

HISTORY OF MEDICINE IN INDIA

Dr. R.D. Lele



National Centre of Indian Medical Heritage
Central Council for Research in Ayurvedic Sciences
Ministry of AYUSH, Govt. of India, New Delhi

2021

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FOREWORD

Dr. R.D. Lele is not only highly accomplished medical doctor, teacher, father of nuclear medicine, but a multifaceted towering personality, recognised as a public health crusader, visionary for religious unity, speedy judicial process, propagator of donor umbilical cord-placenta bank for 150 incurable diseases and prevention of diseases like thalassemia. His autobiography "Pursuit of Excellence" remains of the most inspiring book for scientific and medical professionals.

I still remember, sometime during 1982-83, when I was a doctoral student in Biochemistry and Pharmacology at University of Pune and Haffkine Institute Mumbai, I had an opportunity to attend lectures on Ayurveda and Modern Medicine by Dr. R.D Lele. He was Director of Jaslok Hospital and Research Center in Mumbai. I was absolutely mesmerized by his scholarship to look at ancient sciences with modern eye. During Haffkine days, I was also fortunate to meet other eminent medical scientists including Late Dr. Sharadini Dahanukar, Dr. M.B. Bhide, Dr. R.D. Kulkarni, Vaidya Antarkar, Bagewadikar Shastry and Dr. Ashok Vaidya. Insightful thoughts of these scholars completely changed my perspective to look at Ayurveda as an ancient science of life.

Sometime during that time, Bharatiya Vidya Bhavan had established a research institute known as Swami Prakashanand Ayurveda Research Center in Mumbai, where my mentor Dr Ashok Vaidya was a Director. The vision of this institute highlighted importance of ancient insights for modern discovery captured very well by Dr Lele in a wonderful book "Ayurveda and Modern Medicine". This outstanding best seller book was published by Bhartiya Vidya Bhawan in 1986 with an excellent foreword by Dr Ashok Vaidya. I must admit that Dr Lele's lectures, books and mentorship has greatly influenced me right from the doctoral days and has enriched ideas and induced new insights and shaped my mind over the years. He was able to achieve mastery in the modern medicine as well as Ayurveda to establish interlinkages and scientific basis. He was able to integrate both the concepts elaborating relevance to modern scientific disciplines such as Physics, Chemistry and Mathematics in medicine. In my opinion this was a beginning of a new era of evidence-based integrative medicine. This best seller book by Dr Lele remains a landmark, which facilitated progress of scientific research in Ayurveda. I was fortunate to be blessed with two other medical scientists from the same batch of Dr Lele. First, late Dr N.S. Deodhar who introduced me to the basics of public health in Pune and then Dr Gururaj Mutalik who at the age of 93 continues to inspire me from the USA.

Dr. R.D. Lele has been promoting scientific research in Ayurveda and Modern Medicine and has advocated evidence based integrative approaches for over five decades. The history of Ayurveda and integrative medicine cannot

be complete unless we acknowledge pioneering contributions of many vaidya, doctors, scientists and thinkers, including Gana Nath Sen, Ram Nath Chopra, Madan Mohan Malavia, Maharshi Mahesh Yogi, Pade Shastry, K.N. Udupa, P.M. Mehta, C. Dwarkanath, D.S. Antarkar, B.P. Nanal, Veni Madhav Shasty, Sharadini Dahanukar, Ranjit Roy Chaudhury, K.M. Parikh, Krishna Kumar, M.S. Baghel, Bhrihaspati Dev Triguna, P.S. Warriar, Gururaj Mutalik, G.V. Satyavati, C.K. Atal, B.N. Dhavan, Nitya Anand, S.S. Handa, M.S. Valiathan, B.M. Hegde, G.P. Talwar, Sukh Dev, R.A. Mashelkar, Ashok Vaidya, V.M. Katoch, Y.K. Gupta, S.I. Nagaral, R.H. Singh, H.R. Nagendra, B.N. Gangadhar, G.G. Gangadharan, Narendra Bhat, Darshan Shankar and even a Britisher from a Lord lineage Alex Hankey. This list is really endless full with several unsung heroes.

Today, when the world has realized value of personalized and integrative medicine and moving in a direction of holistic health care, it is important to know the history, heritage and evolution of Medicine in India. Dr. Lele's book precisely bring this treasure of knowledge in a scientific yet lucid style. At the age of 93, he has brought his lifetime experience in form of a new book entitled "History of Medicine in India". Dr. Lele has covered a wide span of important developments in medicine and surgery from Charaka, Sushruta era to the most recent trends in biomedical sciences, molecular biology, genomics, personalized and integrative medicine. Throughout this book Dr. Lele has highlighted contemporary relevance of Ayurveda as a life science. His scholarly interpretations regarding ancient Indian insights and their relevance to modern research and discoveries in covered a wide range of interesting subjects including physiology, pathology, pharmacology, nutrition, behavioral sciences, mental health, surgery and such are indeed very novel and thought provoking. This excellent book is a must especially for medical students, teachers, researchers and practicing doctors of modern medicine and AYUSH systems.

In addition to the fascinating historical account, this book includes brief biographies of representative scholars from Indian Systems of Medicine, Allopathy and relevant scientific disciplines, which can be very inspiring especially for the young generation.

A summary of contributions by Ministry of AYUSH and its Councils especially CCRAS has also been provided. Some other useful resources such as number of AYUSH colleges and prominent research institutions is provided as web links.

I would like to congratulate Ministry of AYUSH and CCRAS for publishing this historical Book as a tribute to significant contributions by Dr R.D. Lele in the field of Ayurveda and Modern Medicine.

Dr. Bhushan Patwardhan
National Research Professor – AYUSH
Savitribai Phule Pune University

PREFACE

In 1978, The Bharatiya Vidya Bhawan launched a project: "Ancient Indian Insights and Modern Discoveries.", Dr. Raja Ramanna Chairman of the Life sciences division, entrusted me with the task of studying Ayurveda through the eyes of a 20th Century physician of modern medicine, specialized in Nuclear medicine.

I studied Charak, Shushrut, Vagbhat and others for seven years and after seven years of study; my book "Ayurveda and Modern Medicine" was published in 1986 by Bhartiya Vidya Bhawan. Dr. Tari Zakaria, Honourable Minister of Health Maharashtra state reviewed the book in The Times of India which gave the book wide publicity. A second edition came out in 2001. I have extensively quoted sections from my book for the current publication by the Central Council for Research in Ayurvedic Sciences (CCRAS), Ministry of AYUSH, Government of India.

I acknowledge with gratitude the permission given by the Trustees of Bhartiya Vidya Bhawan to reproduce many sections in the new book - HISTORY OF MEDICINE IN INDIA.

I have reviewed a wide variety of topics in medicine which was indeed a Herculean task. Apart from reproducing my own published articles on a variety of topics, I have included an entire spectrum of published articles by various Indian authors, mentioned in respective topics. In addition, with the assistance of Dr. Pradeep Thanekar, Transcriptionist and Quality Analyst, an extensive search was made on the Internet for the mentioned topic in the appropriate selection; hence I hope no infringement of Copyrights has been done in this publication. I consider this to be the most valuable resource to all students of Medicine and Biomedical Sciences.

On 16th January 2021, I completed 93 year of my life. My autobiography "Pursuit of Excellence", with foreword by Shri Anil Kakodkar, President National Academy of Medical Sciences, India, was published in 2017, wherein I described myself as an old man In a Hurry with a yet to be finished long standing agenda.

I thank Vaidya Rajesh Kotecha, Secretary, Ministry of AYUSH, Government of India, Prof. Vaidya K.S. Dhiman, Director General, Dr. N. Srikanth, Deputy Director General, Dr. Shruti Khanduri, Research Officer (Ay.), Dr. Vinod Kumar Lavaniya, Research Officer (Ay.), Dr. M.M. Sharma, Research Officer (Ay.), Dr. Rakesh Narayan V., Research Officer (Ay.),

Dr. Mukesh Chincholikar, Research Officer (Ay.), Central Council for Research in Ayurvedic Sciences, New Delhi and Dr. G.P. Prasad, Assistant Director (Ay.), Dr. V. Sridevi, Research Officer (Ay.), Dr. T. Saketh Ram, Research Officer (Ay.), National Centre of Indian Medical Heritage, Hyderabad and all others from the Ministry of AYUSH who facilitated publication of this book. I also thank Dr. Rajeshwari Singh, Research Officer (Ay.), and Dr. Galib for contributing chapters on contributions of Ministry of AYUSH and profiles of few distinguished scholars who have contributed to Ayurveda science and research.

My favorite dictum is **"THINK AS THOUGH YOU WERE GOING TO LIVE FOREVER, ACT AS THOUGH YOU WERE GOING TO DIE TOMORROW"**.

Dr. R.D. Lele

DISCLAIMER

It is my sincere endeavour to accumulate and compile information on various topics of The Modern History of Indian Medicine for the convenience of readers and students to the best of my knowledge and with my conclusive and substantial experience in the field of medicine since 1950.

All the information of this book is for knowledge and education purpose only. These topics and relative text are covered to highlight the Modern History of Indian Medicine as a whole and should not be credited to me as a compiler. I disclaim any ownership or intellectual property right or any copyright of the content herein with.

The topics of this book are attributed to the correct sources, i.e., other books, manuscripts, websites, electronic media, research papers, lectures, et al. Appropriate sources and references are mentioned at the end of each topic.

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AYURVEDA: SCIENCE OF LIFE

Ayurveda (Science of Life) embodies ancient Indian experiential wisdom of over 5000 years. Rig Veda (10,000 BC mentions the concept of Tridosha and Triguna and several diseases with their treatment. There is mention of 120 herbal medicines in one "Aushadhi Sukta", used for treating diseases and also as preventive medicine. **Atharva Veda**, precursor of Ayurveda contains 114 hymns devoted to medical topics - fever, consumption, vidradhi (wounds) leprosy, heart disease, epilepsy and insanity, eye and ear disease, worms etc. Kautilya's Arthashastra includes scientific thoughts about plants.

Mahabharata classifies plants into Vriksha, gulma, lata, valli, tvak and sara. Indian culture considers trees as living beings having inner consciousness, likes and dislikes which they may be expressing but human are unable to perceive them. Historians determine the time of Charaka and Sushruta anywhere from 2000 BC to 200 BC. Charaka classified 50 groups of plants with 10 in each group, total 500 plants according to their actions. Early Greek and Arabic Medicine imbibed many concepts of Ayurveda. The Buddhist period (323 BC to 642 AD) saw great strides in the academic progress of Ayurveda; the most notable was the work of Nagarjuna (4th Century AD) who updated Sushruta's classic works. The ideas of hospitals originated first in Buddhist India. The Buddhist missionaries spread the reputation of Ayurveda beyond the borders - of India-to-Greece, Rome and China.

In 7th Century AD Vagbhat, next in authority to Charaka and Sushruta, wrote a treatise "Ashtanga Hridaya" which consolidated teachings of Charaka and Sushruta with gleanings from Agnivesha, Bhela and Harita and introduced a number of new drugs and modifications and additions in surgery. He mentioned 42 single herbal remedies. Loha (iron) has been described as the chief dravya for pandurog (anaemia). The whole work is in Sanskrit verses (7471 verses in 6 sections and 120 chapters). His other work **Ashtanga Sangraha** throws lights on several obscure passages in his predecessors work in a clear and concise style. Charaka, Sushruta and Vagbhat are known as the **Big Three: Vriddha Trayee**.

During the 7th Century Ayurveda attracted the attention of Arab scholars, and its leading books were translated into Arabic and Persian. In the 8th Century AD Ayurvedic physicians from India were invited by the Khalifa of Bagdad and Jundishpur and put in charge of the hospitals. Abu Bakr al Raze (Rhazes) 865-925 AD quotes both Charaka and Sushruta in his Firoozse Hikmat. Avicenna (980-1038 AD) in his writings indicates a fairly intimate

acquaintance with Ayurvedic medical writings. The Unani system prevalent in India is a blend of Greeco-Arabic Ayurvedic medicine.

In the 7th Century, Madhavacharya wrote **Madhava Nidana** which dwells exclusively on the diagnosis of disease, in 69 chapters and 1552 verses. Madanapala Nighantu was written in 1375 AD. In the 14th Century Sharangadhara wrote the **Sharangadhara Samhita** which is systematised materia medica as a whole and is still the most popular and reliable, treatise on the subject of drugs. Raj Nighantu was compiled in 17th Century.

In the 16th Century Bhav Mishra wrote the last authoritative text in Ayurvedic literature **Bhava Prakash**, containing 10831 verses in 3 sections, in a simple delightful style. In Bhav Mishra's time, Portuguese were attracted to India by the great possibilities of trade. Syphilis was brought to India by the Portuguese with Vasco De Gama landing at Calicut, described by Bhava Mishra as "Phiranga Roga" foreigners disease. He described three stages - Bahya (external), Abhyantara (internal) and Bahirantra (external-internal). He recommended mercury and arsenic as specific remedies. He was the first to mention medicinal drugs of countries other than India Badakshani Naspasi – Amruta - fruit of Badakshan; Khorasani Vacha - Acorus calamus of Khorasan; Sulemani Khajura - Date fruit of Suleman. Garcia de Orta spoke to many Indian vaidyas yogis from Delhi and traders from all parts of the world to gather information but there is no indication that he had knowledge about the Ayurvedic classics. Orta mentions a citation from Charaka, but there is no mention of Sushruta, Vagbhata, Madhava; Bhavamishra or Sharangadhara (16th Century). Garcia de Orta's book was finished in 1563. By the end of the 17th Century, Garcia D Orta's books were translated into many European languages. Ambrose Pare, the eminent French physician translated the book and from there the English derived more detailed knowledge of medicines in India including treatment of mental disorders. By the late 17th Century, the use of Indian plants for the treatment of melancholy was already known. A very eminent East India Chyrghion stated "the Indians are very excellent Botanists, admirably skilled in the nature and use of plants and having an extra-ordinary variety of them have improved Galeniactal physic to a very great height." One of the drugs identified was Sarpagandha (also known as Chandrika-the link between the moon and madness having universal acceptability), now identified as *Rauwolfiaserpentina*, which has been described in Ayurveda. This plant is mentioned at number 42 Orta's list.

Interestingly in the 20th Century the most important single event that aroused the interest of modern medicine in the Ayurvedic Pharmacopoeia was Dr. Rustom Jai Vakil's 1949 report in the British Heart Journal on the usefulness of sarpina (whole extract of Sarpagandha –*Rauwolfia serpentina*) in the treatment of hypertension. Its pharmacological properties had been

investigated earlier in 1931 by Sen and Bose, and in 1942 by Paranjpe. The active principle of Sarpagandha-reserpine was identified in 1978. Transporters for the three biogenic amines nor-epinephrine (NET), dopamine (DAT), and serotonin (SERT) were discovered in the 1990's. The vesicular monoamine transporters (VMATs) were discovered in 1998. VMA1 is localized in endocrine tissue and VMAT2 is localized in neurons. Reserpine is a unique molecule that blocks both VMAT1 and VMAT2. According to Braunwald (Heart 6th ed. 2001) reserpine reduces blood pressure by inhibiting vesicular uptake of NE in post - ganglionic adrenergic neurones. Single daily oral dose of 0.05 mg makes reserpine the most effective inexpensive single drug for the control of hypertension but it is ignored as it has no commercial sponsor. Ayurvedic drug companies have a great opportunity to extend the benefits of this unique Ayurvedic anti-hypertensive for the entire world. Ayurveda has described ten herbal drugs as Medhya Rasayanas Amalaki, Ashwagandha, Bramhi, Jatamansi, Jyolishmati, Mandukparni, Shankhapushpi, Vacha and Yashtimadhu. Today, there is no effective treatment for Alzheimer's disease yet US \$ 15 billion are spent by patients annually on its treatment. My proposed study on Transgenic mice with Alzheimer's disease seeks to validate the ability of Ayurvedic Medhya Rasayanas to prevent and reverse Alzheimer's Disease which will make a huge world market available for Ayurvedic medhya rasayans.

Many Ayurvedic drugs such as Arjun, Ardrak, Guduchi, Guggul, Shatavari, Haridra, Haritaki, Pippali, Katuka, Kumari, Kutaja, Lashuna, Neem, Tulsi etc. have important anti-inflammatory (NF- κ B suppression), anti-oxidant and immune modulatory and anti microbial and anti-cancer properties.

Sushruta Samhita recommended Dhatura as a prophylaxis to be given by mouth immediately after a dog bite. In 1982 TL Lentz (Science Jan 1982) reported that muscarinic acetyl choline receptors provide entry point for the rabies virus. In my letter to the Editor Science (8th October 1982), I pointed out that the active principle of Dhatura blocks Mach Receptor hence Sushruta's prescription of Dhatura represents the first documented example of chemoprophylaxis of infection by receptor blockade.

In the 21st Century another example is a acernannan (active principle of Kumari (*Aloe vera*) which blocks the binding of HIV virus to CCX4 receptors on T cells. I have suggested Celegans, a nematode as an ideal model to study Ayurvedic antimicrobial herbs. This is of utmost urgency in view of the rising microbial resistance to current antibiotics worldwide. There is a Sanskrit proverb which appreciates the value of hard work exemplified by Orta's book: describing his pains-taking efforts for 30 years in search of Indian herbal drugs.

vidvaneva vijanathi vidvajjana parishramam I
na hi vandhya vijanathi gurveem prasava vedanam II

*Only the learned can appreciate the efforts of the learned.
A sterile Woman can not appreciate the severity of labour pains."*

The World Health Organization (WHO) estimates that 4 billion people (80% of the world population) presently use herbal medicines for some aspect of primary health care ([www.who.int/ topics/ traditional medicines/ en/](http://www.who.int/topics/traditional_medicines/en/)) Current global herbal market of US \$ 70 billion is growing annually at 10-15%. Global nutraceutical market is US \$ 142 billion. I congratulate the Asiatic Society of Mumbai for taking up the reprinting of Orta's book which spread knowledge about Indian medicinal plants to Europe in 17th Century. I hope this publication will provide a new stimulus to re-enter the world in the 21st Century with over 40 validated Ayurvedic herbal drugs. What we need is vision, imaginative thinking and swift action as outlined in my four published articles for validation of Ayurvedic herbal drugs to be implemented rigorously by AYUSH.

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AYURVEDA THROUGH MODERN EYES

Introduction

Historians of Modern Cosmopolitan Medicine consider Hippocrates (460-370 BC) as the founder of medicine as we know it today. Hippocrates gave medicine its scientific spirit, replaced superstition by rational observation and inference, gave a rational diagnosis, prognosis and treatment, and gave medicine its ethical ideas. The Hippocratic Oath is taken even today and the Hippocratic aphorisms are admired as gems of human clinical wisdom even by the student of medicine in the 20th Century. Take for instance, the following aphorism: "In case of jaundice, hardening of the liver is a bad sign." Without detracting a bit from the tributes rightly paid by medical historians to Hippocrates, it can be affirmed that Charaka and Sushruta deserve the same primacy and the same place of honour as Hippocrates.

Indian historians claim that Charaka and Sushruta came before the time of Hippocrates, while some western historians put the time of Sushruta much later (1st Century A.D.). The controversy and dispute about the determination of the exact time of Charaka and Sushruta are irrelevant to the proposition that Charaka & Sushruta deserve the same pre-eminence as Hippocrates, as founders of Medicine. Despite the great contributions made by the western Indologists in the last 100 years, in establishing the greatness of ancient Indian Medicine, ignorance and/ or prejudice of western medical historians continue even today as evidenced by the fact that a most recent (1978) *Life Magazine* publication on the history of Medicine does not even mention Charaka and Sushruta.

The History and Literature of Ayurveda

The term Ayurveda means "Knowledge" (*Veda*) concerning maintenance of "life" (*ayus*). The origins of this knowledge are already evident in the Atharvaveda (the contents of which can be dated between circa 1500-1000 BC). The treatment of disease (*Chikitsa*) in the Atharvaveda is largely religious and ritualistic, emphasizing such practices as the "sacred utterances" (*mantra*), penances (*niyama*), amulets (*mani*), sacred oblations (*mangala homa*), fasting (*upavasa*), and purificatory rites (*prayaschitta*), but the Atharvaveda also contains material about human anatomy, herbal medicines (*bhaisajya*), and the classification of diseases (*lingi vyadhi*). Reference is made to "wandering medical practitioners" (*charan-vaidya*) and those who are "trained in medical science" (*Vaidya*). Mythologically the first exponent of the medical science was none other than the creator *Brahma* himself. *Brahma* shared this knowledge with Prajapati, who in turn passed on the tradition to the Ashwini Kumaras and Indra. Surgery (*Shalya*) was revealed by Indra to Divodasa, the King

of Kasi who was also an incarnation of the divine *Dhanvantari*, culminating finally in the classical *Sushruta* tradition of Ayurvedic surgery and medicine. Internal medicine (*Kaya-Chikitsa*) was revealed by Indra primarily to Atreya Punarvasu, culminating finally in the classical *Charaka* tradition of Ayurvedic general medicine. Ayurveda is considered as a supplement (*upanga*) or as an *upaveda* (supplementary veda) of Atharvaveda, or even as a "fifth veda" (the four vedas being Rig, Sama, Yajur and Atharva).

Numerous other texts of medicine, other than *Charaka Samhita* and *Sushruta Samhita* were regularly composed through the centuries, such as the *Bhela Samhita*, *Kashyapa Samhita*, and *Agnivesha tantra* (which were even earlier than *Charaka Samhita*). Other notable contributions were *Ashtanga Hridaya* of Vagbhata (600 AD) and *Madhava Nidana* (700 AD). The Ayurvedic tradition continued as a vigorous and expanding scientific tradition down into the 16th Century. Its medical literature is oriented practically and operationally, although apparently it had an "elective affinity" for and an ongoing exchange with the classical Indian philosophies. The dominant intellectual influences on Ayurveda are those of the *Samkhya* and *Vaisheshika* Indian philosophies, although one also finds terms and notions from the *Vedanta*, *Nyaya*, *Yoga* and early Buddhist and Jain reflections.

For the modern reader, the texts present a symposium-like format in which a practical problem like fever (*Jvara*) or diarrhoea (*Atisara*) or a disease such as pulmonary tuberculosis (*Rajayakshma*) is discussed, classified as to type, contextualised (with respect to prodrome, syndrome, prognosis) and finally dealt with therapeutically. Ayurvedic texts were translated into Greek by Cnidos (300 BC), Tibetan and Chinese (300 AD), Persian (700 AD) and Arabic (800AD).

The Scope & Contents of Charaka Samhita

Charaka Samhita (literally, treatise compiled by Charaka) is a Sanskrit work of great antiquity. It is an exposition of Ayurveda, the science of life, defined as the Science of the causes and symptoms of disease, of their treatment and of the maintenance of health (*Sutra 1, 23*). It also deals with the origin of medical science, the fundamental causes of conception and birth and of physical deformities. The treatise contains a detailed classification and nomenclature of diseases, their *Vyakhya* (definition), *Vyutpatti* (etymology), *Nidana* (etiology), *Poorva Roop* (prodromata) and *Roop* (clinical picture), *Samprapti* (pathophysiology), *Sadhya-asadhyata* (prognosis), *Chikitsa Sutra* (line of treatment), *Aushadha* (drugs), *Anna* (diet) and *Vihara* (practices) etc. This conceptual framework and approach appear strikingly similar to contemporary medicine.

According to Charaka, Ayurveda has eight branches (**Sutra 30/28**)

1. *Kaya-Chikitsa* (Internal medicine & therapeutics)
2. *Shalakyā* (The science of management of diseases of eye, ear, nose, throat and head)
3. *Shalyapahartrika* (Surgery)
4. *Visha gara vairodhika prashamana* (Toxicology)
5. *Bhuta vidya* (Psychiatric knowledge)
6. *Kaumarabhritya* (Pediatrics)
7. *Rasayana* (Rejuvenation)
8. *Vajikaran* (Virilification)

For the discussion of the above topics the treatise is divided into eight sections. (**Sutra 30/35**)

1. *Sutra Sthana* deals with general principles, philosophy etc.
2. *Nidana Sthana* deals with causes of diseases
3. *Vimana Sthana* deals with taste, nourishment and general pathology etc.
4. *Sharira Sthana* deals with anatomy and embryology
5. *Indriya Sthana* deals with diagnosis and prognosis
6. *Chikitsa Sthana* deals with treatment of diseases
7. *Kalpa Sthana* deals with pharmacy
8. *Siddhi Sthana* deals with the cure of disease.

In all there are 120 chapters on specific topics. There are at places some later revisions and interpolations, as repeatedly admitted by the redactor at the end of each and every chapter. In fact, Dradhbala states that he had to rewrite and complete the last section *Siddhi Sthana* from the material available to him (*Siddhi Sthana 12/55*).

The Scope and Contents of Sushruta Samhita

The approach of *Sushruta Samhita* is similar to *Charaka Samhita*, but with special emphasis on surgery, which Sushruta describes as the first and foremost specialty. He has described various types of inflammation and various stages of inflammation, accidental wounds, burns and fractures. Sushruta describes many major abdominal operations for intestinal obstruction, bladder stones etc. and also plastic surgery like rhinoplasty, crushing and extracting the foetus, delivering the foetus through abdominal operation, amputation of limbs and extraction of foreign bodies.

Sushruta described "*Shalya*" or surgery as the highest in value among the therapies because of its ability of producing instantaneous relief by means of instruments and appliances. Sushruta has described 101 kinds of blunt instruments and 20 kinds of sharp instruments. The 101 blunt instruments are subdivided into:

SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA

Name	Number
<i>Swastika</i> or Cruciform	24
<i>Samdamsa</i> or pincer-like	2
<i>Tala</i> or pick lock-like	2
<i>Nadi</i> or tubular	20
<i>Shalaka</i> or pricker-like	28
<i>Upayantras</i> or accessories	25

The very first of these, *Simhamukha Swastika* (lion-faced forceps) is the precursor of the modern lion's forceps. The blunt instruments cover a wide range including forceps, pincers, trocars, speculums (nasal, aural, vaginal), finger guards, syringes, cannulae, dilators, catheters, clusters with eight kinds of bags and tubes, catheters, tubular appliances for inhalation, fumigation and disinfection of rooms, rods, probes of different shapes and sizes, foetus traction hooks, bone levers, directors and many others.

The accessories include thread (also caustic coated thread—“*Kshara sutra*” for the operation of fistula-in-ano), twine for ligature, bandages of 14 types, dressings, abdominal binders, various types of leather bags, bands and bandages, splints (made of bamboo and inner bark of trees), crutches, tendrils and creepers, cloth, spittle, suture material, caustic medicines and goat's guts.

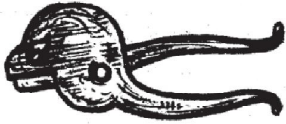
The sharp instruments include knives and scalpels (many varieties), saws, ring scalpels, needles, scissors, *trikurcha* (triple-needle trocar), axes, awls, tooth-scalers and sharp hooks. Sushruta emphasises that “the hand of the surgeon is the best, the most useful and the most important of all surgical instruments”.

Thirty two surgical manoeuvres are described by Sushruta. Some examples: *Nirghatana* (extraction by moving to and fro); *Vyuhana* (raising up and incising a part bringing together the lips of the wound); *Vartana* (contracting or curling up); *Chalana* (moving a foreign body); *Vivartana* (turning round); *Peedana* (pressing out); *Vikarsana* (loosening); *Ahama* (pulling up); *Unnamana* (elevating depressed cranial bones); *Darana* (splitting); *Chhedana* (excision); *Bhedana* (incision); *Un-mathana* (probing); *Achusana* (suction); *Lekhana* (dissection); *Vyadhana* (puncturing); *Visravana* (draining) and *Sivana* (suturing).

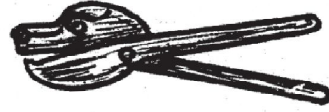
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SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA

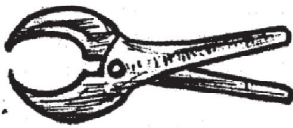
Surgical Instruments mentioned in Sushruta Samhita are



1. Vyāghra-mukha (tiger-faced)



2. Svana-mukha (dog-faced)



3. Tarakshu-mukha (hyena-faced)



4. Vrka-mukha (wolf-faced)



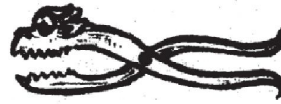
5. Bhrnga-mukha (bee-faced)



6. Kaṅka-mukha (heron-faced)



7. Ṛiksha-mukha (bear-faced)



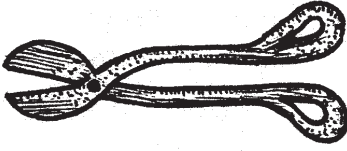
8. Sīmha-mukha (lion-faced)



9. Kāka-mukha (crow-faced)

1 to 9 Svastika-yantras (Forceps for extraction of foreign matter lodged in the body)

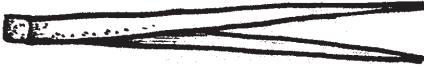
SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA



10. Antarmukham (scissors)



11 Kila-baddha-samdamsa
(gripping instrument)



12. Shaḍānga



13. Vimuktāgra

12 and 13 Pincers for extraction of splinters from below the skin, flesh or deep-seated tissues.



14. Ekatālam

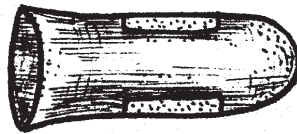


15. Dvitālam

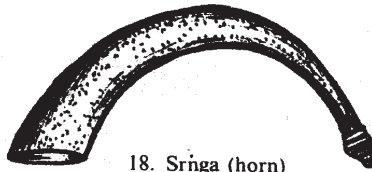
14 and 15 Single-blade and double-blade picklocks for extraction of splinters, growth from inside nose, ear and other orifices.



16. Muchuṇḍī (forceps)

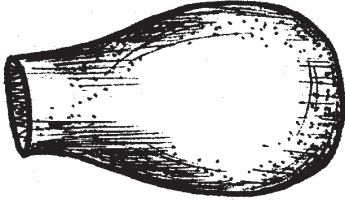


17. Ānguli-trāṇaka (finger-cap)



18. Srṅga (horn)

SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA

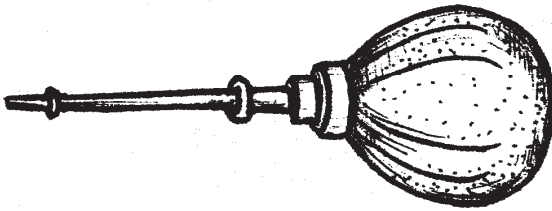


19. Alābu (gourd)

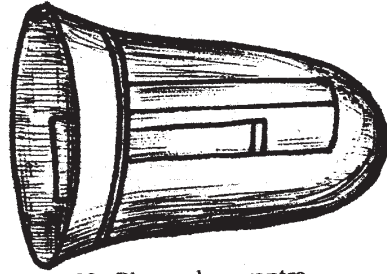


20. Ghatī-yantra (pitcher)

18 to 20 Instruments for cupping; for surgical bleeding, probing into bodily orifices etc.



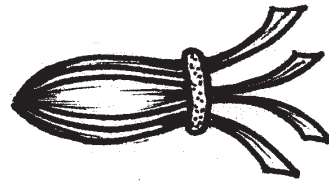
21. Uttara-vasti (urethral syringe or vaginal enema)



22. Bhagandara-yantra (used in fistula-in-ano)



23. Arso-yantra (used in piles)



24. Yoni-vranekshaṇam (used in vaginal examination)



25. Nādi-vranābhyañjanam (used in washing away the pus of an abscess)

SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA



26. Dhūma-yantram (used for fumigation)

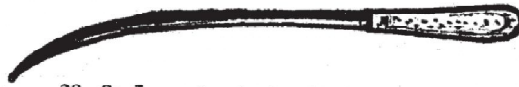


27. Mandalāgram



28. Maṇḍalāgram

27 and 28. Round-headed knives for scraping, scarifying and incising.



29. Sarpāsya (snake-headed instrument)



30. Sarāri-mukha



31. Sarāri-mukha

30 and 31 Instruments for exudating and secreting.



32. Vrihi-mukham (trocar of puncturing)



33. Kusa-patram (used for extraction of fluids)



34. Trikuccham (trocar for evacuating abscesses)



35. Salākā (rod-shaped probe, bougies)

SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA



36. Badisa (sharp hook for extraction of foreign bodies)



37. Kara-patra (saw)



38. Vrddhipatra



39. Vrddhipatra



40. Vrddhipatra



41. Vrddhipatra

38 to 41. Razor-blades with handles for incision and excision.



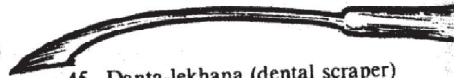
42. Utpala-patram (phlebotome)



43. Adhyardhapatra (scalpel)



44. Nakha-sastra (nail-parer; used for incising and excising)



45. Danta-lekhana (dental scraper)



46. Anguli-sastra (finger-instrument)



47. Karna-vedhini (ear-piercer)



48. Karna-vyadhana (used in cutting by uplifting in the ear-cavity)



49. Karna-sodhana (ear-cleanser)

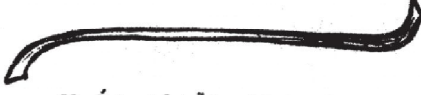
SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA



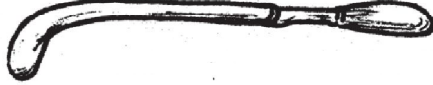
50. Pramarjini (swab cleanser)



51. Eshaṇī (surgical probe for ascertainment of course of fistulous track)



52. Śalya-hāriṇī (used for removal of foreign bodies)



53. Asmaryāharaṇam (used in urinary calculi)



54. Jāmbavaśṭham (used for surgical probing)



55. Antra-vrddhi-dahana-salaka (used in hernia)



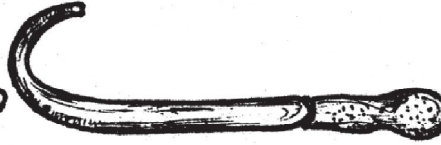
56. Vyūhana-śaṅku (hook or pincer for lifting)



57. Chālana-sanku (hook or pincer for transferring)



58. Āharaṇa-śaṅku (hook or pincer for extraction)



59. Garbha-sanku (hook for foetal operation)



60. Ivasārsorbuda-dāhana-salākā (used in nasal polyps and tumours)



1. Danta-pātana-yantra (instrument for tooth-extraction)

SURGICAL INSTRUMENTS IN SUSHRUTA SAMHITA



62. Sanku (hook or pincer)



63. Ara (awl for puncturing)



64. Danta-sanku (dental pincer or tooth scaler, used for extraction of sordes and tartar from tooth)



65. Yonyavekshana-yantra (used in vagina examination)



66. Yugma-sanku (twin hooks)



67. Snuhi-yantra



68. Tāla-yantra (picklock-like instrument)



69. Sūchi (needle for suturing or puncturing)



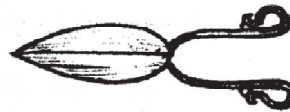
70. Nādi-yantra (tubular instrument)



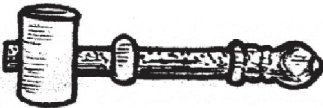
71. Ardha-dhārā (lancet or scalpel)



72. Āti-mukha (used for drawing fluids)



73. Antarmukha-kartari (scissors for evacuating abscesses)



74. Mudgara (hammer for loosening foreign matter embedded in bone)



75. Kuthārikā (mallet)

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AYURVEDA AS A LIFE SCIENCE

One is impressed by the vast conceptual canvas and framework of Ayurveda. It is important to realise that Ayurveda is not confined to Medicine only; it tackles the whole subject of life in its various ramifications. This can be seen by the variety of topics discussed therein, such as re-birth, renunciation, salvation (*Moksha*), soul (*Atma*) etc.

The *purpose of life* is four-fold, to achieve *dharma* (virtue), *artha* (wealth), *kama* (enjoyment) and *moksha* (salvation). In order to attain success in this four-fold purpose of life, it is essential to maintain life not only in a disease-free state but also in a positively healthy state of body, mind and spirit.

The emphasis on the *maintenance of positive health* or *Swastha Vritta*, is a distinguishing feature of Ayurveda. In order to maintain positive health, Ayurveda prescribes specific daily routine "*dinacharya*" and also a seasonal regime "*ritucharya*". In "*dinacharya*" great importance is given to *diet* which is to be taken in a proper way with regard to quality, quantity as well as frequency. Emphasis is given to physical exercise and personal hygiene. The daily regime advocates not to suppress certain natural physical urges like micturition, defecation, hunger, thirst, sleep etc. On the other hand suppression of harmful psychic urges is advocated—like greed, fear, anger, vanity, jealousy, malice and excessive attachment to anything.

Equal importance is given to *mental health*, for which a regime of *Sadvritta* (ethical life) is prescribed. Strict mental discipline and strict adherence to moral values is considered a pre-requisite for mental health.

"That is named the Science of Life wherein is laid down the *good* and *bad* life, the *happy* and the *unhappy* life, and what is *wholesome* and what is *unwholesome* in relation to life, and also the *measure* of life." (*Charaka Samhita*, Sutra Sthana, 1, 41).

An interesting concept worth emphasizing here is that of *Vyadhi - Kshamatva*, that is resistance to disease (or immunity in modern parlance). The aim of Ayurveda is to promote health—"Svasthasya Svasthya rakshanam", increase immunity and resistance—"Vyadhi Kshamatva" and to cure disease—"Aturasya Vyadhi parimokshah".

In spite of the fact that Ayurveda has laid great stress on "*Bhuyo Darshana*" (repeated observation) and acceptance of data as reliable only on the basis of "*Anvaya*" (uniform consistency), unmarred by any "*Vyatireka*" (contradiction), *intuition* has played a major role in the development of Ayurvedic

concepts. But it is remarkable, from a clinician's viewpoint that the clinical approach of the Ayurvedic physician seems strikingly similar to that of the modern physician, as will be seen from the next section.

The Clinical Approach in Ayurveda

According to Charaka, there are three means open to the physician for ascertaining the nature of any sickness; they are:

- i. theoretical knowledge of the possible causes and symptoms of all known diseases;
- ii. meticulous observation of the patients' symptoms, signs and complaints;
- iii. inference based on previous experience. In the absence of one or more of the three aids to diagnosis, or with their fragmentary or incorrect knowledge, the physician cannot come to a true conclusion (Vimana, 4, 3-5).

If one reads Sushruta's description of the clinical methods it appears very contemporary.

"The physician should interrogate (*"prashna"*) the patient about his complaints in great detail. He should use the five senses of sight, touch, hearing, smell & taste, in addition to oral inquiry".

"Fullness or emaciation of the body, state, and indications of vitality, strength, complexion etc. are perceived by the sense of *sight*".

"The heat and coldness of the body, gloss, roughness, hardness or softness of the skin of the affected part as in fever or in an edematous swelling of the body, are perceptible by the sense of *touch*".

"The *Vayu* making the blood ebullient forces it up with a distinctly audible report and thus affects the sense of *hearing*. Diseases which can be diagnosed with the help of hearing will be fully dealt with in the chapter on *Vrana Srava*".

"The characteristic smell emitted by an ulcer in its critical stage (*"Arista"*) should be determined with the help of the organ of *smell*.

"Secretions or discharges should be tested with the organ of *taste*. In *"prameha"* & *"Madhumeha"* (diabetes) one should watch the urine being or not being swarmed with hosts of ants or flies".

"Such facts as the *time* or *season* of the first appearance of the disease, the caste to which the patient belongs, and things or measures which tend to bring about a manifest amelioration of the disease or prove comfortable to the patient (*"Satmya"*), similarly the factors which cause aggravation of the pain, the strength of the patient, his appetite and state of digestion, the emission of stools, urine and flatus or their stoppage, the maturity of the disease as regards time, should be specifically ascertained by directly interrogating the patient on those subjects".

“A disease wrongly observed or incorrectly described is sure to mislead the physician”.

The *observational* or *empirical approach*, the classified entity being a phenomenon that has actually been witnessed, formed the basis on which the Ayurvedic physician made inferences based on the “*Tridosha*” theory.

Every disease, whether acute or chronic, mild or severe, pass through certain stages. These stages are called *kriyakala* or the time for treatment. They are six in number:

(1) *Sanchaya* or accumulation of morbid *dosha* (2) *Prakopa* or vitiation of dosha (3) *Prasara* or spread of dosha (4) *Sthana-sanshraya* or localization of dosha (5) *Vyakti* or manifestation of disease and (6) *Bheda* or chronicity, complications etc.

In the clinical assessment in Ayurveda, there are two words used—*Rogi pariksha* (examination of patient) and *Roga pariksha* (examination of disease). *Rogi pariksha* (examination of the patient) is carried out to assess his life span, “*Ayushah-pramana strength*, “*bala*”; and intensity of morbidity, “*Dosha pramana*.”

In assessing the strength and morbidity of the patient, the following ten points are to be examined:

- (1) Constitution of the patient or “*Prakriti*”
- (2) Pathological condition or “*Vikruti*”
- (3) Perfectness of body tissues or “*Sara*”
- (4) Compactness or “*Sanhanana*”
- (5) Proportions of the limbs or “*Pramana*”
- (6) Homologation or suitability—“*Satmya*”
- (7) Psychology or “*Satva*”
- (8) Capacity for food and its digestion, “*Ahara Shakti*”
- (9) Capacity for work and exercise, “*Vyayama Shakti*”, and
- (10) Age of the patient, “*Vaya*”

Based on all these ten factors, the strength of the patient can be assessed as either high—“*Pravara*”, medium “*Madhya*” or low—“*Avara*”.

The concept of therapeutic test or *Upashaya* is worthy of note. There are certain diseases where the diagnosis becomes difficult or impossible. In such cases, Charaka recommends *Upashaya*, or the use of medicines, diet and regimen which are antagonistic directly or in effect to the causative factor, disease or to both.

Other points to be taken into account are the exciting factors or “*Prakopana Nidana*”, onset or “*Utthanam*”, location or “*adhithana*”, stage of aggravation or “*Vridhi*”, abatement or “*Kshaya*”, sequelae or “*Udarka*”

The assessment of the results of treatment or "*Karya phalam*" is to be based according to Charaka on four criteria or "*Chabis-shreyas*".

The indications of cure from a disease are described as:

1. "*Rug-upashamanam*" or relief from pain & disease.
2. "*Swara-vama yoga*" or accession of voice and complexion.
3. "*Sharira upachaya*" or increase in body weight.
4. "*Bala Vriddhi*" or regaining strength and vitality.
5. "*Abhyavaharya Abhilasha*" or desire for food.
6. "*Ruchini Ahara kala*" or relish while eating.
7. "*Samyak Jaraman*" or timely and proper digestion of food.
8. "*Nidra labha yathakalam*" or sleep at proper time.
9. "*Vaikarikanam Swapnanam adarshanam*" or not seeing frightful dreams.
10. "*Sukhena pratibadhanam*" or happy awakening.
11. "*Vata-mutra purisha retasam Mukti*" or normal elimination of flatus, stool, urine and semen.
12. "*Sarvakaraihi Mano Buddhi indriyanam Avyagatti* or freedom from impairment of any kind of the mind, intellect and sense organs.

The scope of Ayurvedic, treatment consists of a salubrious use of (a) "*aushadha*" (drugs), (b) "*Anna*" (diets) and (c) "*Vihara*" (practices), prescribed jointly and severally:

- i. Contrary to the cause of disease, or
- ii. Contrary to the disease itself, or
- iii. Contrary to both the cause and disease, or
- iv. Similar to the cause of disease, or
- v. Similar to the disease, or
- vi. Similar to both the cause and disease.

"Shodhana" and "Shamana" concepts:

"*Shodhana*" means purification of the body through *vamana* (emesis), *virechana* (purgation), *Basti* (enema), *Shirovirechana* (nasal medication) and *rakta mokshana* (bloodletting). It is also called "*Pancha Karma*" or five-fold line of treatment. "*Shamana*" means subsidence of disease and symptoms by *Kshut* or *langhana* (fasting or light diet), *Trit Nigraha* (restriction of fluids), *Vyayama* (exercises), "*atapsevan*" (sun rays) and *maruta seven* (breeze of air).

Certain other methods of treatment or *Upakramas* are "*Brimhana*" or Methods to increase body weight (as against methods to reduce body weight by "*langhana*"). *Snehana* or administration of oily or fatty substances by food and drinks, enema or through the skin by oily massage (as against *Rukshana* or reduction of fat). *Stambhana* or procedures by which the flow of fluids in the body is lessened or checked (as against *Swedana* or procedure to induce sweating, by applying dry heat, steam, poultices or hot liquids).

Another interesting concept is *Srota-Suddhikara Chikitsa* or to get normal flow of the flowing materials in the body. *Rasayana chikitsa* is aimed at controlling the ageing process and increasing strength and vitality. *Vajikarna* is aimed at increasing pleasure in the sex act and procuring healthy progeny.

Optimal timing of drug administration in relation to meals:

Ayurveda describes the following ten timings of giving of drugs in relation to meals:

1.	"Abhakta"	on empty stomach
2.	"Pragbhakta"	pre-prandial
3.	"Adhobhakta"	postprandial
4.	"Antarabhakta"	in between meals
5.	"Madhyabhakta"	in the middle of the meal
6.	"Sabhakta"-	mixed with the meal
7.	"Samugda"	given in the beginning and at the end of the meal
8.	"Muhurmuhu"	repeatedly
9.	"Sagrassa"	with every morsel of food
10.	"Grasantar"	in between morsels.

It is interesting that we use similar considerations today with the aim of improving absorption and minimizing gastric irritation.

1. Drugs taken 1 hour before or 2 hours after a meal for more rapid absorption Oral antibiotics penicillamine.
2. Drugs taken half an hour before meals anti-cholenergics—to decrease gastrointestinal motility Appetite depressants - to reduce food intake.
3. Dopamine antagonist (metoclopramide) - to prevent nausea..
4. Drugs taken with meals to prevent gastric irritation or improve absorption of lipid- soluble drugs.
5. Drugs taken half hour after mealsto relieve gastric upset-antacids.

Cimetidine	Oral	Hypoglycemic
	Hydralazine	
	agents	
Corticosteroid	potassium, iron supplements	Hydrochlorothiazide
Theophylline	Anti-TB drugs	Propoxyphene
Anti inflammatory drugs	Urinary antiseptics	Griseofulvin
Aspirin	Propranolol Diphenyl hydantoin	Spirolactone Carbamazopine

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RELEVANCE OF AYURVEDA TODAY

Eminent modern medical men in India have written extensively about our glorious ancient medical heritage (Kutumbiah, Bhatia, R. J. Vakil, Keswani etc.). The Government Medical College & Hospital at Aurangabad in Maharashtra, with which the author was associated, is an institution of Modern Medicine; the staff and students of this Institution unanimously named the College & Hospital campus after Charaka, Sushruta and Dhanvantari.

As a student of Modern Medicine, having studied both Hippocrates and Charaka & Sushruta, I find remarkable similarity of approach between the Greek and Indian Masters. It is quite likely that these great masters were contemporaries and were influenced by the ideas of each other, as happens in contemporary cosmopolitan medicine. One major difference is that in Hippocratic literature there are 42 clinical cases, almost the only records of the kind for the next 1700 years. In *Charaka Samhita* and *Sushruta Samhita* we do not find such individual clinical case records. What we find are declarative statements which represent the crystallisation of an accumulated experience derived from observation of natural phenomenon and the application of logic, both inductive and deductive, to make generalisations, which have a universal appeal.

For the benefit of those who have not had the opportunity of studying the original texts, I have compiled selected passages and Ayurvedic Aphorisms which to my mind have relevance even today.

Ayurveda as a Life Science

“Health is the supreme foundation of virtue, wealth, enjoyment and salvation. Diseases are the destroyers of health, of the good in life, and even of life itself. Thus has arisen the great impediment to the progress of humanity”.

“That is named the Science of Life wherein are laid down the good and the bad of life, the happy and unhappy life, and what is wholesome and what is unwholesome in relation to life, as also the measure of life”.

“The Science relating to life is regarded by the philosophers as the most meritorious of all the sciences because it teaches mankind what constitutes their good in both the worlds”. “Life is spoken of as the union of the body, senses, mind and spirit. The body, mind and spirit together are, as it were, the tripod”.

RELEVANCE OF AYURVEDA TODAY

"The body and the mind are both considered to be the abodes of disease, likewise, of well-being. The cause of well-being is their harmonious and concordant interaction. The cause of disease, psychic or somatic, is either erroneous, absent or excessive interaction". "The objective of the Science of Life is establishing equilibrium of the body elements".

"The morbidity of the body is remedied by medication; the morbidity of the mind by spiritual knowledge, philosophy, fortitude, remembrance and concentration".

The Nature of Happy Life

"Life of such a man is called happy as is not afflicted with either bodily or mental ailments, as is endowed with youth, strength, virility, reputation, enterprise and boldness befitting his abilities, is actuated in his deeds by the combined urge of knowledge, science, the senses and the sense objects, is possessed of multifarious and delightful amenities occurring from great wealth, whose efforts are prosperous and who can plan as he likes. A life to the contrary is deemed unhappy".

The Nature of Good Life

"The life of that man is said to be good who is a well-wisher of all creatures, who does not covet other people's goods, who is a teller of truth, who is peace-loving, who acts with deliberation, is not negligent, is devoted to the three ends of life viz., virtue, wealth and enjoyment, without letting anyone to come into conflict with the other two, who is reverential to those who are worthy of reverence, who is of a scholarly, scientific and retiring disposition, partial to the company of elders, who can curb his passions of desire, anger, envy, pride and conceit, who is constantly given to charitable acts, and contemplative of the good in this world and the next, and endowed with memory and understanding." Life of the opposite nature is said to be "not good".

Code of Conduct for Healthy Living

"The wise man who seeks happiness both here and hereafter, should exercise the highest care in selecting what is wholesome in the matter of food, conduct and behaviour."

"The length of life is a matter of care and husbandry. The opposite condition leads to death. He who rightly observes the rules of health as laid down here will not be deprived of the full measure of hundred years of disease free life."

Virtues of Clean Habits

“Virtues of cleaning the teeth, scraping the tongue and cleansing the mouth, massage and bathing, wearing of clean apparel, trimming of hair, beard and nails, frequent ablution of the feet and the excretory orifices, have all been emphasized. Like the lord of a city in the affairs of his city, a charioteer in the management of his chariot, so should a wise man be ever vigilant in the care of his own body.”

“By degrees, the wise man should free himself from unwholesome, habits; also by degrees, he should develop wholesome habits. By gradual withdrawal, addictions do not revert; and wholesome habits, gradually acquired, become firmly implanted”.

Virtues of Measured Diet

“Food is the principal factor which materially contributes to the strength, complexion, vitality of animated beings”.

“That should be known as the proper measure of food which when taken, is digested in due time without impairing one’s health”.

“An excess or surfeit of food is markedly harmful unless the gastric fire is increased by hard exercise.”

Importance of Exercise

“That activity of the body, which is meant to increase its strength and firmness is regarded as physical exercise. It should be practiced regularly in the right measure. Lightness, capacity for work, firmness, tolerance to hardship, subsidence of humoral discordance and stimulation of gastric fire accrue from exercise.”

“Fatigue, exhaustion, wasting, thirst, asthma, cough, fever and vomiting result from over-exercise.”

Ethical Conduct

“Mind control consists of restraining the mind from the desire for unwholesome objects”.

“A wise man should not suppress the natural urges of urine, faeces, semen, sneezing, yawning, hunger, thirst, sleep, tears, and deep breathing after exertion.”

RELEVANCE OF AYURVEDA TODAY

“On the other hand, those desirous of their welfare both in this and the next world should suppress the rash and evil impulses of the mind, speech and body. The wise man should control the impulses of greed, grief, fear, anger, vanity, impudence, jealousy, excessive attachment, and malice. One should control the impulse of speech that is harsh, extravagant, insinuating, untrue and untimely. One should control the impulse for all such activities as are injurious to others such as adultery, theft and violence.”

“One should have recourse to such means of livelihood as are not contrary to the dictates of religion. One should be devoted to peace and scholarship. Living thus, one attains happiness.”

“Do not give way to anger and joy, do not nurse your sorrows, be not arrogant in success and dejected in defeat, remind yourself constantly of the vanity of things, be decided as to causes and their effects and consequently devote to benevolent enterprises; do not grow complacent with your achievements; do not lose heart; do not recall calumny.”

“Diseases occur in those who do not observe the rules of healthy living. Hence the healthy man should be diligent in the observance of the rules of healthy living”.

“He alone can remain healthy, who regulates his diet, exercise and recreation, controls his sensual pleasures, who is generous, just, truthful and forgiving, and who gets along well with his relatives.”

Homeostasis, the Aim of Therapy

“Medicine is that, which being well administered becomes an equaliser of increased and diminished elements at the same time. It brings down the excessive element and augments the deficient one.” “Indeed this alone is the end sought in the employment of medicine, as also in the observance of wholesome habits, that the equilibrium of the elements may be achieved or maintained as the case may be. For it is only with a view to help maintain the balance of the elements that the intelligent will make use of a balanced diet. By the use of like and unlike food and exertion, the increase and diminution of body elements are brought about opportunely to restore equilibrium.”

“There is in the World no substance that may not be used as medicine, in this or that manner, for this or that purpose.”

“Medicine is of two kinds—one kind is promotive of vigour in the healthy. The other is destructive of disease in the ailing.”

"The opposite of medicine is also of two kinds— the one causing immediate disorders and the other causing remote ill-effects".

"That which is of contrary character to medicine is to be known as 'contra-medicine'. It is unfit for use. We shall confine to describing that which alone is fit for use".

The Four Pillars of Treatment

"The physician, the drugs, the attendant and the patient constitute the four basic factors of treatment. Of these four, the physician occupies the chief place, being at once the knower of disease and drugs, the instructor of the attendant and patient, and prescriber of medicine and regimen."

The Qualifications of a Physician

"Clear grasp of theoretical knowledge, wide practical experience and skills, purity of body and mind, these are the tetrad of desiderata in a physician".

The Qualifications in a Nurse

"Knowledge of nursing, skill, affection for the patient, and cleanliness. These are the tetrad of desiderata in the attendant".

The Qualifications in a Patient

"Recollection, obedience to instructions, courage, and ability to describe his ailment are the tetrad of desiderata in a patient". Drugs, their Potency and Sources "Substances are classified into three groups:

1. Some rectify the discordance of body elements.
2. Some vitiate the body elements.
3. Some are conducive to the maintenance of good health.

"Again, substances can be classified differently in three groups as animal, vegetable and mineral."

"He is the best of physicians who knows the science of administration of drugs with due reference to climate and who applies it only after examining each and every patient individually."

"A drug that is not understood perfectly is comparable to poison, weapons, fire and the thunderbolt, while the perfectly understood drug is comparable to ambrosia. The drug whose name, form and properties are not known, or the drug, which though known, is not properly administered, will cause disaster."

RELEVANCE OF AYURVEDA TODAY

“Even acute poison is converted into an excellent medicine by the right method of preparation. While, even a good medicine may act as an acute poison if improperly administered.”

“Therefore, the intelligent man who desires health and long life, should not take any medicine prescribed by a physician who is a stranger to the art of application. One may survive the fall of a thunderbolt on one's, but one cannot expect to escape the fatal effects of medicine prescribed by an ignorant physician.”

“That is the right medicine which makes for health and he is the best physician who relieves people of disease.”

“A single drug may have many appellations owing to its diverse actions. If we could indeed find any one drug possessed of all the properties, and capable of meeting all requirements, who would then put himself to the trouble of committing to memory the names and qualities of any other drugs?”

Aims of Therapy

“The physician will try to cure the diseases which are curable; adopt palliative measures in cases where palliation is the only remedy that can be offered; and give up a case which is beyond all medical treatment, and mostly, those which are more than a year's standing”.

“The physician who undertakes to treat incurable disease will invariably suffer loss of income, will tarnish his learning and fame, and earn for himself disrepute and taboo in society”.

“The curable diseases are of two kinds: those that are easily cured and those that are cured with difficulty. The incurable diseases also fall into two categories: those that are palliable and those that are absolutely irremediable”.

Principles of Therapeutics

“That should be known as the proper medication which requires to be taken in small doses, which is quick in action and is curative of even an excessive degree of morbidity, which is easy to take, which is light in digestion, palatable, pleasing, curative of the particular disease, not harmful even if complications arise, not very depressant, and is possessed of the most agreeable smell, colour and taste.”

“The physician must take into consideration that drugs differ with respect to land, season, source, flavour, taste, potency, post-digestive effects, and specification, and also that men differ with respect to their body, constitution, age,

vitality, gastric fire, morbid tendency, proclivities, homologation and state of the disease.”

“An under dose of medication cannot cure the disease just as a small quantity of water cannot quench a great fire. And medicine given in overdose will prove harmful just as excessive watering harms the crops. So, after carefully considering the severity of the disease and the strength of the medication, the physician should administer it neither in too large a dose nor in too small a dose.”

Cautious Therapy

“It is better to take a potion of a mild medication repeatedly as it is attended with only slight discomfort and no risk, than to take a very strong medication which is attended with immediate danger to life”.

“The purificatory dose if improperly administered is like poison, and if properly administered, is like nectar.”

“All therapeutic measures designed to alleviate disease, however wholesome and however skillfully given, fail to bring about the alleviation of disease if they are used either in insufficient or excessive measure or at the wrong time or in the wrong manner”.

“There is no substance which is absolutely of good or bad qualities. Hence our concern should be to select such substances as possess more of the required good qualities”.

Approaching Death

“The knower of the medical science should not declare the approach of death, if he is not questioned concerning it, although he clearly perceives the signs prognosticate of the end”.

“Even if he is questioned, the physician should not immediately pronounce the prognosis of death where such inconsiderate action on the part of the physician may cause shock to the patient and distress to others”. “While refraining from announcing the approach of the end, the experienced physician should not, however, undertake treatment in a case where he finds that the prognostic signs of death are present”.

“But if the physician observes signs which are of a contrary character to those laid down as prognosticative of death, he should certainly declare the approach of recovery as indicated by the auspicious nature of the signs”.

Qualities of a Good Physician

“Clear grasp of theoretical knowledge, wide practical experience, skill, and purity of body and mind - these are the tetrad of desiderata of a good physician”.

“The physician who possesses knowledge, clear interpretation, right application and practical experience is to be regarded as a the reclamer of life”.
“He who practices medicine neither for gain nor for gratification of the senses, but moved by compassion for creatures, surpasses all”.

“Those, who, for the sake of a living, make merchandise of medicine, bargain for a dust of heap letting go a heap of gold”.

“There is no benefactor; either moral or material, comparable to that physician who regains those who are being dragged away by fierce disease towards the abode of death, back to life, by severing the noose of death. For, there is no other gift greater than the gift of life”.

“He who practices medicine, holding compassion for creatures as the highest religion, is a man who has fulfilled his mission and attains supreme happiness”.

“The physician who is endowed with character, intelligence and reason, and has mastered the science of healing, deserves to be venerated as a mentor of all men. He is indeed regarded as Life's guardian, (*“Pranacharya”*)

Medical Knowledge & Experience

“A physician well-versed in the principles of Ayurveda but unskilful in his art through want of practice, loses his wit at the bedside of his patient, just as a coward is at his wit's end to determine what to do when for the first time he finds himself in the ranks of a contending army”.

“On the other hand a physician experienced in his art but deficient in his knowledge, is condemned by all good men as a quack and deserves capital punishment at the hands of the king”.

“Both these classes of physicians are not to be trusted, because they are inexpert and half-educated. They are like a one-winged bird incapable of flight”.

“A physician well-versed in the principles and experienced in the practice of medicine is alone capable of curing disease just as only a two-wheeled cart can be of service in a field of battle”.

RELEVANCE OF AYURVEDA TODAY

"The endeavours of a man who has studied the entire science but fails to make a clear exposition of the same, are vain like the efforts of an ass that carries a load of sandalwood without ever being able to enjoy its pleasant scent".

"For the learned man there are only two methods of examination-direct observation and inference".

"Practice bestows on a man true insight which leads to success in treatment even as the skill to distinguish between the good and the bad among precious stones is not derived from a mere acquaintance with the theoretical knowledge of gems".

"A surgeon who is fully conversant with the symptoms which are respectively exhibited by a swelling in its unsupported, suppurating and suppurated stage is alone worthy of the epithet. The rest are but impostors".

"The *Vaidya* who opens up an unsupported or unripe swelling out of ignorance, as well as the one who neglects a fully suppurated one, should be looked upon as the vilest *chandal*, for his wrong or incorrect treatment".

"A patient who is discreet, and is not in a special hurry to end his earthly sojourn, would do well to shun the presence of a bungling, unskillful surgeon who cannot even keep himself unhurt in the course of a surgical operation".

Physician-Patient Relationship

"The patient, who may mistrust his own parents, sons and relations, should repose an implicit faith in his own physician and put his own life into his hands without the least apprehension of danger. Hence a physician should protect his patient as his own begotten child".

"No thoughtful man, who seeks enduring life, should ever covet the possessions of the 'guardian of life' or revile him or do any harm to him".

"Whoever having been treated by a physician does not recompense him whether or not there be a previous understanding for remuneration that man is beyond redemption".

"The physician should regard all his patients as if they were his own children and vigilantly guard them from all harm, considering this to be his highest religion".

Scientific Attitude

"One should not suffer disputants who are of little learning, foolish and blatant, not because of considerations to oneself, but with a view to keeping the light of knowledge unobscured".

RELEVANCE OF AYURVEDA TODAY

“Those whose compassion for all creatures is great and who are devoted to truth are ever zealous in putting down false doctrines”.

“The whole of suffering which cleaves mind and body has ignorance for its basis, and conversely all happiness is found in clear scientific knowledge”.

“However, this very knowledge of mighty import is no illumination to those who are devoid of understanding, as is the orb of the sun to those who have lost their eyesight”.

“Of all types of evidence, the one that we observe with the eye is the best”.

“Everything spoken must be supported by reason. Such statements, with their support in reason and clear in their nature, are of use in the science of treatment, for they help to clarify the intellect. The unimpeded intellect achieves the fulfillment of all its efforts”.

Concept of Periodic Health Check up

“The ignorant man fails from stupidity or negligence to note the incipient state of a disease, just as a simpleton fails to recognize a potential enemy.”

“Disease, from atomic beginning, assumes enormous proportions. Therefore, before even diseases show themselves or while yet they are in the incipient stage, one who cares for one’s happiness should endeavour to have them treated with proper medication”.

The Ever-sick Patients

“The ever-sick class comprises the priests, the King’s officers, the merchant and the courtesan”.

“The priest, engaged as he is constantly in the study and recitation of the scriptural texts, observance of the vows and the daily rites, fails to attend to his bodily good”.

“The King’s officer similarly fails in his duty towards his own body by his preoccupation with the gratification of the royal mind, and by the demands made on him by the other dependants of the King, the constant anxiety caused by the various responsibilities of his position, as also the constant fear of incurring the displeasure of his masters”.

"The Courtezan, being dependent on the whims and moods of men, devotes herself to their service and is constantly engaged in acts of toilet and beautification. The merchant is perforce victim to a sedentary mode of life, suppresses the natural urges and can hardly even afford to have timely meals and exercise".

The Eight Censured Types

"In respect of their bodily conditions, eight kinds of persons are found censurable. They are the very tall and the very short; the very hairy and the hairless; the very dark and the very fair; the very corpulent and the very emaciated".

"Of these again, the very corpulent and the very emaciated suffer from specially censurable traits; the corpulent person is affected with eight disabilities, viz. diminution of life, lack of agility, difficulty in sex act, debility, fetor, distressing sweats, excessive hunger and excessive thirst".

"Such excessive corpulence is caused by overeating, by the use of articles that are heavy, sweet, cold and unctuous, by lack of exercise, by day sleep, by lack of mental exertion and by inherited tendency".

"That man is spoken of as over corpulent who on account of the inordinate increase of fat and flesh is disfigured by pendulous buttocks, belly and breasts, and whose increased bulk is not matched by a corresponding increase in energy. Thus, the evils of corpulence together with its causes and symptoms have been set out".

Evils of Emaciation

"The emaciated man cannot stand the strain of exercise or of a full meal or of hunger or thirst, or of disease or of strong medication. Similarly he cannot bear great cold or heat or the strain of the sex act".

"Splenic disorders, cough, wasting, dyspnoea, *gulma*, piles, abdominal affections and disorders of assimilation generally assail the emaciated man".

"That man is said to be over-emaciated who is lean of buttocks, belly and neck, who is covered with a network of prominent vessels, who is reduced to skin and bones and who has prominent joints".

"These two, the very corpulent and the very emaciated, are perpetually afflicted with diseases and are to be treated with constant slimming and nourishing remedies respectively. For reducing the corpulent heavy but non-nourishing food should be given; while for building up the emaciated, light but nourishing food should be given".

“Of the two conditions, emaciation is the lesser evil, though both alike require to be remedied. When both are overcome by disease, it is the corpulent that suffer more”.

“The man is well-proportioned in flesh, well-knit in figure and firm by senses, is not overpowered by the violence of disease. He is able to endure hunger and thirst, heat and cold and the strain of exercise, and has normal digestive and assimilative powers”.

Assessment of Fatal Prognosis

“Just as the blossom is the harbinger of the coming fruit, so is the evil symptom known as fatal prognosis the harbinger of the death of the patient. The appearance of fatal symptoms never ends except in death and there is no death that is not preceded by the appearance of fatal symptoms”

“The ignorant are deluded into mistaking for fatal symptoms what are not such, and the really fatal symptoms go unrecognized by them. This is the result of delusive knowledge.”

“That man is regarded by the wise as manifesting fatal symptoms, who exudes day and night, smell, resembling those of various flowers in a forest abounding in various trees and creepers bursting into bloom. Such a man is certain to die before a year.”

“A man whose body exudes a mixture of unpleasant smells, or a single unpleasant smell, is to be regarded by the physician as one showing fatal prognostic symptoms.”

“Flies, lice, wasps and mosquitoes get repelled and turn away from the bad taste of the body of the man about to die.”

The Method of Investigation

“The physician should palpate the patient’s entire body with his hands which must be in a normal condition. While feeling the patient’s body the following are the abnormalities to be noted.”

“They are:—the absence of throbbing in those parts which are always throbbing; coldness of those parts which are always warm; rigidity of those parts which are always soft; roughness in those parts which are always smooth; the disappearance of those parts which should normally exist; the looseness, sagging or dislocation of joints, the paucity of flesh or blood; hardness; excessive perspiration; also whatever else that is abnormal and unaccountable.”

RELEVANCE OF AYURVEDA TODAY

"If the patient's respirations are either too long or too short, it is to be concluded that he is nigh unto death. If the two sides of the neck, on being felt, are observed not to pulsate it is to be concluded that he is nigh unto death.

If the patient's eyes are not normal but evince abnormal tendencies, that is to say if they are too protuberant, too sunken, too-oblique, too asymmetrical, either perpetually open or perpetually closed, then it should be concluded that the patient is near death's door."

"If the physician tugs at a few hair on the head or body and they come out with the roots without causing pain, then it is to be known that the patient is soon to depart from life."

"If the veins in the abdominal region become conspicuous, it is to be understood that the patient is not going to survive".

"If the nails are drained of blood, or if they look dark blue resembling the colour of ripe fruits of the *Jambu* tree, it is to be gathered that the patient's days are numbered".

"If a debilitated patient develops abdominal distension and diarrhoea, his life is difficult to save".

"If constipation and excessive thirst make their entry into an already weakened man, life deserts him ere long".

"A full conception of the science will never be attained by the knowledge of only a part of it".

"Thus believing to have a perfect approach to the whole subject by the knowledge of one branch only, the physician blunders".

"Those who are mistaken in the diagnosis of disease will be also be misled in deciding the line of treatment".

"Being deluded by a misconception of the nature of the disease they administer wrong medication, which either kills the patient or brings down upon him greater affliction".

"The physician, knowing all that is to be known, examining everything in every respect possible and diagnosing after full investigation, will never be mistaken and will be able to achieve the desired result".

"There is no limit at all to the Science of Life; so you should apply yourself to it with diligence. The entire world is the teacher to the intelligent and the foe to the unintelligent. Hence, knowing this well, you should listen and act according to the words of instructions of even an unfriendly person when they are worthy".

The first “flame photometer”

“In case of suspected poisoning of the food, the physician should throw part of it in the fire. The fire burns abnormally when food containing poison is cast into it. The flame becomes variegated in colour like the feathers of the peacock and the smoke is acrid, intolerable, dry and smells like a corpse”.

The first Urine specific gravity test

Yogaratanakara has described “*Taila Bindu Pariksha*” or oil drop examination. A drop of “til” (sesame) oil is gently placed with the help of a hay stick, on the surface of urine collected in a utensil. If the oil spreads over the surface, the disease is curable. If the oil drop remains suspended, the disease is difficult to cure. If the oil drop settles to the bottom, the disease is incurable.”

In praise of discussion

“Discussion with a person of the same branch of Science is indeed what makes for the increase of knowledge and happiness. It contributes towards the clarity of understanding, dispels doubt and confirms the ideas of those that have no doubts. It enables one to learn new things in the course of the discussion”.

“One should persuade gently and in a spirit of goodness. One should not rejoice in the discomfiture of the other party in a discussion. One should not boast before others. One should not get deluded by a partial or imperfect grasp of the subject. One should not expatiate on what the other is not at all acquainted with”.

“Before the assembly of unfavourably disposed persons, one should not engage in debate under any circumstances and with anyone, whether such assembly be composed of men of learning, experience and dialectical skill of statement and rejoinder, or of ignorant persons”.

“In a hostile debate one should speak skillfully and never object to statements backed by authority. The hostile debate which is serious enrages some people. And there is nothing that an enraged man may not do or say; and the wise never commend a quarrel before an assembly of good men.”

“Excellence of speech is that which is neither insufficient in sense nor superfluous, which is full of meaning and not delusive, nor self-contradictory and which is explicit in sense.”

“Everything spoken must be supported by reason. Such statements with their support in reason and clear in their nature are of use in the science of treatment, for they help to clarify the intellect. The unimpeded intellect achieves the fulfillment of all its efforts.

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EXPLORING THE HERBARIUM

Introduction

According to Charaka, "There never was a time when the science of life did not exist, even as it was the case with life". The life-stream carried in its currents its own supporting and protecting wisdom that became manifest at the beginning of each cycle of time to the seers. Man guided by the instinct of lower animals and the intuition of his own species evolved the science of drugs from the vegetables and animal and mineral sources around him. In *Atharva Veda*, the precursor of Ayurveda, one finds the following interesting description:

"The boar knows the plant; the mongoose knows the remedial herb; what ones the serpents, the Gandharvas know, those I call to aid. What herbs of the Angirasas the eagles know, what heavenly ones the Raghatas know, what ones the birds and the swans know, and what all the winged ones, what herbs the wild beasts know, these I call to aid for you. Of how many herbs the inviolable Kine partakes, of how many the goats and sheep, let so many herbs, being brought, extend protection to thee".

Atharva Veda, Kand 8, Sutra 7.

Charaka states, "The goatherds, the shepherds and cowherds and other foresters are acquainted with the names and forms of plants; and their uses".

Learning from Instinct of Animals

One striking example of the instinct of animals in relation to plants is provided by the milkweed *Asclepias curassavica* in Costa Rica. Although it grows abundantly in the grass, large herds of cattle completely avoid it, because they have learnt by experience that it causes sickness and occasional death. The poisons in the asclepiads have attracted much attention among the pharmacologists and organic chemists because the substances are similar to digitalis, the cardiac glycoside. The amount of the glycoside that causes vomiting is just about half the amount required to cause death through its action on the heart. Hence an animal that eats a grass containing the cardiac glycoside will, provided that it is capable of vomiting, rid itself of the poison before a lethal amount can be ingested.

In contrast, milkweeds are the exclusive food of the larvae of an entire group of tropical insects which include the monarch and the queen butterflies. Insect-eating birds avoid these butterflies. Assay of extracts of the butterflies have revealed cardiac glycosides similar to digitalis in their effect — calactin, calotrophyin and calotoxin. The fact that many naturally occurring plant poisons

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including alkaloids and cardiac glycosides are bitter is highly relevant. The bitterness is a clue for conditioning predators to avoid the plants. The poison itself could very well be tasteless, provided that it was always associated with a flavour that could shy away the predators. Certain plants exhibit a form of mimicry — they have flavours usually associated with particular poisons but actually lack the poison still the ploy works to shy away the predators! Analysis of plant selection by the butterfly group (whose caterpillar stage is a formidable eating machine) has made it clear that their choice has a chemical basis.

The plant world's main line of defence (against attack by insects and birds and animals) consists in chemical weapons. Very wide-spread among the plants are certain chemicals that apparently perform no physiological function for the plants themselves but do act as potent insecticides, or insect repellents. Among those are alkaloids, quinones, essential oils, glycosides, flavonoids and raphides (crystals of calcium oxalate). Long before man learned to synthesize insecticides he found that an extract from chrysanthemums, *pyrethrin*, which is harmless to mammals, is a powerful killer of insects.

Particularly interesting are the *alkaloids*, a heterogeneous group of nitrogenous compounds found mainly in flowering plants. They include nicotine, caffeine, quinine, marijuana, opium and peyote (mescaline). Alkaloids give the plants that contain them protection from predators. Plant alkaloids can disturb an herbivorous animal's physiology, and hallucinogenic alkaloids may be "chemopsychological weapons". It is even possible that plants fight insects with tumour-inducing substances; at least one plant alkaloid, nicotine, is known to be a powerful carcinogen in vertebrates.

Through accident, through trial and error and through intelligent observation & inference, mankind has accumulated knowledge about harmful plants (poisons) and useful plants (drugs). As early as 5000 B.C., the Chinese had well developed floral pharmacopoeias, or sets of accepted plant-derived drugs/ So did the Babylonians, the Assyrians and the Hebrews. The Greeks knew many of the currently used plant-derivative drugs. Dioscorides produced in 60 A.D. the great *De Materia Medica*, which dealt with all the medicinal substances known at the time, including some 600 plants. The *Charaka Samhita* describes about 500 herbal drugs and the *Sushruta Samhita* describes approx. 700 plants classified under 37 classes or "*ganans*".

There are as many as 800,000 species of plants on earth of which only a few have been exploited by man. The three major cereals —rice, wheat and maize — and perhaps ten other widely cultivated plant species stand between famine and survival for the majority of the world's human population. A handful of drug plants have served mankind for several thousand years. Table I gives a list of important drugs (and poisons) that originated in folklore and form part of the pharmacopoeia even today. To the ancient Greeks, the word

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“pharmakon” meant not only a curative drug but also a poison, a charm, a spell, or an incantation. Today the word drug still has all these meanings.

Today we understand the nature of drug action a lot better than at any time in history, and our interest in the herbarium continues even today. A most recent example of a herbal remedy of great interest in the 20th Century is Qinghaosu, a medicinal herb used in China since 168 B.C. Chinese chemists have in 1972 isolated the active principle and used it successfully in Chloroquin-resistant Plasmodium falciparum malaria.

Chemistry of Plant Products

As knowledge of chemistry advanced, many plants were subjected to chemical analysis to obtain active principles in pure forms. Thus Serturmer and Pelletier in Germany isolated active principles from opium and Pomegranate peel. With rapid advances in organic chemistry after Wohler's synthesis of urea, there was a great spurt of activity in the field of synthetic chemistry. Today a large majority of drugs in therapeutic use are synthesised. However, pharmacopoeias of most countries still contain a fair number of drugs obtained from the vegetable kingdom.

TABLE - I

Name of Drug	Family or Genus	Part of Plant
Atropine	<i>Atropa belladonna</i> (Solanaceous family)	Whole plant
Castor Oil	<i>Castor Oil Plant</i>	Seeds
Caffeine	<i>Coffea arabica</i> , <i>Thea sinensis</i>	Seeds
Cannabis Indica	Indian Hemp	All parts
Clove	Caryophyllata	Flower
Cocaine	<i>Erythroxylon coca</i>	Leaves
Colchicin	<i>Colchicum autumnale</i>	Roots and Seeds
Digitalis	Fox glove (Purburea)	Leaves
Emetine	<i>Ipecacuanha</i>	Roots
Ephedrine	<i>Ephedra</i>	Stems
Eserine	<i>Calabar</i> beans (<i>Physostigma venenosum</i>)	Seeds
Forskolin	<i>Coleus forskolii</i> (Mainmul)	Fresh roots
Morphine	<i>Papaverum somniferum</i>	Unripe capsule
Nicotine	<i>Nicotina</i> (tobacco)	Leaves
Picrotoxin	<i>Anamitra cocculus</i>	Mushroom
Pyrethrum	<i>Pyrethri flores</i>	Flower
Quinine		
Quinghaosu	<i>Cinchona</i> (<i>Quina quina</i>)	Bark

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Reserpine	<i>Sarpagandha (Rauwolfia serpentina)</i>	Roots
Salicylic acid	<i>Willow</i>	Bark
Scillaren	<i>Squill</i>	Bulbs
Senna	<i>Cassia acutifolia</i>	Leaves
Strophanthus	<i>Strophanthus gratus</i>	Seeds
Strychnine	<i>Nux vomica</i>	Seeds
Tubocurarine	<i>Curare (G. tomentosum)</i>	Bark & Stems
Turpentine	<i>Pine (coniferous tree)</i>	Resin from bark
Vencristine	<i>Vinca rosae</i>	Flowers

Various parts of a plant may be used as therapeutic agents. These may be used in a dried form or after extractions. Such crude preparations of plant origin are called Galenicals after Galen, the ancient Greek physician. Chemical analysis of active principles derived from plants shows they are glycosides, saponins, alkaloids, oils, waxes, resins, compound resins, carbohydrates (gums), tannins.

The pharmaceutical preparations of plant origin are administered either as watery solutions (including mucilages, syrups and elixirs containing syrups & alcohol), or *alcoholic* solutions, or *extractives* — *infusions, decoctions, tinctures fluid extracts, solid extracts etc.*

Alkaloids

The alkaloids are a class of compounds synthesized by plants. Many of them have powerful effects on the physiology of animals and man. Since earliest times they have served man as medicines, poisons and the stuff that dreams are made of.

The alkaloid *morphine*, the principal extract of the opium poppy, remains even today, "The one indispensable drug". *Quinine*, from Cinchona bark, cures malaria even today. *Colchicine*, from the seeds and roots of the meadow saffron, banishes the pangs of gout. *Reserpine*, from snake roots or Sarpagandha, tranquillises the anxieties of the neurotics and psychotics. The coca leaf alkaloid *cocaine* plays Jekyll and Hyde as a useful drug and as a sinister narcotic. The South American arrow poison *tubocurarine* is used today as a muscle relaxant during surgical operations. The belladonna alkaloid *atropine* is a useful anti-spasmodic and mydriatic (dilates the pupils). The alkaloid derived from Calabar beans, used by West African tribes in trials by ordeal, physostigmine is specific treatment for myasthenia gravis. *Caffeine* and *nicotine*, the most familiar of the alkaloids are imbibed and inhaled daily by a large segment of the human population. *Coniine*, the alkaloid poison in the draught of hemlock that killed Socrates, has a simple structure while *Strychnine* from nux vomica has a complicated structure. From the chemical point of view they are all grouped

together only because we do not know enough about them to file them under other headings. One common thing is that amino-acids are the source of most alkaloids. From the same starting material tyrosine, one plant makes reserpine while the other makes strychnine. *Hordenine* is one of the few alkaloids known to undergo further metabolism in plants; it is converted into one of the units that form the long chain molecules of lignin, an essential structural material in many plants.

Lectins

Lectins are proteins found primarily in plants. They combine specifically with sugars on cell surfaces and hence bind cells together. The legumes are particularly rich in lectins. In recent years, lectins have provided a valuable tool for research in immunology, since lectins are valuable as probes for identifying and mapping the sugars on the surface of cells. It has been known for many years that protein extracts of various bean species are able to induce lymphocytes to proliferate. The term *mitogen* is used for these substances because of their ability to stimulate mitosis. The most widely used substance in the immunological sphere is *phytohaemagglutinin* (PHA) and its mitogenic activity was noticed during its use as an haemagglutinating agent in haematology. This mitogenic effect is antigenically non-specific, but most of the mitogens (PHA, Concavalin A, leuco-agglutinin) have been shown to stimulate T lymphocytes. Poke weed mitogen is believed to be primarily a B lymphocyte stimulant and specifically so in low concentrations. While the actual nature and significance of non-specific stimulation of lymphocytes is not understood in general, there is a fair degree of correlation between cellular immune competence and non-specific T-cell stimulation by mitogens. In the study of human disease states, a very large majority of the work has used PHA as the mitogen.

In the 1890's, with the help of ricin & abrin, Paul Ehrlich discovered some of the most fundamental principles of immunology.

Hormones from Plants

After the establishment of the structure of cholesterol in 1932, interest was focused on *plant steroids* as a fertile route for the production of steroid hormones. Digitalis, the cardiac glycoside extracted from plants which had been known for centuries as poisons, was shown to contain a steroid attached to a sugar. The steroid part has a skeleton like that of a bile acid, but one major difference is that the side chain is coiled into a ring.

The digitalis steroids are rather spetial, but steroids with sugars attached are very common in the plant world. One class of these substances is known as *Saponins*, because watery solutions of these foam like soap when shaken. The steroid part of a saponin is called a sapogenin. The most interesting of these substances is *diosgenin*, which has a skeleton remarkably

like that of cholesterol, with 27 carbon atoms and a double bond between the 5th and 6th carbons. The discovery of this structure at once suggested that diosgenin would be useful for producing sex hormones. Diosgenin could easily be converted into pregnenolone, already known as a building material for progesterone.

Another substance called *sarmentogenin* which had been isolated in 1929 from some unknown plant seeds, was shown to carry a hydroxyl group at the position 11, suggested the possibility of converting it into cortisone.

Ethnobotanical Research

Folklore has been considered as the archaeology of the mind. The knowledge about plants that has been accumulated through experience, trial & error, and which has been passed on from generation to generation, whether verbally or in writing, forms the main subject of ethnobotany. The science of ethnobotany has recently received much attention in underdeveloped and developing countries, where large portions of populations still depend upon natural resources in practically indigenous conditions and the impact of modern systems of medicine has not reached them.

Ethnobotanical information is largely based on personal experience of groups of people or tribes, where human beings themselves served as tools of experiments under force of circumstances. It might have cost many human lives over the millennia, to eliminate certain harmful drugs from folk medicine, but there might have been some real gains.

A considerable percentage of India's population comprises tribals. Certain parts of India have predominantly tribal populations such as Central India, the eastern parts of peninsular India and most of the far-eastern states. Ethnobotanical researches have so far brought on record over 500 plants as significantly used by the tribals for various purposes. Organized field work in this subject was started by Dr. S.K. Jain, Director, Botanical Survey of India, in 1960 and an active school of ethnobotany has now come up in this department. The first group of people taken up for studies were the Gonds in Central India, and the work was extended to Bihar, Orissa, Andhra Pradesh, Arunachal Pradesh, Meghalaya, and Manipur. A list of 50 plants used in folk medicine in different parts of India is given by Jain. The uses extend over eye diseases, diarrhoea and dysentery, cough and cold, fever, wounds & fractures, dog bites, snake bites, abortifacients and aphrodisiacs. Of particular interest is the *Saprosma tematum*, a decoction of its leaves being used with ginger in malaria. This deserves further scrutiny in view of the search for new anti-malarials. Similarly *Tamarix ericoides* Rott (Tamaricaceae) leaves as a decoction are reported "to cure enlarged spleen in children as well as in adults", and it is worth scrutinising it for anti-malarial effects.

EXPLORING THE HERBARIUM

Ethnobotanical studies should be profitably utilised for interaction between organized traditional medicine and folk medicine. Most of the primitive tribals will not accept any other medicine except the ones prescribed by their medicine-men. The medium of the medicine-men should be profitably utilized for a choice of appropriate medicines for further critical scrutiny. The immense richness of botanical resources was emphasized by Schultes in 1963 when he pointed out that only a very small fraction of plant resources has yet been utilized by the human race, particularly for their active principles. A study by Schultes in 1969 on hallucinogen of plant origin has yielded results of academic and practical interest. Ethnobotanical research leads to the discovery of new or less-known medical herbs and gives new clues for pharmacological testing. Herbarium sheets and museum specimens and field notes on them have provided a good source of ethnobotanical data.

Jain has discussed the problems related to the authenticity of information collected during ethnobotanical field work. Many plants are referred in literature to their common names and their identity may be disputed. About 20 different plants are attributed to the name SOMA mentioned in the ancient Hindu epics. Other significant examples of disputed identity are the names "Brahmi", "Punarnava", "Jatamanasi", "Rudanti", "Bala" and "Kalpavruksha". The main difficulty in fixing the botanical identity of herbal drugs is the lack of proper descriptions and illustrations. Local names for plants or plant products have not remained the same over the ages. The properties attributed to plants are of help in identification in some cases, brief notes on the structure or morphology of plants but they may lead to greatly varying interpretations. For instance, the description of "SOMA" could be interpreted to tally with branched shrubs like *Sarcostemma* and *Ephedra* on the one hand, climbers like *Cocculus hirsutus* or *Dioscorea bulbifera*, and a polyporus fungus *Ammanita muscaria*. The botanical names of course mean little to the folks in the forests, rural or tribal areas, or, for that matter to the non-botanists. Even the names common in commerce may be completely unknown and foreign to the tribal societies. Thus, if their help is solicited for procuring materials for testing, they will have to be told the names which are familiar to them, and to know these the only means is to do ethnobotanical work with them. Screening of the plant kingdom for new substances of pharmacological value is a continuous quest.

Screening of Indian Plants for Biological Activity

The Central Drug Research Institute (CDRI) at Lucknow started in 1964 a programme for the screening of plant extracts for a wide range of biological activities. The botanical identity of each plant was established before the extract was prepared. Although it is customary to prepare extracts of plant material with a variety of solvents (polar & non-polar) when investigating possible biological effects, they used only a 50 percent ethanol extract in order to be able to cover a large number of plant material. Almost all these extracts have been tested for

antibacterial, antifungal, antiviral, anticancer and a wide range of pharmacological activities. A fair number of extracts have been tested for anti-amoebic, antimalaria, antifilaria and hypoglycaemic activity and a few for activity against helminths and spirochetes and for inhibition of spermatogenesis and prevention of fetal implantation. Antilipemic, diuretic and anti-inflammatory activities were also tested. In all, 2065 extracts from 1973 species were studied. However, in terms of clinical applicability, the bulk of this colossal effort has turned out to be sterile.

Phytoconstituents are known to vary depending on ecological factors such as time of collection, habitat, climate etc. This may explain the discrepancy sometimes found between observations of different workers. Hence time and place of collection should be mentioned along with the experimental data. Indian folklore and Ayurvedic pharmacopoeia mention the use of some plant products as local contraceptives. The CDRI, Lucknow has tested about 1600 plant extracts (50% ethanol) for in vitro spermicidal activity on rat vasal or epididymal contents at 2% concentration. Thirty plant extracts showed spermicidal activity in rats and sixteen out of them caused instantaneous immobilization of human spermatozoa. The list of extracts which have shown promising activity at the CDRI is given in *Appendix L*.

Anti-tumour Plant Agents

Comprehensive reviews of the technical and folklore literature have been published by Hartwell in 1971, wherein citations are recorded for the use of different plant species which have been used or recommended in various parts of the world for the treatment of cancers and other conditions such as warts and tumours. In the U.S.A., the Cancer Chemotherapy National Service Centre (CCNSC), now incorporated into the Development Therapeutic Programme (DTP) has screened thousands of plant extracts against standard tumour systems consisting of solid tumours and leukemias.

At the Cancer Research Institute (CRI) in Bombay, more than 600 species of indigenous plants have been screened using standard transplantable tumours. Eight plants have exhibited meaningful anticancer properties. Phytochemical studies, subsequently undertaken on plant materials, have revealed that some of them contain chemical entities which manifest various degrees of activity in experimental tumours. Isolation and structural elucidation of plant-derived tumour inhibitors are yielding fascinating, novel types of growth-inhibiting compounds containing high electrophilic functions. New compounds possess structures and chemical properties which suggest that they may act by selective alkylation of growth-regulatory macromolecules. This approach may yield useful templates for the synthesis of potentially superior chemotherapeutic agents. New growth inhibitors may provide powerful tools for the elucidation of new biochemical mechanisms of growth control that may be amenable to selective regulation.

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Dr. Ramakrishna Ambage of CRI has reviewed information on some promising plants, novel isolates, their anti-tumour properties and possible mechanisms of action. The most interesting ones appear to be the diterpenes, lignans, quassinoids, ansamacrolides and alkaloids. The X, B unsaturate lactone function has been shown to be important for the tumour inhibitory activity of several classes of cyclic synthetic compounds and naturally occurring terpenoids.

It is evident that anti-cancer activity is encountered in compounds of a wide variety of chemical classes. Many of these are of novel chemical structures, especially those of considerable complexity, requiring the development of methods for the creation of new ring systems.

APPENDIX I

Anti-Cancer Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	41	RT <i>Berberis asiatica</i>	+	
2	36	ST <i>Cedrus deodara</i>	+	
3	36	ST <i>Cedrus deodara</i>	+	
4	18	LF <i>Erythrina suberosa</i>	+	
5	6	BU <i>Urginea indica</i>	+	
6	583	PX <i>Annona squamosa</i>	+	
7	380	PL <i>Bacopa monnieri</i>	+	
8	598	PX <i>Buchanania lanzan</i>	+	
9	428	Calotropis <i>procera</i>	+	
10	443	PL <i>Celsia coromai-deliana</i>	+	
11	477	PL <i>Cleistanthus collinus</i>	+	
12	433	PX <i>Cocculus pendulus</i>	+	
13	554	PL <i>Corchorus aestuans</i>	+	
14	542	PX <i>Cotoneaster marginatus</i>	+	
15	390	PX <i>Flemingia chappar</i>	+	
16	513	PL <i>Gleichenia linearis</i>	+	
17	483	PL <i>Ipomoea leari</i>	+	
18	454	PL <i>Lepidagathis trinervis</i>	+	
19	328	PX <i>Lyonia ovalifolia</i>	+	
20	459	PX <i>Maba buxifolia</i>	+	
21	590	PX <i>Manilkara hexandra</i>	+	
22	303	SB <i>Melia azedarach</i>	+	

EXPLORING THE HERBARIUM

23	557	PL <i>Nicotiana plumbaginifolia</i>	+	
24	326	PL <i>Polygonum recumbens</i>	+	
25	306	SB <i>Quercus semicarpifolia</i>	+	
26	511	PL <i>Selaginella plumosa</i>	+	
27	478	PX <i>Streblus asper</i>	+	
28	469	ST FR) <i>Zizyphus rugosa</i>	+	
29	723	<i>Albizzia procera</i>	+	
30	677	<i>Casearia verca</i>	+	
31	673	<i>Duabanga sonneratioides</i>	+	
32	613	<i>Luffa graveolens</i>	+	
33	654	<i>Photinia integrifolia</i>	+	
34	724	' <i>Pyrus pashia</i>	+	
35	732	<i>Rhus parviflora</i>	+	
36	637	<i>Tetrastigma serrulartum</i>	+	
37	952	PX <i>Aglaia odoratissima</i>	+	
38	938	PX <i>Mallotus stenanthus</i>	+	
39	958	PX <i>Mappia foetida</i>	+	
40	1474	PX <i>Anamirta cocculus</i>	+	
41	1377	PX <i>Anisomeles malabarica</i>	+	
42	1266	SB <i>Castanopsis indica</i>	+	
43	1441	PL <i>Commelina undulata</i>	+	
44	1442	PL <i>Cyanotis fasciculata</i>	+	
45	1446	PX <i>Gymnosporia wallichiana</i>	+	
46	1214	PL <i>Jussiaea suffruticosa</i>	+	
47	1448	PX <i>Passiflora foetida</i>	+	
48	1281	PX <i>Tephrosia candida</i>	+	
49	1212	SB <i>Terminalia paniculata</i>	+	
50	1365	PX <i>Wikstroemia indica</i>	+	
51	1528	PX <i>Argyreia involucrata</i>	+	
52	1523	PX <i>Brucea mollis</i>	+	
53	1522	PX <i>Hippocratea macarantha</i>	+	
54	1586	PX <i>Indigofera mysorensis</i>	+	
55	1603	PL <i>Senecio tenuifolius</i>	+	
56	1601	PL <i>Vanda parviflora</i>	+	
57	1584	PL <i>Vicoa indica</i>	+	
58	2068	PX <i>Aglaia roxburghiana</i> var. <i>beddomei</i>	+	
59	2090	PL <i>Amberboa ramosa</i>	+	

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60	1872	FL Blepharis sindica	+	
61	1871	PL Cistanche tubulosa	+	
62	1865	RT Croton burhia	+	
63	2050	PL Eranthemum purpureum	+	
64	2100	PX Gmelina asiatica	+	
65	2081	PL Impatiens balsamina	+	
66	1961	PL Inula cappa	+	
67	2099	PX Ipomoea dichroa	+	
68	2055	PX Moringa oleifera (Hybrid)	+	
69	1936	PL Parthenium hysterophorous	+	
70	2097	LF Sansevieria cylindrica	+	

List of Plants Fractionated for their Biological Activity

Hypoglycaemic Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	54	RT Aegle marmelos	+	
2	89	LF Anacardium occidentale	+	
3	70	SB Ficus racemosa	+	
4	47	FR Mucuna prurita	+	
5	126	SB Quercus lancaefolia	+	
6	58	RT Ricinus communis	+	

C. N. S. Depressant Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	1244	PX Atylosia trinervia var. Major	+	
2	1404	PL Geranium ocellatum	+	
3	1249	PX Melianthus major	+	
4	1592	PX Ardisia neriifolia	+	
5	1596	PL Cissus repens	+	
6	1594	PX Dysoxylum binectariferum	+	
7	1597	PL Forrestia mollissima	+	
8	1723	PX Saraca indica	+	
9	1621	PX Terminalia aijuna	+	
10	1847	PX Acacia auriculiformis	+	

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11	1850	RT Boerhaavia chinensis	+	
12	1894	PL Cassia pumila	+	

Hypotensive Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	78	SB Alstonia scholaris	+	
2	262	LF Rhododendron arboreum	+	
3	379	SD Argyreia -speciosa	+	
4	433	PX Cocculus pendulus	+	
5	387	PL Croton bonplandianum	+	
6	409	PX Hibiscus rosa-sinensis	+	
7	301	LF Kydia calycina	+	
8	584	SB Madhuca indica	+	
9	838	Ammania sengalensis	+	
10	623	Bridelia stipularis	+	
11	688	Chukrasia tabularis	+	
12	863	Cochlospermum religiosum	+	
13	602	Desmodium pulchellum	+	
14	876	Eriolaena hookeriana	+	
15	787	Kalanchoe integra	+	
16	814	Rhododendron nilagirica	+	
17	859	Zizyphus oenoplia	+	
18	1278	RT Coleus forskohlii	+	
19	1487	SB Miliosma pungens	+	
20	1339	PX Rhododendron falconeri	+	
21	1925	PX Aspidopterys indica	+	

Spasmolytic Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	150	PL Adiantum caudatum	+	
2	247	LF Actinodaphne angustifolia	+	
3	7	SB Myrica nagi	+	
4	274	PL Pyracantha crenulata	+	
5	379	SD Argyreia speciosa	+	
6	487	PL Pholidota articulata	+	

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7	973	SB Balanites aegyptiaca	+	
8	1371	PX Ancistrocladus heyneanus	+	
9	1278	RT Coleus forskohlii	+	
10	1642	PX Clausena pentaphylla	+	
11	1647	PL Hydrocotyle podontha	+	
12	1947	PX Acacia sundra	+	

Spasmogen Activity

1	32	ST Symplocos crataegoides	+	
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Cardiotonic Activity

1	57	PL Asclepias curassavica	+	
2	1049	PX Strophanthus wallichii	+	

Anti-Inflammatory Activity

1	684	Sagittaria sagittifolia	+	
2	1192	PL Hedychium spicatum	+	
3	1759	PX Cyathea gigantea	+	
4	1758	PX Cytherexylum subserratum	+	
5	1594	PX Dysoxylum binectariferum	+	
6	1739	PX Jambosa lacta	+	
7	1794	PL Sonchus brachyotus	+	
8	2011	PL Astragalus chlorostachys	+	
9	2044	PL Desmodium laxiflorum	+	
10	2038	PL Dioscorea pentaphylla	+	

Anti-Strychnine Activity

1	85	LF Leea Indica	+	
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Anti-Acetylcholinisne Activity

1	168	PL Siegesbeckia orientalis	+	
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EXPLORING THE HERBARIUM

Diuretic Activity

1	505	PL <i>Dryopteris crinipes</i>	+	
2	524	PL <i>Pavetta indica</i>	+	
3	521	PL <i>Vittadinia australis</i>	+	
4	1747	PX <i>Linociera malabarica</i>	+	
5	1763	PX <i>Pithecolobium bigeminum</i>	+	
6	1725	PL <i>Plantago lanceolata</i>	+	
7	1501	PL <i>Psychotria monticola</i>	+	
8	1723	PX <i>Saraca indica</i>	+	
9	2030	PX <i>Ficus elastica</i>	+	

From the academic point of view, one would be interested in the mode of action of these diuretics in the light of current knowledge of diuretic action.

From the practical point of view, one will have to consider what will be the particular advantages of these herbal diuretics in competition with the currently available diuretics like the benzthiazide etc.

Abortifacient Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	1768	PL <i>Acrostichum aureum</i>	+	
2	1581	PL <i>Perilla frutescens</i>	+	
3	1766	PL <i>Verbena bonariensis</i>	+	

Antibacterial Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	579	RT <i>Amebia nobilis</i>	+	
2	779	<i>Picea abies</i>	+	
3	1238	PX <i>Evodia lunu ankenda</i>	+	
4	1663	PX <i>Derris scandens</i>	+	

Antihistaminic Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	Activity low
1	32	ST <i>Symplocos crataegoides</i>	+	
2	1764	PL <i>Smithia conferta</i>	+	

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Spermicidal Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	low
1	1639	PL Aeschynomene indica	+	
2	1592	PX Ardisia neriifolia	+	
3	1573	PL Caltha palustris	+	
4	1679	PX Clerodendrum serratum	+	
5	1662	PX Samanea samar	+	
6	1684	PX Schefflera capitata	+	
7	1685	PX Symplocos gardneriana	+	
8	1703	SD Trigonela foenum-graecum	+	

Anti-Amphetamine Activity

Serial No.	CDRI Code No.	Plant	Activity confirmed	low
1	197	PL Fagonia cretica	+	
2	398	RH Alpinia galaega	+	
3	329	PL Conyza stricta	+	
4	351	LF Dillenia indica	+	
5	354	PX Mikania cordata	+	
6	749	Aesculus punduana	+	
7	689	Hiptage benghalensis	+	
8	1075	RH Colocasia fomicata	+	
9	933	PX Daphne papyracea	+	
10	1069	RH Ipomea paniculata	+	

Anti-Viral Activity

1	50	Pod Cassia fistula	+	
2	51	SB Cassia fistula	+	
3	208	PX Cassia auriculata	+	
4	621	Bridelia retusa	+	

Anti-Fungal Activity

1	579	RT Amelia nobilis	+	
2	1204	PX Hypericum mysorensense	+	

EXPLORING THE HERBARIUM

Neuromuscular Blockade Activity

1	340	RT <i>Cocculus laurifolius</i>	+	
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Semen Coagulant Activity

1	1620	SB <i>Albizzia odoratissima</i>	+	
2	1629	FR <i>Caesalpinia coriaria</i>	+	
3	1582	PX <i>Callitris robusta</i>	+	
4	1707	PX <i>Cassia javanica</i>	+	
5	1600	PX <i>Cupressus funebris</i>	+	
6	1748	PX <i>Diospyros insignis</i>	+	
7	1777	PX <i>Embelia viridiflora</i>	+	
8	1548	PX <i>Eriolaena quinquelocularis</i>	+	
9	1599	PX <i>Eucalyptus cloeziana</i>	+	
10	1612	PX <i>Garcinia indica</i>	+	
11	1651	SB <i>Grewia tiliaefolia</i>	+	
12	1737	PX <i>Humboldtia brunonis</i>	+	
13	1718	PX <i>Ixora coccinea</i>	+	
14	1518	PX <i>Leea aquata</i>	+	
15	1740	PX <i>Syzygium montanum</i>	+	
16	1795	PX <i>Tectaria cicutaria</i>	+	
17	1621	PX <i>Terminalia arjuna</i>	+	
18	1502	PX <i>Vaccinium pleschnaultti</i>	+	
19	1749	PX <i>Vateria indica</i>	+	
20	1771	PX <i>Vatica chinensis</i>	+	
21	1589	PX <i>Wendlandia wallichii</i>	+	

Hypertensive Activity

1	1871	PL <i>Cistanche tubulosa</i>	+	
2	1245	PX <i>Sophora glauca</i>	+	

Antifertility Activity

1	1822	PL <i>Lamium album</i>	+	
2	2055	PX <i>Moringa oleifera</i> (Hybrid)	+	

Anti-helminthic Activity

1	2036	TU <i>Momordica dioica</i>	+	
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EXPLORING THE HERBARIUM

Table I: Plant origin of drugs used in Modern medicine

Drug	Plant source	Clinical	Molecular Mechanism observation of action
Artemether	Qinshausu	Chloroquin resistant malaria	Heme-mediated decomposition of endoperoxide generating free radicals
Atropine	Atropa belladme	Antispasmodic	MAch receptors
Caffeine	Coffee arabica	Stimulant	Adenosine receptors
Cannabis indica	Indian Hemp	Sedation, antiemetic	Cannabinoid receptors CB1 CB2
Cocaine	Leaves of Coca	Addictive drug	Blocks DAT, NET, SERT
Colchicine	Colchicum autumnale	Relief of pain in gout	Inhibits release of leucocyte-derived chemotactic factors
Digitalis	Foxglove	Relief of dropsy	N ⁺ /K ⁺ ATPase
Emetine	Ipecacuana	Amoebtic dysentery	Inhibits protein synthesis in eukaryotic cells.
Ephedrinc	Ephedra	Bronchodilator	a,p adrenoreceptor agonist.
Eserine	Calabar beans	Pupil constriction	Reversible cholinesterase inhibitor
Morphine	Papavarum somniferum	Analgesic	Opioid receptors
Nicotine	Tobacco plant	Stimulant	Nicotinic Ach receptors
Quinine	Cinchona bark	Fever due to malaria	Inhibits haemozoin crystallization - aggregation of
Reserpine	Sarpagandha	Sedation Lower BP	cytotoxic heme Block VMAT, VMAT2
Salicylicacid	Salix alba Willow bark	Fever and pain relief	Cox inhibitor NF-κB i inhibitor
Strychnine	Nux vomica	Hyperexcitability convulsions	Blocks glycine receptors
Vincristine	Vinca rosae	Anti-cancer	Binds to tubulin disrupts microtubule assembly.

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NUTRITION - ANCIENT AND MODERN

Introduction

Mankind has always been interested in food. The practice of dietetics is an ancient, empirical and sometimes elegant art. It is only in the present Century that it has also become a science that tells us what nutrients we need, why we need them and from what foods they may be obtained.

Charaka says in praise of food: "The life of all living things is food and the entire world seeks food. Complexion, clarity, good voice, long life, understanding, happiness, satisfaction, growth, strength and intelligence are all established in food."

"Food is the foremost among those that sustain life; water among these that are refreshing agents; wine among acopies; milk among vitalizers; flesh among roborants; meat juice among demulcents; salt among appetisers; acid juices of fruits among cordials; the flesh of the cock or hen among promoters of strength".

"*Aharatattva*" or dietetics forms an important part of Ayurveda. *Charaka Samhita* describes in great detail the digestibility, nutritive value and medicinal value of hundreds of different palatable substances of various classes. It points out that all such substances can gain in nutritive value or become harmful by combination with other items, by cooking or preparation, and according to quantity taken, payability, appetite, bodily health, local climate, season and eating habits. A list of substances which are incompatible with each other, or unwholesome in particular seasons, is given.

"Wholesome" and "Unwholesome" Food

In *Charaka Samhita* one finds the following interesting dialogue: "What is the factor that promotes the growth of man?"

"The use of a wholesome diet is the only factor that promotes the healthy growth of man, and the factor that makes for disease is the indulgence in unwholesome diet"

"How shall we know unerringly the characteristics of both the wholesome and the unwholesome varieties of diet?"

"That class of foods, which helps the harmonised body elements to retain their state of equilibrium and the discordant body elements to gain equilibrium, is the wholesome one, and the unwholesome one to be that which acts in the

opposite manner. This definition of the wholesome and the unwholesome will be found to be infallible”.

“Food is all of one kind, eatability being the common feature. But it is of two kinds as regards its sources, one is inanimate and the other animate; it is also two-fold in respect of its effects, being either wholesome or unwholesome”.

Thanks to the tremendous advances in physiology and biochemistry, the Twentieth Century Science of Nutrition has been able to elaborate in great detail the “wholesome” and “unwholesome” aspects of diet, as we shall see in this chapter.

Energy Requirements

Charaka states: “Even light, easily digested and nutritious food should not be taken in excess of bodily requirements, or after the appetite has been satisfied. Food difficult to digest should not be taken habitually. If ever used, the quantity should not exceed a fraction of a full meal”.

What constitutes excess over the normal body requirements as indicated by Charaka? How to assess normal body requirements of food? The science of Nutrition has been able to tackle these questions and provide useful answers, although some nutritionists think we still do not know what optimum nutrition is.

Antoine Lavoisier (1743 -1793) proved that there existed a close similarity between breathing of air by the human body and the combustion of a substance in air. In both, the oxygen in the air was consumed, being replaced by carbon-dioxide. He further observed that a man at work consumes more oxygen than the one at rest. It thus became known that the food we eat is somehow transferred into energy and heat inside the body.

Animals including man get their energy from their food in a chemical form, in the form of carbohydrates, fats and proteins. The energy is liberated and utilised for the performance of mechanical work, for maintaining the metabolic activity of liver, kidneys, brain and the other organs, for maintaining the body temperature and for promoting growth by synthesis of new chemical substances rich in energy.

The unit of energy is the joule (J) and is the energy expended when 1 kilogram (kg) is moved 1 metre (m) by a force of 1 newton (N). Physiologists and nutritionists are concerned with large amounts of energy and the convenient units are the kilojoule (KJ or 1000joules) and the mega joule (MJ or million joules). Formerly energy was always expressed quantitatively in units of heat, the unit being the kilo calorie, defined as the amount of heat required to

raise the temperature of a litre of water from 15°C to 16°C. Conversion of Calories to joules is made by multiplying by 4.186, or roughly by 4.2.

The total energy expenditure is quantitatively related to the oxygen consumption. The measurement of oxygen consumption in man has been made with many different types of apparatus. The Benedict Roth apparatus is very simple to use and gives a direct reading of the oxygen consumption without the necessity of gas analysis. For measurement of energy expenditure during everyday activities of living, and during industrial work, the Max Planck respirometer is extremely useful. Many thousands of measurements of energy expenditure of men and women undertaking a great variety of activities have been made.

When a subject is at complete rest and no physical work is being carried out, energy is required for the activity of the internal organs and to maintain body temperature as already mentioned. This energy is called the *basal metabolic rate*, or BMR; it is expressed in KJ/ Kg of body weight. Animals as diverse as man, mouse, dog and horse have very different BMRs. But if expressed in KJ/M²/hour (Surface area of the body) the figures for each species are remarkably similar. A nomogram is available to predict surface area from measurements of height and weight.

There are wide variations in the energy requirements of individuals, even of those following the same occupation and apparently leading similar kinds of lives. But when food is freely available, a healthy individual instinctively assesses his own energy needs with remarkable precision. The energy requirements of individuals are dependent upon four variables viz. physical activity, body size and composition, age and climate. There are also extra needs for growth in childhood and adolescence, and for pregnancy and lactation.

Recommended Daily Allowance

One of the earliest and best known attempts to make recommendations regarding nutritional needs of populations was made under the auspices of the League of Nations. This report was published in 1936 and influenced the thinking of nutrition workers throughout the world. The recommended dietary allowances for calories for Indians, made by the Indian Council of Medical Research are given in Table I, according to the type of work.

**TABLE I:
Recommended Allowances for Calories per day (ICMR)**

Man (55 kg)	
Sedentary work	2400
Moderate work	2800
Heavy work	3900

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Woman (45 kg)	
Sedentary work	1900
Moderate work	2200
Heavy work	3000
Pregnancy (later half)	+ 300
Lactation	+ 500
Children	
Under 1 year (0-6 m)	120 / kg.
(7-12 m)	100 / kg.
1-3 years	1200
4-6 years	1500
7-9 years	1800
10-12 years	2100
Girls:	
13 - 15 years	2200
16-19 years	2200
Boys:	
13 - 15 years	2500
16-19 years	3000

Sedentary work: This category includes clerks, teachers, journalists, doctors, lawyers, shop-keepers, architects, drivers and pilots.

Moderate work: This category includes light industry and assembly plants, railway workers, postmen, plumbers, bus conductors, farm workers and builders' labourers.

Heavy work: This category includes coal miners, steel workers, dock workers, foresters and army recruits.

A simple common sense guide for the adequacy of a given Calorie allowance is to watch the weight over a period of weeks. Steady weight in an adult would indicate adequacy, loss of weight would indicate deficit, and gain in weight would indicate surplus of calories over needs. If one overeats to a very slight extent of 0.05 percent, he will acquire a modest middle-age spread amounting to some 28 pounds of weight. The gain in weight, though usual, is not healthy.

Self-regulation of feeding

A good example of the "wisdom of the body" in self-regulation of food intake was provided in 1969 by Ashworth. He provided unlimited food for eight children who were markedly underweight. At first their intakes were very large, about 670 KJ (160 KCal/kg/-day). However, when they had reached the normal

weight for their height, they began to refuse food and reduce their intakes to 485 KJ (116 KCal/kg/day) sufficient to meet the normal requirements of growing children.

Feeding is controlled by situated in the hypothalamus, which is that small area of the brain lying beneath the main bulk of the cerebrum. If in rats the two ventro-medial nuclei of the hypothalamus (VMH) are destroyed by stereotaxic techniques using fine needles, the animal begins to eat voraciously and becomes obese in a few weeks. This can be attributed to the loss of a "*Satiety Centre*". On the other hand, if the two ventro-lateral hypothalamic nuclei (VLH) are destroyed, the animal refuses to eat, though otherwise normal; unless fed forcibly it will die of starvation; this can be attributed to the loss of a "*Feeding Centre*". Several regulatory processes have been proposed as modulators of these hypothalamic. Meal-induced gastric distension, level of insulin, total adipose tissue mass, may all influence the activity of the hypothalamic centre. Additionally the hypothalamic are sensitive to catecholamines; and beta-adrenergic stimulation inhibits eating behaviour. This provides at least one rationale for the appetite-suppressing effects of amphetamines.

Ultimately the cerebral cortex controls eating behaviour and impulses from the feeding centre to the cerebral cortex are only one input. Psychological, social and genetic factors also influence food intake.

Changing Energy Requirements

Until 200 years ago, up to the Industrial Revolution, human muscles, supplemented by those of oxen and horses, mules and donkeys, provided the power that made civilization possible. Muscles did the work of the field, thrashed and ground the corn, built the great temples and palaces, transported men and their armies, and spun and wove the fabrics for clothing and tapestries. In the modern industrial societies all this has changed. With a flick of a switch now one can harness great power. There is little need now to use muscles for anything but the lightest activity. Hard labour, walking, running and bicycling are becoming more and more unnecessary due to increasing mechanisation, motorisation and automation. Evidently, *homo sapiens*, having become *homo sedentericus*, is paying the price for the change. Degenerative diseases including heart failure in middle age are more common in sedentary persons than in active ones. The importance of regular physical exercise has therefore become all the more crucial, in the maintenance of health today, than ever before. (See chapter 14: "Exercise in Health & Disease")

Modern Concept of "Proper Nutrition"

The body contains many thousands of species of organic molecules but requires for health the intake of only 23 *organic compounds*, in addition to a

source of energy and water: nine essential amino-acids, one essential fatty acid and 13 vitamins or accessory food factors. The vast majority of organic molecules in food, although metabolized or assimilated by the body, are non-essential in the sense that their deletion from the diet does not cause illness. The simplicity of nutritional requirements of the healthy subjects compared with the complexity of the chemical composition of the body is the result of the remarkable capacity for endogenous biosynthesis (see the chapter on "The Chemistry of Life").

Of the limited number of *inorganic compounds* in food, the majority of their constituent elements, which are 15 in number, are considered to be nutritionally essential; these are calcium, phosphorus, iodine, iron, copper, cobalt, zinc, magnesium, potassium, sodium, chloride, chromium, manganese, molybdenum and selenium.

The symptoms and manifestations of nutritional deficiency are now well recognized. The requirement of an essential nutrient is the smallest quantity that maintains normal mass, chemical composition, morphology and physiological functions of the body and prevents any clinical or biochemical signs of corresponding deficiency state. In children, an additional criterion is a normal rate of growth.

Minerals

Ayurveda describes various kinds of salts and several kinds of minerals for use in human diet and therapeutics. These are described in Table II.

**TABLE II:
Salts and Minerals in Ayurveda**

Salts

1. Samudraka (Sea salt)
2. Baluka (Salt from saline sands)
3. Romaka, Pamsuja (Salt from saline soils or clay)
4. Maulaka (Black salt)
5. Udbhida (Fossil salt)
6. Saindhava (Salt from ashes of marine plants)
7. Agrya lavana (Rock salt)
8. Sauvarchala (Salt obtained by boiling alkali with myrobalan)
9. Anupalavana (Salt obtained by evaporating well water)

Mixture of salts

1. Dvi lavana (mixture of rock salt with alkaline salt)
2. Lavana traya (mixture of three salts)
3. Lavana chatvari (mixture of four salts)
4. Lavana panchaka (mixture of five salts)

Minerals/Metals

1. Ayas, Mandura, Loha (Iron)
2. Tamra (Copper)
3. Gandhaka (Sulphur)
4. Trapu (Tin)
5. Mrt (Clay)
6. Istaka Churna (Brick powder)
7. Adrijatu, Shilajatu (exudate from ores)
8. Sarvaloha (tin, lead, iron, copper and silver)
9. Hema (Gold)

Mankind has used salt since antiquity. The first known salt mines have been found in the Austrian Tyrol and date from the late Bronze Age, about 1000 B.C. For at least 3000 years sodium chloride or common salt has played an amazingly important part in the lives of men. Wars have been fought over its sources and for centuries its trade was more important than that of any other material; this was because salt was the best preservative available.

A full account of the symptoms and signs of salt deficiency based on experimental depletion was given by Me Cance in 1936, using himself and his pupil as subjects. The characteristic symptom is muscular cramp, which is well known to miners who work in hot pits, thereby losing a lot of salt through their sweat. Other symptoms are loss of appetite and vomiting, and mental apathy. Similar experimental depletion of many other elements has been studied in man, and animals.

The theory that man is descended from some remote marine ancestor is expressed in the Sanskrit description "*Amrutasya Putra*", "son of the sea". It is consistent with the fact that his extra-cellular fluid has definite similarities in mineral composition to that of the sea as it was likely to have been many millions of years ago. Sea water contains measurable quantities of chloride, sodium, magnesium, calcium, sulphur, nitrogen, potassium, carbon, iodine and iron. It also contains traces of phosphorus, although the greater part of this element is taken up immediately by plankton, the floating organisms of the sea, and incorporated into their organic structure. All of these elements contribute to the nutrition of the human body. The knowledge about the importance of trace elements is very recent.

Many carcasses of small animals have been analysed chemically, but the results do not necessarily apply to man. A complete chemical analysis of the human cadaver is a formidable task which has been carried out on a number of occasions, but not sufficiently often to give the range of variations in people of different age and sex (Widdowson et al., 1951).

Twentieth Century Science & Technology have given us a new tool for the study of trace elements, which is most sensitive and most accurate. As many as

70 elements can be measured in the range of 10^6 to 10^{12} g by the method of *neutron activation analysis*.

The principles on which activation analysis is based are fundamental to the physical basis of nuclear medicine. In a typical analysis, the sample to be analysed is exposed to an intense beam of neutrons which interact with the nuclei of the atoms in the sample to produce radioactive and stable isotopes. Each radioactive isotope is uniquely characterized by its rate of decay and the type of radiations emitted; therefore positive identification and quantitative measurement of the radionuclide is possible. The amount of an element in a sample can be determined directly from the radioactive measurement because the induced radioactivity is directly proportional to the number of the atoms of the stable isotope in the original sample and to the neutron flux that interacts with the stable nuclei.

The role of trace elements in biology has been recently appreciated. Deficiency diseases can be caused by a lack of essential trace elements, and high dietary concentrations can be toxic.

It is worth knowing why the 15 elements considered to be essential for nutrition, are so important. *Calcium* is the most abundant mineral in the body. It makes up about 1.5 to 2 percent of body weight and 39 percent of the total mineral content. In addition to the major function of calcium to build and maintain bones and teeth, the remaining 1 percent of the body's calcium is found in the body fluids and soft tissues. Ionic calcium is essential for the activity of certain enzymes, notably ATPase in the release of energy for muscle contraction and for the activity of c AMP. In the blood clotting process, calcium must be present to initiate the changes needed for the formation of the clot, fibrin. Calcium affects the transport function of cell membranes, possibly acting as a membrane stabilizer.

Calcium also influences transmission of ions across membranes of cell organelles, the release of neurotransmitters at synaptic junctions, the synthesis, secretion and metabolic effects of protein hormones and the release or activation of intracellular and extracellular enzymes. There are minute amounts of calcium in the cytosol; it is found in mitochondria and endoplasmic reticulum as a phosphate salt.

Calcium is required in nerve transmission and regulation of heart beat. The proper balance of calcium, sodium, potassium and magnesium ions maintains muscle tone and controls irritability.

Phosphorus is one of the most essential elements, second to calcium in abundance, comprising 22 percent of the total body mineral content. In addition to its structural role, phosphorus has numerous functions more

than any other mineral element. Phosphorus is an essential component of nucleic acids; and phospholipids are key components in the structure of cell membranes. Glucose is phosphorylated as the first step in its utilization and at other steps. High energy phosphate compounds play a central role in many reactions, as does cyclic AMP. Phosphorus is part of some conjugated proteins, for example milk casein. Many of the B vitamins function as coenzymes only when in combination with the phosphate. The phosphate buffer system is important particularly in intracellular fluid, where its concentration is much higher than in extracellular fluid, and in the tubular fluids of the kidney.

Sulphur occurs principally as a constituent of the amino-acids cystine, cysteine and methionine. It is present in all proteins but is most prevalent in the keratin of the skin and hair (4 to 6 percent sulphur) and in insulin (3.2 percent sulphur). Glutathione, a tripeptide containing cysteine, is important in cellular reactions involving the sulphur amino-acids in protein. Sulphur exists in a reduced form (-SH) in cysteine and in an oxidised form (-S-S-) as the double molecule, in cystine. This is important in the specific configuration of some proteins and in the activity of some enzymes. Sulphur also occurs in carbohydrates such as heparin, and chondroitin sulphate in bone and cartilage. Two vitamins, thiamine and biotin contain sulphur. The poisonous effects of many heavy metals (arsenic, mercury, lead) are due to their ability to combine, with sulphhydryl groups.

Magnesium is essential for the production and transfer of energy for protein synthesis, for contractility of muscle and excitability in nerves. It is an essential co-factor in numerous enzyme systems related to other functions. Magnesium and calcium, having similar functions, may antagonise each other. An excess amount of magnesium will inhibit bone calcification. In normal muscle contraction, calcium acts as a stimulator and magnesium as a relaxer. An excessive amount of calcium may induce signs typical of magnesium deficiency.

Iron plays a crucial role in the transport of oxygen from the lungs to the tissues, in the transport of CO₂ away from the tissues to the lungs, and in the process of cellular respiration. Haemoglobin, myoglobin and the cytochromes are the iron-containing proteins and enzymes mediating oxygen transport. There is evidence from animal studies that in dietary iron deficiency the concentration of the respiratory cytochrome enzymes may drop before the haemoglobin level in the blood drops. Iron may play a role in the conversion of beta-carotene to Vitamin A, the synthesis of purines, the clearance of blood lipids and the detoxification of drugs in the liver. Lactoferritin in breast milk is an iron-containing protein effective against *E. coli* of the gastrointestinal tract of infants.

Fluorine is mainly important in relation to protection of tooth enamel against caries, but it seems to be an essential trace element in animal feeding

experiments. The skeleton of the average man contains 2.6 gm. of fluorine. The fluoride content of food varies according to the content of the soil in which it is grown. In certain parts of India the water sometimes contains 10-45 ppm (parts per million parts). Over a period of years it produces excessive fluoride deposition in bones and consequent pressure effects on the nerves and the spinal cord. The disease is called fluorosis.

Zinc plays a role in a number of metabolic activities. There are 70 or more metallo-enzymes that require zinc to function. These include carbonic anhydrase, alkaline phosphatase, lactic dehydrogenase and carboxy peptidase. Zinc functions by maintaining spatial and configurational relationships necessary for enzyme action. In this role it helps to bind enzymes to substrates and may modify the molecular shape of enzymes by simultaneously combining with amino-acids at different places on the protein, thus affecting secondary, tertiary and quaternary protein structure. A number of zinc metallo-enzymes are involved in the regulation of cellular growth.

In addition to its function in enzymes, zinc participates in the metabolism of nucleic acids and the synthesis of proteins. Zinc may also have an important role in cell division since zinc deficiency causes adverse effects on the incorporation of labelled thymidine into the DNA of rats. Zinc is required for DNA synthesis, and the DNA-dependent RNA polymerase is a zinc dependent enzyme; so is thymidine kinase. Zinc is essential for wound healing, for defence against infection especially of the skin surface. Zinc deficiency causes ageusia, loss of hair, night blindness and a skin rash, often associated with the staphylococcal and yeast infection which respond only to zinc supplementation.

Sodium Chloride: Sodium, chloride and potassium are so intimately related in the body that it is most convenient to discuss them together. Sodium constitutes 2 percent, potassium 5 percent and chlorine 3 percent of the total body mineral content. They are distributed throughout the body fluids and tissues, but sodium chloride is primarily extracellular while potassium is mainly an intra-cellular element. All three are involved in at least four important physiological functions of the body, namely water balance, osmotic equilibrium, acid-base balance and normal neuro-muscular irritability. Hormonal control of sodium, potassium and chloride is mediated through the adrenal cortical hormones. Adrenal cortical insufficiency or certain conditions such as marked vomiting and diarrhoea, burns, prolonged diuretic therapy will result in "low salt syndrome".

Potassium, apart from playing an important role in the maintenance of water balance, osmotic equilibrium and acid base balance, is also important along with calcium in the regulation of neuro-muscular activity. Potassium

level in the muscle is related to muscle mass; therefore if muscle is being formed, an adequate supply of potassium is essential. The same applies to glycogen storage. Very low serum levels (less than 2mEq/L) of potassium lead to sudden cardiac death, while very high serum levels (over 8mEq/L) can lead to death by cardiac asystole.

Iodine is unique among the essential mineral elements in that it is an essential component of specific thyroid hormones. The adult human body normally contains 20 - 50 mg. of iodine of which 8 mg. is concentrated in the thyroid. In Himalayan and other mountainous regions of India and the rest of the world, the deficiency of iodine leads to goitre; such gland contains less than 1 mg. of iodine. Addition of sodium iodide to the common salt sodium chloride (in a proportion of 1 part to 50,000 parts) has beneficial consequences. Sea-food (fish) is an excellent source of iodine.

Cobalt is unique in that it must be supplied entirely in its physiologically active form, cyanocobalamin or hydroxycobalamin (vitamin B12), which contains 4 percent cobalt, and is the only cobalt-containing compound present in the body.

Chromium in the form of a low molecular weight organic complex, glucose tolerance factor (GTF), is required for normal glucose metabolism in several animal species including man. Deficiency of chromium leads to glucose intolerance and neuropathy in patients receiving long-term total parenteral nutrition, which is reversed by chromium supplementation.

Copper is a component of many enzymes including Cytochrome C oxidase and is important in cardiovascular and skeletal integrity, central nervous system structure and function, and erythropoietic function.

Selenium is an important constituent of glutathione peroxidase in erythrocytes; this enzyme protects against excessive accumulation of hydrogen peroxide. Deficiency of selenium has been associated with congestive cardiomyopathy and possibly muscle disease, in China.

Manganese activates a host of critical intracellular enzymes. Deficiency Syndrome in man has been described (weight loss, change in hair colour and slow growth of hair). Manganese toxicity in miners leads to a picture similar to Parkinson's Disease & Wilson's Disease.

Protein — Energy — Malnutrition

In a child deprived of food, growth stops almost immediately because of the high requirement of energy necessary to build protein. A child who has suffered undernourishment very early and for an appreciable length of time will never reach normal size for his age even though he is later fed well enough to

restore a normal rate of growth. This is part of the reason for the small body size of many people in impoverished countries. The first year of life or the pre-weaning period is particularly critical for the brain is still growing and developing during this time. In experimental studies on rats and in analysis of the brains of children who had died of marasmus (emaciation due to energy deprivation), the underfed brain had a subnormal content of DNA. Starvation had interfered with cell division and left the animal or child with a permanent deficit in the number of cells in the brain. When the mother was underfed during pregnancy, in the rat experiments, malnutrition of the offspring after birth had an even more devastating effect on the brain.

Unfortunately, millions of Indian children are victims of protein energy malnutrition. "Kwashiorkor", was first described by Dr. Cecile Williams in 1933 in Ghana. The meaning of the word given to her by the Ga tribesmen was "the sickness the older child gets when the next baby is born". The typical clinical signs are apathy, loss of appetite, edema and changes in the skin and hair. On close examination of the blood and other tissues there is a marked drop in the concentration and activity of key enzymes, which are themselves proteins.

Nearly half the world's population is underfed or otherwise malnourished. The lives of the people in the developing world are dominated by the scramble for food to stay alive. Such people are perpetually tired, weak and vulnerable to disease. Because their undernourishment begins soon after birth, it produces permanently depressing and irremedial effects on the population as a whole.

Importance of Breast Milk

Ayurveda stresses the importance of breast milk for infant feeding. *Kashyapa Samhita* (which deals with Pediatrics) defines "pure breast milk as that with which the baby thrives well and both the mother and baby remain happy, healthy and free from any ailment. Breast milk promotes growth and development, and acts as a tonic for all tissues. It increases the body resistance to various diseases. It promotes healing of wounds".

"Love and affection for the baby are essential for the secretion of breast milk. Hence looking at, handling, carrying the baby or even remembering the baby promotes secretion of milk. Happy state of mind and adequate rest and sleep are important for increasing breast milk supply. The mother should take plenty of milk, meat, ghee and oil and plenty of fluids to help increase the quantity of milk".

"Absence of maternal instinct, or fear, anger, sorrow and grief suppress the secretion of breast milk. Starvation, fasting, or inadequate diet, exertion and fatigue suppress the breast milk".

"If the mother does not have enough breast milk or if she is sick or her milk is grossly vitiated, it is better to employ a "Dhatri" or wet-nurse as no other

milk can compete with human milk. The wet-nurse should belong to a good family, should be healthy, well built and good complexioned; she should take regular well-balanced diet and should not be suffering from any disease. Her breasts should be well-developed and nipples well-formed and protruding". Vagbhata suggests that "it is better to employ two wet-nurses so that they can feed their own babies adequately. However, it is important not to have more wet-nurses as the mixture of milk with different qualities can upset the baby".

A wide variety of medicines have been prescribed in Ayurveda for "purification of breast milk". Ayurveda also gives details of the qualities of cows' milk, also milk from goats, buffaloes, asses, horses, sheep, camel and elephants. Supplementary feeds are recommended at the age of 6 months when the infant cuts its teeth. Even if the infant does not cut its teeth, the supplementary feeds must be started by the age of 10 months.

The current enthusiasm in the western world about the breast feeding of babies is "rediscovering the wheel" so far as the Indian mothers are concerned.

Nutritional Needs for Lactation

The period of lactation is a time of even greater nutritional stress for the mother than that of pregnancy. It is estimated that 1000 food calories are required to produce 600 calories of human milk. The fact that many Indian mothers in low-income groups have been observed to lose weight while nursing a baby indicates clearly that their calorie and possibly their protein need is not adequately met. Mothers with deficient diets produce milk with low vitamin and mineral content. Table III compares the vitamin content of human milks from different countries.

TABLE III
Comparison of Vitamin Content of Milk

Country	Vitamin A IU/100 ml	Riboflavin mg/100 ml	Vitamin C mg/100 ml
India (Low socio-economic level)	70	17	2.6
Great Britain (Low nutritional intake)	153	26	3.2 to 4
USA (Superior nutrition)	180	47	4.4

The calcium and phosphorus in milk are supplied from the mother's diet or withdrawn from her bones. It is not surprising that women losing 300 mg. of calcium per day in milk and consuming low calcium diets for a succession of pregnancies suffer severe calcium deficiency. This has been most frequently observed in regions where there is lack of vitamin D. In overcrowded, congested areas in Bombay where Muslim women observe purdah and live indoors, there is no opportunity to absorb the ultraviolet rays of the sunlight to produce calciferol in

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the skin. Hence it is comparatively common to find osteomalacia associated with pregnancy and lactation.

Dr. Gopalan at the National Institute of Nutrition, Hyderabad, has pointed out that in spite of their inadequate diets poor Indian mothers are able to breast-feed their infants successfully over long periods. Many produce from 400 to 600 grams of milk daily for periods extending over a year. The concentrations of calcium and iron in their milk samples were comparable to the normal range, although the mothers had poor calcium intake and were anaemic. Through this adaptive mechanism nature protects the baby at the cost of the mother.

In India, the high maternal mortality rate is influenced by the prevalence of iron-deficiency anaemia. Fetal iron stores are influenced by the mother's iron nutrition, during pregnancy. The normal full-term infant born of a non-anaemic mother usually possesses adequate iron store so that little is needed for several months. This is important because breast milk does not contain much iron. The high incidence of anaemia in many groups of Indian infants under six months suggests low iron storage before birth, because the mother's diet was lacking in iron. Experiments with radioactive iron indicate that the transfer of iron from the mother to the baby is most pronounced in the last 10 weeks of pregnancy. This explains the wide prevalence of severe anaemia in the later months of pregnancy. The iron deficiency can be very effectively treated by the use of medicinal iron.

Recognition of the nutritional needs of pregnancy are indicated in the difference between the recommended daily allowance for the nonpregnant women. The ICMR recommendations (1968) are shown in the Table IV below:

TABLE IV

Condition	Calories	Proteins grams	Calcium grams	Vit. A I.U.	Riboflavin mg.	Thiamine mg.	Niacin mg.	
Non-Pregnant	1900	45	0.4-0.5	3000	1.0	1.0	13	(sedentary work)
Pregnant (last-half)	2200	55	1.0	3000	1.2	1.2	15	
Lactating mother	2600	65	1.0	4600	1.4	1.4	18	

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CONCEPT OF HARMFUL FOODS

In Ayurveda there are descriptions of combinations of foods which are to be avoided. Some examples:

“Fish should not be eaten in conjunction with milk; one is cold, the other is hot. Being thus incompatible they tend to vitiate the blood and tend to cause obstruction of the channels”.

Modern science of nutrition does *not* validate this belief. It is difficult to differentiate facts from fancy because in all societies many superstitions and food fads have existed since time immemorial. Some examples:

“The flesh of domesticated wet, land or aquatic creatures should not be eaten in conjunction with honey, til, gur, milk, black gram, garden radish, lotus stalks or sprouted grains.

There is a long list of foods containing pharmacological or toxic agents known to have an adverse effect on human health, for which scientific explanation is available.

A monograph prepared by the Food Protection Committee (1966) of the U.S. Food and Nutrition Board, and another by Liener (1969), contain much curious information, and both are very readable.

Nature of “Harmful Foods

Foods which contain all of the important nutrients needed by the body may yet not be safe to eat. This may be true for a variety of reasons.

“It is on account of such mixed diet that one develops deafness, blindness, tremors, idiocy, indistinctness of speech, nasal articulation, or comes by one’s death”.

“Jatuka-Shaka and ripe nikucha must not be eaten with honey or milk. Such practice brings about death or the loss of strength, complexion, radiance, virility and potency”.

One wonders what could have been the basis for these statements. What is the modern counterpart of “harmful” foods?

Wholesome foods are sometimes adulterated by the addition of harmful substances and thus become unsafe. Substances used to destroy insects or pests may be present in food and may make it harmful. The food

may contain harmful micro-organisms or their products. Food-borne infection is a reflection of poor hygiene. In India, salmonellosis including typhoid fever, amoebic and bacillary dysentery, abdominal tuberculosis and brucellosis are common problems spread by contaminated food and water. Animal parasites (Trichinosis, flukes, tapeworms, roundworms) are also conveyed by foods.

Some of the most potent toxins are found in fungi which may contain otherwise healthy foods. *Ergot* is a fungus infesting rye, and outbreaks of ergotism have occurred in times of food scarcity. *Aflatoxins* can contaminate many human foods like groundnuts. Aflatoxins damage the liver and lead to cancer in many animals e.g. monkeys. Their role in human cirrhosis and liver cancer is conjectured. Some discussion of dietary carcinogens would be appropriate at this point.

Dietary Carcinogens

Dr. Bruce Ames has reviewed in 1983 (*Science*, issue of 23rd September) the increasing body of evidence that large numbers of potent carcinogens arise from natural processes. Mutagens are present in substantial quantities in fruits and vegetables. Carcinogens are found in cooking as a result of reactions involving proteins or fats. A variety of hydroperoxides, enals, epioxides and other reactive chemicals are produced by rancid fats, and rancid meat. Dietary practices may be an important determinant of current cancer risks.

Carcinogens and mutagens are present in mould-contaminated foods such as corn, nuts, peanut butter, bread, cheese and fruit. Some of these contaminants, such as aflatoxin are among the most potent known carcinogens and mutagens. Nitrosamines and nitroso compounds are suspect as causative agents of stomach and esophageal cancer in humans. In the digestive system these nitrogen compounds are formed from nitrate and nitrite. Beets, celery, lettuce, spinach, radishes and rhubarb all contain about 200 milligrams of nitrate per 100 grams portion.

Rancid fats are possible causative agents of colon and breast cancer in humans. However, there are no direct estimates of the amounts of oxidized fats ingested by humans, and the unpalatable nature of rancid fats precludes their ingestion in significant quantities. Burnt and browned materials formed by heating proteins during cooking are highly mutagenic. Chemicals isolated from such products have been found to be carcinogenic when fed to rodents. In addition, the browning reaction products from caramelization of sugars or the reaction of amino-acids and sugars during cooking contain a large variety of DNA-damaging agents.

Epidemiologists have noted marked differences in cancer rates between population groups. The general indication is that an increase in

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consumption of fibre-rich cereals, vegetables and fruits, and decrease in consumption of fat-rich products and excessive alcohol, would be prudent.

Fortunately we have in our diet many defence mechanisms to protect ourselves against mutagens and carcinogens. For instance tocopherol (Vitamin E) has protective effects against radiation-induced DNA damage and mutation, and dimethyl hydrazine induced carcinogenesis. *Beta carotene* is another antioxidant in the diet that could be important in protecting body fat and lipid membranes against oxidation. Carotinoids are free-radical traps and remarkably efficient quenchers of singlet oxygen (a very reactive form of oxygen which is mutagenic). However, a recent large scale case control study produced no evidence "relating intake or serum levels of anti-oxidant vitamins to a reduced cancer risk". A low-fat high-fibre diet not only decreases intake of fat soluble synthetic carcinogenic contaminants but also reduces the risk of cardiovascular disease and of diverticulitis.

Mustard Oil

In Bengal and Bihar mustard oil is the chief cooking fat. In many episodes of epidemic dropsy, the clues were analysed in the best detective manner by Lai and Roy and other workers, who showed that mustard oil was responsible for this disease. The toxin was not present in the oil from the mustard seeds themselves, but in oil from seeds of a poppy weed (*argemone mexicana*) which commonly grows in the mustard crops. The Argemone seeds contain an alkaloid sanguinarine which is toxic. *Sanguinarine* inhibits the oxidation of pyruvic acid, and as in wet beriberi, pyruvic acid may accumulate in the blood of patients suffering from epidemic dropsy. The anaemia which is common in these patients has the features of a pyridoxine responsive anaemia (Lele and Krishnaswamy, 1979).

Lathyrism

Hippocrates had noted that "At Ainos those men and women, who continually fed on pulses, were attacked by a weakness of the legs which remained permanent". As we recognize today, the description fits the condition of lathyrism which results from excessive consumption of *Lathyrus Sativus*. The condition has been seen in some parts of India. An excellent account of the ravages of this ancient disease can be found in "Rambles and Recollections of an Indian Official" published in 1844 by a British soldier, General Sleeman. "During three successive years 1829-1831 the wheat crop was destroyed by severe hailstorm, lack of rain and blight. During that period the "teori" or "Kesari", a kind of wild vetch, which though not sown itself but is left to grow carelessly among the wheat and other grain, and given in the green and dry state to cattle, remained uninjured and thrived with great luxuriance. The villagers ate this, and in 1833 the sad effects began to manifest themselves. The younger population of

this and surrounding villages, from the age 30 downwards began to be deprived of the use of their limbs below the waist, in all cases sudden, but in some cases more severe than in others. About half the youth of both sexes became affected during 1833 and 1834 and many of them lost the use of their lower limbs entirely”.

In some parts of India 4 percent of the rural population even today is affected by lathyrism. Kesari dal has been deliberately sown along with wheat by farmers particularly in Madhya Pradesh, as a drought-resistant crop. If the rains are good, the wheat outgrows the lathyrus, of which little is harvested. If the rain fails and there is a poor crop of wheat, a useful harvest of lathyrus may be reaped and consumed for subsistence. A poor monsoon is generally followed by an epidemic of lathyrism. All individuals who obtain more than a quarter of their caloric intake from *Lathyrus sativus* are liable to get lathyrism.

A neurotoxin has been isolated from the seeds of *Lathyrus sativus*, known as BOA A (B-N-Oxalyl-amino-L-alanine). On analysis at the National Institute of Nutrition in Hyderabad, this substance has been found in samples of seeds in amounts up to 2 gm per 100 gm.

The relation between intake of BOA A and the clinical features of lathyrism has not been worked out. Other neurotoxins have been isolated from seeds of the common Vetch (*vicia sativa*) which frequently grows as a weed in lathyrus crops.

Concept of Lethal Synthesis

Peters in 1963 coined the term “lethal synthesis” when he discovered that the *Jhoracatv* of a plant that poisons cattle in the Transvaal region of South Africa, makes use of the enzymatic machinery of the body to convert itself by synthesis into a very toxic *fluorocitric acid*. According to Peters a similar mechanism might be operating in lathyrism. “The example of lathyrism is so striking that it may prove to be a key problem whose solution may lead to other things.”

Concept of Deficiency Disorders

Five major diseases, scurvy, beri-beri, keratomalacia, pellagra and rickets arise as a result of *deficiency* of certain specific essential chemical factors. In the writings of Hippocrates or in Ayurveda one does not find the clear concept of a specific deficiency disorder.

Undoubtedly there was a lot of *intuitive wisdom in folklore* regarding the causation and prevention of these disorders, but it took mankind a long, long time to understand the basis of this intuitive wisdom. The story of scurvy is of great educational interest.

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Scurvy was not clearly recognized by the Greek, Roman or mediaeval physicians. There is no word for it in Ayurveda although one might conjecture that some haemorrhagic manifestations described were due to scurvy. In the 15th Century enterprising Europeans undertook long sea voyages. In 1497 Vasco de Gama sailed round the Cape of Good Hope to reach Calicut on the Malabar Coast in South India. Scurvy broke out among his crew, killing 100 out of his 160 men. For the next three hundred years scurvy was a major factor determining the success or failure of all sea voyages, undertaken for trade, exploration or war. As early as 1535 the French explorer Jaques Cartier, whose crew was severely affected by scurvy in Newfoundland had noted that the local Canadian Indians knew that the juice of the leaves of a certain tree had remarkable anti-scorbutic properties. Similar value of a decoction of spruce or pine needles was well known to the Swedes at least as early as the 16th Century.

The first controlled therapeutic trial ever undertaken was in relation to scurvy. James Lind, a Scottish Naval Surgeon in 1747 showed "the most sudden and visible good effects from the use of oranges and lemons in two scorbutic sailors who received them, while there was no change whatsoever in ten other scorbutic sailors who had identical clinical condition but did not receive them." Lind published in 1753, "A Treatise of the Scurvy". This information was successfully utilised by Captain James Cook during his long voyage round the world from 1772 to 1775. He took great care to replenish his supplies of fruits and vegetables whenever he touched land, with the result that there was not a single case of scurvy in his crew. The effect of Lind's study on state policy was delayed by some forty years. It was not until 1795 that the British Royal Navy enforced the practice of supplying oranges and lemons to the crew. The disease, however, continued to linger for a further 50 years in the merchant navies of the world. In South Africa from 1898 onwards, serious outbreaks of scurvy occurred in people working in the gold mines, and by 1902 it was stated that the number of cases of Scurvy exceeded that of accidents. Although a recommendation for a supply of fresh vegetables and lime juice for the miners was made by a knowledgeable doctor, it took the Government there another 22 years to issue a minimum ration scale for miners, which not only abolished scurvy but led to a marked improvement in their health and efficiency.

Unfortunately good health lessons are often soon forgotten. In 1912, Captain Scott, a naval officer, ignoring the experience of the Royal Navy in the eighteenth century, planned an expedition to the South Pole without a single source of ascorbic acid in his food rations. The story of that expedition is now tragic history.

In 1907 Holst and Frolich discovered that guinea-pigs, like man and monkeys, are susceptible to scurvy. Thereafter the search for the active principle was directed towards isolating from citrus fruit juices the pure

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chemical substance that would cure scorbutic guinea-pigs. In 1932 Glen King isolated the vitamin from lemon juice and identified it with ascorbic acid which the biochemist Szent-Gyorgyi had isolated from adrenal glands, oranges and cabbages in 1928. Szent-Gyorgyi was primarily interested in the nature of substances with reducing properties in biological materials; he had not recognized the properties of ascorbic acid as a vitamin. Ascorbic acid is a simple sugar, and a most active reducing agent known to occur naturally in living tissues. Its chemical structure was elucidated by Haworth and Hirst in Birmingham, England and its synthesis accomplished in 1933.

In experimental ascorbic acid deficiency in guinea-pigs Wolbach of Harvard studied its effects on the microscopic structure of tissues. Ascorbic acid is necessary for the proper formation of the intercellular ground substance or matrix that binds together the cells in such tissues as capillaries, bone, teeth and connective tissue. In connective tissue fibroblasts synthesize the protein collagen which then forms extracellular fibrils, strands and bundles. Ascorbic acid is in some way necessary for the formation of hydroxy-proline, an amino-acid which forms about 13 percent of the collagen molecule. In scorbutic guinea pigs the collagen gradually disappears and the supporting structure of the connective tissue collapses. Lack of intercellular cement substance in the walls of the capillaries leads to their rupture and the production of petechial haemorrhages. (Bleeding spots)

Although the guinea pig enabled ascorbic acid to be discovered, it could not provide the information on human needs for the vitamin. The first man to attempt to induce Scurvy in himself was an Edinburgh-trained physician William Stark, who died in the attempt in 1770. This dangerous experiment was not repeated until 1940 when a young American Surgeon John Grandon fed himself on a diet devoid of ascorbic acid. In a later experiment, use of radio-isotopes helped to establish that the size of the ascorbic acid pool in a well-fed man is about 1.5g of which about 45 mg is utilised daily. Clinical signs of scurvy appear usually after 30 to 70 days when the pool is reduced to below 300 mg and the rate of utilisation below 9 mg/day.

The Story of Beri-beri

Beri-beri was a common condition in many parts of the world. Towards the end of the 19th Century several investigators were looking for the causative factor or factors. The impact of the newly emerging science of bacteriology was so great that everyone was thinking in terms of causative germs; in fact 17 different organisms were confidently claimed to be the cause by various investigators!

Takaki, a Japanese naval doctor in the 1880's studied the conditions in which the disease occurred in the Japanese navy, and after detailed

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investigations of its incidence in relation to many environmental factors, he came to the conclusion that it was not an infection but a *dietary deficiency* which caused the disease. The proportion of polished rice in the Japanese diet was excessive, so Takaki thought that beri-beri resulted when the ratio of protein to carbohydrates was too low. Takaki tested his dietary hypothesis by sending a crew on a voyage with an improved diet, wherein a part of the rice ration was replaced by wheat bread and the allowance of milk and vegetables was increased. While experience on a naval training ship had earlier shown 169 cases of beri-beri out of 300 crewmen on a voyage lasting nine months, on the voyage this time only 14 cases of beri-beri occurred, all in individuals who had refused to take the condensed milk and meat ration. Takaki, later as Surgeon General enforced the improved diet in the navy with the virtual disappearance of beri-beri within a year though for reasons which were entirely different from what Takaki imagined.

In 1890 the Dutch physician Eijkman, stationed in a military hospital in Java, observed a disease in chicken and pigeons resembling human beri-beri. He fed some domestic fowls on the food provided for his patients suffering from beri-beri. He noticed that the birds developed weakness of the legs and head retraction. A new head cook at the Hospital discontinued this supply of superior "military rice" (highly polished rice). So that thereafter the birds had to be fed on "inferior" whole grain "civilian rice". The result was that the fowls recovered! Eijkman wrote: "A chance circumstance threw suspicion on the fowls' feed. The onset and cessation of the epidemic in the fowls, which lasted six months, coincided respectively with the introduction of refuse of cooked polished rice, and its subsequent replacement with raw whole rice".

Next came the experiment in which Eijkman proved that there was something existing in very small amounts in the germ and pericarp of rice, that was water-soluble and that protected fowls from a disease resembling human beri beri. Eijkman deservedly won the Nobel Prize many years later for his discovery which showed how beri-beri could be prevented and cured.

No less instructive in this story is the nature of the medical profession's reaction to Eijkman's studies, they were doubted and questioned for a decade. Manson, in his presidential address to the Epidemiological Society in London in 1901 entitled "the Etiology of Beri-beri", was not impressed by Eijkman's theory. According to Martson, the disease was purely an intoxication produced by a toxin elaborated by a germ. In Osier's "Principles and Practice of Medicine" of 1909 (7th Edition), the germ and food theories received equal notice, and the latter offered no hint that something might be *deficient* in a polished rice diet. In the same year Fraser and Stanton in Kuala Lumpur finally showed that human beri-beri responded in the same way as that of Eijkman's birds.

In 1911 Funk prepared an extract of rice pericarp which was therapeutically active in beri-beri.

Proof of Accessory Food Factors

Between 1906 and 1912, Frederick Hopkins in Cambridge, England carried out experiments which showed that young rats fed on a diet of milk protein casein, starch sugar, lard and inorganic salts failed to grow and finally died. The addition to the diet of only 3 ml of milk daily, supplying not more than 4 percent of the total energy enabled the rats to thrive. He thus demonstrated the existence of an "accessory food factor" in milk. In 1913 two groups of American workers extracted this growth factor with ether, thus showing that it was fat-soluble. In the same year E. V. McCollum in U.S.A. showed by studies with rats that milk contained two growth-promoting factors: the one in butter he called "fat-soluble A", and the one in the fat-free portion was termed "water-soluble B". It was realised that there were several accessory factors, and as they were discovered they were called Vitamin A, B, C, D etc. The word "vitamine" was suggested by Funk in 1912 because he believed that all the accessory factors were vital amines. We know now that only a few of the vitamins are amines, but the name has stuck, albeit without the last "e". In the last 50 years most of the vitamins have been isolated, synthesised and given chemical terminology. For instance Vitamin A is *retinol*, Vitamin B1 is *thiamine*, and B2 *Riboflavin*, B6 *pyridoxine*, B12 cyanocobalamin *and* so on. It has also become possible to define in biochemical terms their exact role as co-factors in certain essential chemical reactions in the body. To learn exactly how this knowledge came about, we will go back to the story of beri-beri where we left it.

Concept of Biochemical Lesion

Thiamine (anti-beri-beri vitamin) was the first vitamin whose precise activity in the body was stated in biochemical terms. This was achieved at Oxford between 1928 and 1935. Peters (1963) has written a historical account of the work of his school, which illuminates the process of scientific discovery and development of new concepts. In brief, it was first demonstrated that lactic acid accumulates in the brains of pigeons in which thiamine deficiency is experimentally induced, causing head retraction and opisthotonus. It was then found that minced brain tissue from such pigeons took up less oxygen than brain tissue from normal pigeons in the presence of added glucose or lactic acid, *in vitro* (in a test tube). This failure of oxidation could be corrected by adding thiamine in catalytic amounts to the brain tissue. It was thus established for the first time that a vitamin could be an essential part of an enzyme system. It was found that pyruvic acid also accumulated in the brain and blood of such pigeons and it disappeared on the administration of thiamine. It is now known that the pyrophosphate of thiamine is the coenzyme of carboxylase, the enzyme concerned with the decarboxylation and oxidation of pyruvic acid. It was a lucky circumstance that this work developed with thiamine and the pigeon's brain, as this vitamin and this tissue show the *biochemical lesion* better than any other yet found.

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The clinical and pathological features of Wernicke's encephalopathy were described in 1881. It was usually encountered in chronic alcoholics and occasionally in excessive vomiting of pregnancy, and in terminal cachectic states. In 1934 it was observed that rats made deficient in thiamine developed focal vascular lesions in the brain stem. In 1938 it was observed that the characteristic lesions in the brain in Wernicke's encephalopathy were experimentally produced in thiamine deficient pigeons. Subsequent studies confirmed the value of thiamine in this disorder. After the grim experience of prisoners of war in the Far East after the 1939-1945 world war, Wernicke's encephalopathy came to be regarded as cerebral beri-beri.

Today a specific test for thiamine deficiency is the measurement of the transketolase activity in the red blood cells with and without the addition of thiamine pyrophosphate (TPP). If TPP increases activity by more than 25 percent, this indicates thiamine deficiency. It is unfortunate that beri-beri still exists in many rice-eating communities. Infant beri-beri results from a thiamine-deficient milk from a deficient mother; it is responsible for a large proportion of infant death in the Philippines, Burma, Vietnam and probably also in other rice eating areas.

The Story of Pellagra

Pellagra was not known to classical and mediaeval physicians. There is no description in Ayurveda which suggests this condition. In India pellagra occurs sporadically in those parts where maize is a staple cereal. For instance, Shah and Singh in 1967 reported 128 cases, all maize eaters, admitted to the Udaipur Hospital in one year. Pellagra also occurs in the Jowar eaters in Andhra Pradesh, where it accounts for 1 percent of general admissions and 10 percent of mental hospital admissions in certain seasons. The history of the search for the cause of pellagra illustrates very well how the growth of knowledge can bring together apparently contradictory theories and shows in the end that each has a substance of truth. The maize theory was the obvious one because pellagra occurred in maize eaters; it was attributed to some hypothetical toxin in the maize, perhaps produced by bacterial fermentation during storage. The protein deficiency theory was based on the observation that the diet of pellegrins was very poor in proteins. Goldberger in U.S.A. between 1913 and 1928 made a systematic study of pellagra and its causation by a combination of the epidemiological and experimental approach. He demonstrated that pellagra is a deficiency disease and that the pellagra-preventing factor was water-soluble and heat-stable, and occurred in the same food stuffs as thiamine; but he died before the identification of nicotinic acid. Maize actually contains more nicotinic acid than oats, rye, white wheat bread and rice. The explanation is that most of the nicotinic acid in maize is present in a bound form, unavailable to the consumer. Also, the protein of maize is deficient in tryptophan, from which the body is able to make nicotinic acid.

Rickets

The discovery of the cause and cure of rickets is one of the great triumphs of biochemical medicine. Most people recognise rickets as a deficiency disease resulting from a lack of Vitamin D. Few people will know that rickets was the earliest air pollution disease. In England when soft coal was used in industry, near about 1650, rickets was first described in children belonging to poor people living in narrow, sunless alleys of factory towns and big city slums. This, as we know now, was because of a deficiency of solar ultra-violet radiation, which is necessary for the synthesis of Calciferol, the calcifying hormone released into the blood stream by the skin. Without calciferol not enough calcium is laid down in growing bones and the crippling deformities of rickets are the consequence. Either adequate sunlight or the ingestion of minute amounts of calciferol or one of its analogues therefore prevents and cures rickets.

Solar radiation may be blocked by many means among them being the industrial smog in London. The long dark winter of many north European countries forced prolonged confinement of infants indoors during winter.

In 1906, it was noticed in Germany that all children who were born in the fall and died in the spring had rickets; those who were born in the spring and died in the fall were free of the disease. In 1909, G. Schmorl documented this marked seasonal variation in the frequency of rickets with a series of 386 post-mortem examinations carried out on children less than four years of age.

In 1908, Theobald Palm, an English medical missionary who went to Japan, was struck with the absence of rickets among Japanese as compared to its lamentable frequency among the poor European children. He wrote to other medical missionaries round the world. From the data it was deduced that rickets was caused by the absence of sunlight. "It is in the narrow alleys, the haunts and playgrounds of the children of the poor, that this exclusion of sunlight is at its worst, and it is there that the victims of rickets are to be found in abundance". The systematic use of sun baths was a logical preventive and therapeutic measure.

The first successful attempt to induce rickets experimentally in animals was made in 1908 at the University of Glasgow by Leonard Findlay. Puppies confined indoors in cages developed rickets; unconfined animals did not become rachitic.

Harry S. Hutchinson conducted a most clear-cut investigation in Bombay in the beginning of this century. He found no rickets at all among poor Hindus who subsisted on a pitifully inadequate diet but who worked outdoors all day, "and while at work left their young infants at some nearby point in the open air". In contrast he

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found that rickets was exceedingly common among well-fed Muslims and upper-class Hindus, whose women usually married at the age of 12 and entered "purdah" where the ensuing infants usually remained with their mother for the first six months of life in a semi-dark room in the interior of the house. Hutchinson concluded that "the most important etiological factor in the production of rickets is the lack of sunlight, fresh air and exercise". He proved the point by taking out 10 children of purdah-induced rickets out into the open air, "showing that removal of the cause removes the effect. All other factors remained constant and no medicine was given".

In 1919, a Berlin Paediatrician, Kurl Huldshinsky tried the light from a mercury-vapour quartz lamp which includes the ultra-violet wave-lengths, on four cases of advanced rickets in children. He obtained complete cures within two months. In addition to providing a truly effective method of curing rickets, he proceeded to show that an endocrine hormone must be involved. He irradiated one arm of a rachitic child with ultra-violet rays. Then he showed, with X-ray pictures, that calcium salts were deposited not only in the irradiated arm but in the other arm as well. This proved that on irradiation the skin released into the blood stream a chemical that had the needed power to induce healing at a distance—in other words, a hormone. In June 1924, Alfred Hess in New York found that ultra-violet irradiation rendered linseed and cotton seed capable of curing rickets. Hess proceeded to show that a crude cholesterol and plant sterols, as well as the skin, acquired the property of curing rickets when irradiated by ultra-violet rays. In 1927 Otto Rosenheim and Thomas Webster showed that the plant sterol ergosterol (derived from ergot, a fungus) became enormously anti-rachitic when irradiated with ultraviolet light. A description of the nature of the skin hormone naturally released by irradiated skin was finally provided in 1936 by Adolf Windaus at the University of Gottingen. He demonstrated that 7-dehydro cholesterol is the natural pre-hormone that is found in the skin and showed how it became calciferol on ultra-violet irradiation.

Modern studies support the long-suspected fact that fish, unlike birds and mammals, are able to synthesize calciferol enzymatically without ultraviolet light. Shielded by water, fish receive essentially no ultra-violet (290 - 320 millimicron) radiation, and yet the blue fin tuna fish has up to a milligram of calciferol per gram of liver oil, enough to provide a daily protective dose of calciferol for 100 children. In the north of Europe fish has always been a staple diet, and so the normal diet tended to protect children against rickets. Slowly, over the years, the people of Scandinavia and Baltic regions became aware of the specific therapeutic value of cod liver oil which contains enough calciferol to protect against rickets if consumed in amounts equal to 4 grams of oil per day; and oil or fat containing calciferol preserves its efficacy for a long time. In a controlled trial in Negro children in New York City, Hess in 1917 proved the prophylactic value of routine administration of cod liver oil. Mellanby in London in 1919 suggested that the efficacy of cod liver oil was "most probably due to vitamin A deficiency", which

was obviously wrong. Me Collum, the American nutritionist in 1922, went on to establish the difference between the active anti-rachitic factor in cod liver oil and vitamin A by showing that after having been aerated and heated cod liver oil could still cure rickets but had lost the ability to cure Xerophthalmia, which is due to lack of vitamin A. On this basis he called the cod liver oil factor "Vitamin D". Final recognition of the uniqueness of fish liver oils came from the finding that animal fats such as butter and lard have essentially no calciferol, particularly in winter; no non-fish diet of any kind could protect against rickets in a sunless environment. It was quite clear that cod liver oil was a medicine, and not a food. No specific medicine such as cod liver oil can be called a dietary vitamin unless it is present in normal foods in significant amounts. Orally administered thyroxine cannot be regarded as "Vitamin T" even though patients with thyroid deficiency are cured by thyroid extract. Both endocrine secretions (thyroxine and calciferol) require external factors, incidentally, iodine in the case of Thyroxine and ultra-violet rays in case of calciferol.

It should therefore be considered that Calciferol is a hormone rather than a "Vitamin D"—it is a steroid hormone whose production rate is under physiological control rather than being left to the vagaries of diet. The recognition of calciferol as an ultra-violet-dependent hormone gives fresh meaning to a number of seemingly unrelated physiological and cultural adaptations. Tropical man probably avoids the danger of too much calciferol production by virtue of his dark skin; the melanin granules in the outer layer protect the lower layers of the skin. European man, on the other hand, needed to use all the scanty ultra-violet light available and consequently was gradually selected for an unpigmented skin.

It is paradoxical that in our land with plenty of sunshine, where the sun is worshipped as God Suryanarayana, rickets and osteomalacia should occur due to inadequate exposure to sunlight. The capacity of the skin to synthesize Vitamin D on exposure to sunlight is not affected by under nutrition and there is significant increase in serum 25HCC after as short an exposure to sunlight as 6.5 minutes.

Vitamin D (1,25.2 OHD)

Vitamin D (1,25.2 OHD) has receptors (VDRs) in multifile cells including neurons and dial cells in the human brain. Vit. D is involved in the regulation of nuclear treatmentation of 200 genes involved in cell differentiation, proliferation and apoptosis. Vitamin D normal level above 30-40 mg/ml. less than 20 mg/ml indicates deficiency. More than 80 mg/ml toxic levels. In spite of abundant sunshine Indians have Vit. D deficiency in large populations including doctors and nurses ! Vitamin D deficiency is linked to Alzheimer's disease, strokes bones (rickets, osteomalacia osteoarthritis), epilepsy, cancer (prostate, crest, colon), TB and antoimmunine diseases.

Science and Technology for the Conquest of Hunger

Starvation and hunger have haunted mankind throughout recorded history. It was Malthus, more than any other single author who first put the omnipresence of hunger in a universal perspective. He argued that unless man regulated his rate of population growth, his numbers would soon exhaust the available food supplies and therefore perish.

Unfortunately, apart from that due to famines and floods, hunger is often man-made. Mahatma Gandhi, himself a strict vegetarian and an apostle of non-violence, said during the devastating Bengal famine in 1943 that with the vast availability of fish and sea-foods there was no reason why people should starve to death.

Modern Science and technology have shown spectacular ways for better food production as well as better food conservation and preservation. Chemical fertilisers, insecticides and pesticides, plant growth regulators, soil conditioners, all require capital investment but they would pay for themselves many times over in higher yields. Modern genetics has created high-yield disease-resistant varieties of seeds that can increase food production several-fold. Irrigation of land and mechanisation of farming have contributed to the green revolution. Scientific animal husbandry can provide greater yield of milk and poultry products. Scientific storage of food at the right temperature and humidity with protection from rodents and insects, protective packing with polyethylene and other synthetic wrappings permit better food preservation.

Artificial enrichment of food with vitamins and minerals is another modern development that can help millions of needy people tremendously. Iodized salt can dramatically reduce the incidence of endemic goitre. Enrichment of wheat flour with thiamine, riboflavin and niacin, and that of rice with thiamine plus iron and calcium, will produce significant improvement in the health of most of ill-fed populations. The addition of lysine to wheat flour or bread can raise the proportion of the wheat's usable protein from about a half to two-thirds; and the amino-acid threonine could make grain protein almost as fully usable as the protein of meat and milk. The main problem so far is the cost of synthesis of amino-acids. As more of them are synthesised and the price is brought down, these products of laboratory chemistry will make it possible to turn grain into "meat" for the vast segment of world population which is vegetarian either by choice or by economic necessity.

When a properly processed oil seed meal (made from cakes that are left when the oil is pressed out of the seed) is mixed with a food grain in the ratio of 1:2 the combination contains about 25 percent protein of meat-like high quality. With the addition of a small amount of yeast and vitamin A it will make a highly nutritious food.

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In 1975, when the world population touched nearly 4 billion, the global food production was estimated at 3.3 billion tons. This target was achieved nearly 12,000 years after agriculture came into existence on planet earth. With the world population threatening to reach about 8 billions in the next 40 years, what is going to be mankind's response? The synthetic chemists do not share the pessimism of Malthus, since they visualise the prospects of manufacturing completely synthetic foods at a low enough cost, to end all food worries. After all, the essential nutrients man requires are basically chemicals whose formulae are well known. Modern technology could make microorganisms do the food production for us when the resources of land and sea are exhausted.

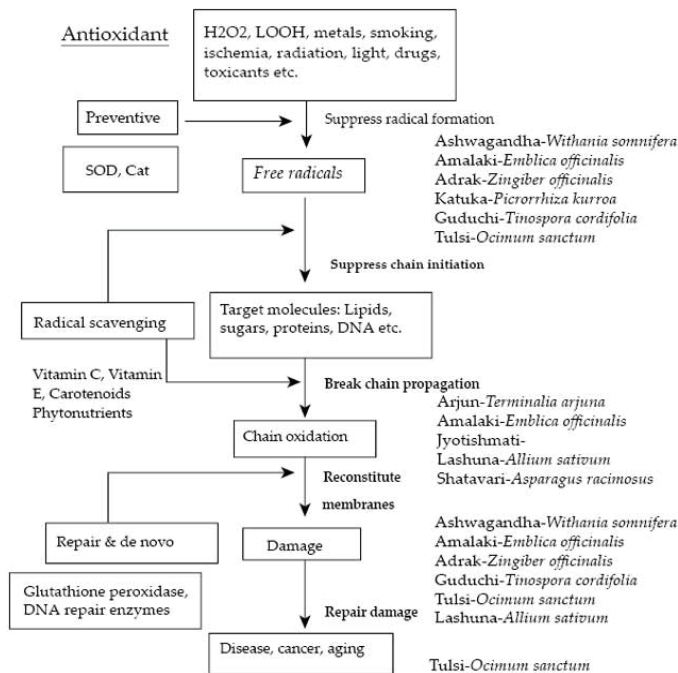
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ANCIENT INDIAN INSIGHTS AND MODERN DISCOVERIES IN NUTRITION, EXERCISE AND WEIGHT CONTROL

Introduction

Ayurveda (“Science of Life”) the ancient Indian System of Health Care represents experiential wisdom of over 5000 years. The following description from “Charaka Samhita” (600 BC) sounds refreshingly contemporary

“A person who is habituated to pampering his belly even when a previous meal has not been thoroughly digested; who is addicted to a habit of sleeping in the day or leading a sedentary life, who is averse to taking any sort of physical exercise, will suffer from excessive stoutness. He is likely to be afflicted by many diseases that invariably terminate in death, due to obstruction of internal channels due to deposition of fat. Hence all things and conditions which foster the growth of abnormal Fat should be carefully avoided.”¹



Level of Antioxidant Action Non-enzymatic, enzymatic and ancillary enzymes & Defense systems in vivo against oxidative damage.

Fig. 1: Depicts the Ayurvedic anti-oxidants according to the various levels at which they act. (Devasagayam et al., 2004)².

"The excessive corpulence is caused by over eating, lack of exercise, lack of mental exertion and by inherited tendency".

The corpulent person is afflicted with eight disabilities viz. diminution of lifespan, lack of agility, debility difficulty in sex ant, fetor, distressing sweats, excessive appetite and excessive thirst".

Importance of "Ahar" – Diet

Charaka Samhita discusses "Wholesome" and "unwholesome" food. "The use of a wholesome diet is the only factor that promotes the healthy growth of humans; and the factor that makes for disease is the indulgence in unwholesome diet". "That class of food which helps the harmonised body elements to retain their state of equilibrium, and the discordant body elements to gain equilibrium, is that which acts in the opposite manner".

Regarding Energy requirements, Charaka States: "Even light, easily digested and nutritious food should not be taken in excess of bodily requirements, or after the appetite has been satisfied. Food difficult to digest should not be taken habitually. Even if used the quantity should not exceed a fraction of a full meal". "An excess or surfeit of food is markedly harmful unless the gastric fire is increased by hard exercise".

Sushruta, advised the corpulent diabetic to indulge in vigorous physical exercise such as walking of at least 100 "yojanas" or physical effort (such as digging a well). At the same time Sushruta extorted the thin diabetic not to exert too much.

Ayurveda describes 3 kinds of "ahar" or diet – "Satwik", "Rajasik" and "Tamasik". The "Rishis" took "Satwik ahar" consisting of kanda, moola, phala (vegetables and fruits) and lived for hundred years. In today's parlance, this represents a 1300 caloric diet (which causes the least oxidative stress), high fibre, low fat, low sodium, high potassium & minerals and plenty of anti-oxidants (Figure 1). Excessive oxidative stress is central in most human disorders including ageing process as shown by increased levels of F2 Isoprostanes in peripheral blood and urine, and increased F4 neuroprostanes in the CSF.

Osmotin, a recently discovered plant analogue of mammalian adiponectin, is abundant in fruits & vegetable and acts through adiponectin receptors (Narsimhan LM et al., 2005)³ Adiponectin and osmotin ant via AdipoR1 receptors in muscles in muscles and Adipo R2 receptors in liver and act as insulin sensilizers and regulators of energy homeostasis via AMPK activation (Wolf G 2003)⁴. Part of the beneficial effects of fruits and vegetables is due to their osmotin content, which remains stable in the digestive tract.

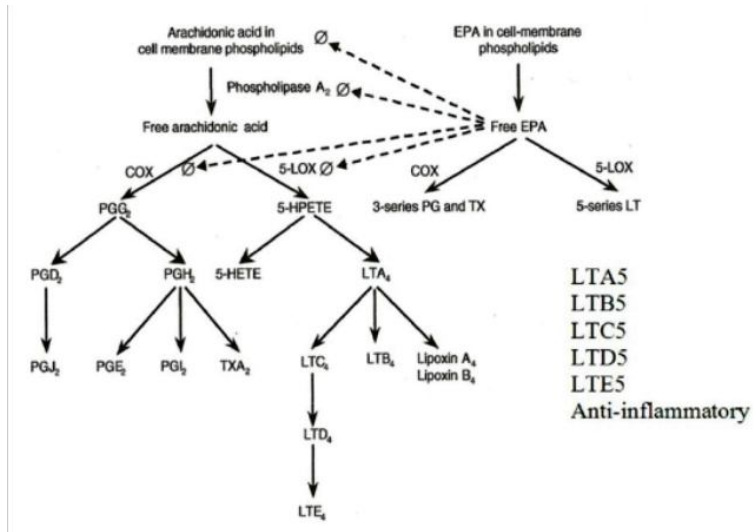


Fig. 2: Beneficial effects of EPA/DHA in cells membrane phospholipids

Kashyapa Samhita (which deals with pediatrics) stresses the importance of breast milk as essential promoter of growth and development and tonic for all tissues. "If the mother does not have enough breast milk, it is better to employ a "Dhatri" (wet nurse) as no other milk can compete with human milk".

Ayurveda also gives details of the qualities of Cow's milk, also milk from buffaloes, goats, sheep, camels, horses and elephants.

The insight about mother's milk is fully vindicated today in terms of its ideal content of essential fatty acid EPA/ DHA and their effects on the composition of the cell membrane (as discussed in the next section).

Essential Fatty Acids

Polyunsaturated fatty acids of omega 6 class linoleic acid (LA) and omega 3 class (alpha)linolenic acid (ALNA) are essential dietary sources since they cannot be synthesized by the organism. W6 are present in maize, sunflower and sesame oil; W3 are present linseed oil, nuts, soyabeans, wheat and cold water fish.

All cell membranes contain W6 arachidonic acid and W3 Eicosapentanoic acid EPA and docosa-hexanoic acid DHA (Fig. 2). The ideal ratio of W6 : W3 in 2:1, maximum 6:1 Any higher ratio is detrimental since it

leads to increase in the arachidonic-acid induced proinflammatory cytokines (PGE1, IL-1, IL-6, IFN γ and TNF) EPA/DHA lead to decreased production of pro-inflammatory cytokines and increased production of anti-inflammatory lipoxins, resolvins and protections and IL-10, which play active role in the resolution of inflammation (Ariel and Serhan 2007)⁵ (Bannenberg and Serhan 2010).⁶ EPA is a source of resolvins (rvE1, E2), DHA (RvD1D2D3D4) and protections (PD1 and NPD1) DHA derived Neuroprotections (NPD1) protect against neuronal decline through excessive oxidative stress and apoptosis, while promoting cell survival and maximising cognitive function throughout the human life span (Uavy & Dangour 2006).⁷

W3 FAs maintain membrane fluidity and longer residence of transporters such as GLUT. Brain cell membranes have a high content of EPA/DHA, essential for neurotransmission, brain development and function including learning tasks. Epidemiological data indicates the association of low EPA/ DHA with depression (with higher levels of inflammatory markers including hsCRP, ICAM-1, I1-6) and coronary Heart Disease (Empana JP et al., 2005).⁸ Some epidemiological data supports a relationship of higher fish intake and lower depression and suicide (Colin A et al., 2003).⁹ Dietary supplement of DHA for three months prevented young students from developing aggressive behaviour during time of stress (Hamazaki et al., 1996).¹⁰ EPA / DHA play essential role in maintaining normal endothelial function and inhibiting endothelial inflammation, the starting point of atherosclerosis. The EARLY study evaluated the role of DHA in restoring endothelial function in children with hyperlipidemia, as measured by increased flow-mediated vasodilation (FMD) (Engler MM et al., 2004)¹¹. Higher concentrations of EPA/DHA improve brachial artery dilatation in patients with coronary artery disease. (Tagawa H et al., 1999)¹². Red cell membrane EPA/DHA level of 5% of total fatty acids is associated with a 70% reduction in the risk of primary cardiac arrest (Siscovik DS et al., 1996)¹³.

Higher concentrations EPA/DHA decrease the risk of sudden cardiac death (Albert et al., 2002)¹⁴ EPA/DHA ensure plaque stability via reducing abundance of macrophages (Thises et al., 2003)¹⁵. I Low EPA/DHA is associated with acute coronary syndrome (Block RC et al., 2008).¹⁶

Dietary PUFAs function as fuel partitions, including FA oxidation and reducing fatty acid synthesis and reduce fat deposition. High intake trans-fatty acids (TFAs) in cafeteria foods, bakery and meat products, margarine, frying oils and desserts reduce the conversion of ALA to DHA, and promote abdominal obesity hence reducing the dietary intake of TFAs is an important health goal. (Kummerow FA et al., 2004).¹⁷

Diet and Inflammation

Prof. PC Calder (2002)¹⁸ has given an excellent review of inflammation in health and disease. He has emphasized the important role of dietary essential fatty acid omega 3 PUFA EPA and DHA, in the suppression of pro-inflammatory cytokines and production of anti-inflammatory lipoxins, resolving and protections in the resolution of inflammatory response (Fig. 2). This is crucial in many disease states including inflammatory disorders (such as arthritis), atherosclerosis, asthma and cancer. Zinc, selenium, Vit. A, Vit. C, Vit. E, folic acid Vit. B6 and Vit. B12 are important nutrients whose deficiency affects susceptibility to infection and host immune response. The role of Vit. D. in relation to immune competence has only recently been discovered. Dendritic cells and macrophages have receptors for Vit. D. Deficiency of Vit. D and Vit. D receptor polymorphism increase susceptibility to tuberculosis (Wilkinson 2000).¹⁹

There is a two-way interaction between nutrients and human genes (Roche HM 2004).²⁰ How genetic variation influence response to nutrients and how nutrients influence gene expression, transcription and metabolism are the subject of Nutrigenomics. The effect of metabolism are the subject of Nutrigenomics.

The effect of material malnutritional on suppression of foetal insulin IRS-PI3K, AKT pathway is well known as the basis of Metabolic Syndrome and insulin resistance with consequent hyperinsulinemia.

Diet and Chemoprevention of cancer

Diet contains several non-nutritional phytochemicals whose active principles have been identified: Haldi (Curcumin), red chilli paper (capsaicin), ginger (gingerol), green tea (epigallocatechin), honey (caffeic acid) garlic (diallylsulphide), cabbage (indole-3-carbinol) broccoli (sulpharaphane), carrot (carotene), grapes (resveratrol), grape seeds and pine bark (procyanadine), tomatos(lycopenes)

Table 1: Mode of action of dietary phytochemicals

1.	Curcumin	Inhibits TNF α induced COX2 gene transcription and NFKB & AP1 activation; anti-proliferative, proaplotic and anti-metastatic activities via suppression of B cantenin.
2.	Capsaisin	Blokade of IKb α degradation and NFKB translocation into nucleus; induces apoptosis by activation of CJUN. NH terminal kinase (JNK) and p 38.

3.	Gingerol	Inhibits EGF-induced AP 1 activation and neoplastic transformation.
4.	EGCG Epigallocatechin 3 Gallate	Blocks activation of API & NFkB, inhibits P13K. AKT-NF-κB and HER/NEU receptor tyrosine phosphorylation; inhibits VEGF, β calenin expression G0/G1 phase arrest and apoptosis.
5.	Genistein	Inhibits API, cFOS and ERK activity, inhibits AKT mediated NFkB activation.
6.	Resveratrol	Inhibits PMA-induced COX-2, PKC and AP1, MMP-9 NFkB; induces apoptosis via activation of p53 via Erk and p 38 Down-regulates β catenin.
7.	Procyanidin	Naturally occurring polyphenolic bioflavonoid in grape-seed & pine bark; powerful antioxidant.
8.	Caffeic acid phenethylester (CAPE)	Disrupts the NRF2-KEAP1 complex. Decrease β catenin expression; suppress NFkB activation.
9.	Diallyl sulphide	Prevents mutagenesis by suppressing ROS.
10.	Indole-3 Carbinol	Decreases β catenin, inhibits adhesion, migration and invasion of cancer cells.
11.	Sulphoraphane	Directly interacts with KEPA1; stimulates nuclear translocation of NRF2 which subsequently activates ARE for expression of many antioxidant or detoxification enzymes.
12.	Lycopene	Anti-oxidant - suppresses ROS.

Their mode of action at the molecular level is described in Table 1. Non-nutrient dietary phytochemicals exert their substantial anti-mutagenic and anto-carcinogenic properties by blocking cell signalling pathway that regulate cell proliferation and differentiation-such as the family of mitogen activated protein kinases (MAPKs), NF-κB-API, NRF2 as well as catenin a component of cell-cell adhesion machinery. Carcinogenesis is a multi-step process, the initiation of which can be blocked or suppressed by dietary phytochemicals. They can also halt or retard the progression of pre-cancerous cells into malignant cells (Surh YH 2004).²¹ How dietary phytochemicals can modify gene expression or transcriptional gene silencing is the subject of nutrigenomics and epigenetics.

Current Knowledge about Adipose Tissue

Ability to store energy in excess of what is required for immediate use is essential for survival. White adipose tissue plays a central role in the regulation of energy balance and conservation of body heat through thermogenesis. Functions of adipose tissue include (1) storage of triacylglycerol in the body, and aromatization of sex steroids, storage of fat soluble vitamins and (2) protection of vital structures-orbits, palms & soles, vulva, perineal, periarticular, pericalyceal and epidural regions. It is interesting to note that this supportive function of fat is preserved in lipodystrophy suggesting separate embryonic origin and genetic regulatory mechanisms of supportive fat. (3) Adipose tissue is an endocrine organ which produces several adipocytokines. Leptin, visfatin, adiponectin, resistin, TNF, IL-6 PAI-1 etc. (Fig.3).

Newly formed adipocytes produce adiponectin, an insulin sensitizer while distended adipocytes produce leptin, resistin, TNF, IL-6. TNF induces insulin resistance by causing serine phosphorylation of IRS-1 in muscle and IRS-2 in liver thereby abrogating the IRS-P13K-ACT signalling pathway necessary for GLUT4 translocation, glucose transport and glycogen synthesis in muscle.

Adipose tissue is a dynamic structure with a good blood supply. The stored fat in adipose tissue is continuously undergoing lipolysis (hydrolysis) and lipogenesis (reesterification). These two processes are not forward and reverse phases of the same reaction but have entirely different pathways in the control of synthesis and hydrolysis. Insulin plays a central role in stimulation lipogenesis and preventing lipolysis. Due to differences in receptors and post-receptors events between human visceral (Omental) and subcutaneous adipose tissue, antilipolytic effects of insulin are 3 fold higher in subcutaneous fat than omental. Although the receptor number is similar (~ 300,000 sites per cell), receptor affinity is higher in subcutaneous fat. I-25 labeled insulin dissociates more rapidly from omental than subcutaneous adipocytes.

There is a remarkable heterogeneity in the distribution and metabolic response in adipose tissue in different sites. At any BMI adult females have more body fat than males as reflected in plasma leptin levels. Insulin stimulates adipogenesis and prevents lipolysis at all sites. Growth hormone reduces truncal fat and promotes fat deposition in palms and soles. Estrogen promotes fat deposition in hips, legs, brast and subcutaneous tissue. Prolactin promotes adipogenesis in (femorogulateal & mammary regions. Adrogens favour visceral and subsutaneous abdominal fat deposition. Male hypogonadism is associated with increased adipose tissue distribution in female pattern. Glucocorticoids promote re-distribution of fat from peripheral to central location - truncal and supraclavicular (buffalo Halo hump). Lipody strophy related to HIV treatment resembles Caushing's syndrome but cortisol levels are not high.

B adrenoceptor agonists (isoprenaline) accelerate lipolysis while α_2 adrenoceptor agonists (clonidine) retard lipolysis, more in females. Noradrenaline – induces lipolysis is ten fold more in abdominal than gluteal fat-this difference is 20 fold in females. Regional differences in nor-adrenaline induced lipolysis are not seen when post receptor acting compounds are used such as forskolin (adenylyl cyclase & CAMP), enprofylline (phosphodiesterase) or dibutyryl cAMP (protein kinase). (Bolinder J et al)²². Visceral adipose tissue cells grow slower in culture than subcutaneous adipose cells. Thiazolidine drugs cause proliferation of subcutaneous adipose tissue (but not visceral adipose tissue) and increased UCP2 mRNA expression.

Understanding Obesity at the Molecular Level

Obesity can occur as a result of genetic and acquired changes in three main types of biochemical processes which are now understood at the molecular level (Palou A et al., 2000).²³

1. Feeding control, which determines the sensation of satiety and hunger through processes that depend on an interplay between internal signals (notably leptin) and environmental factors. Leptin regulates food intake by central action inducing expression of SOCS-3 mRNA in the hypothalamus and it stimulates fatty acid oxidation in adipose tissue
 - i. By reduction in SREBP-1 (sterol regulatory element binding protein) an insulin-stimulated lipogenic transcription factor.
 - ii. By upregulation of carnitine palmitoyl transferase 1 (CPT-1), acyl coA oxidase (ACO), PPAR1, UCP-1, UCP-2 and UCP-3 in WAT and liver, causing fatty acid oxidation and disappearance of fat store within adipocytes and liver. However, leptin resistance is a feature of obese humans. Excessive SOCS-2 activity in leptin responsive cells is a potential mechanism of leptin resistance. Protein tyrosine phosphatase PTP1B regulates leptin signalling pathway probably by targeting the Jak2 protein molecule, a characteristic feature of human obesity. PTP1B may be a novel target to treat leptin resistance in obesity.
2. Energy efficiency, particularly activation of UCP-1, UCP-2 and UCP-3, convert calories contained in food as heat instead of accumulating them as fat.
3. Adipogenesis, controlled by an interplay of transcription factors including PPAR, C/ ebp and ADD families. The knowledge of a growing number of genes and molecules implicated in these 3 types of processes of their metabolic relationship provides a molecular level understanding of body weight regulation and suggesting new methods of obesity control (TFA)

found in extensive in cafeteria foods, margarine, frying oils, desserts, bakery products, promote abdominal obesity.

Human Obesity Gene Map

As of October 2005, 175 human obesity cases due to single gene mutations in 11 different genes were reported. There are 244 genes that when mutated or expressed transgenes in mouse, result in phenotypes that affect body weight and obesity. 253 QTLs for obesity-related phenotypes have been mapped from 61 genome-wide scans. The obesity gene map shows putative loci on all chromosomes except Y. The electronic version of the map the links to useful publications and relevant sites can be found at the Pennington Biomedical Research Centre Human Genomics Laboratory. <http://obesity.pbrc.edu>

Vit. A and Vit. D

Vit. A has a role in the regulation of the level and functioning of body fat reserves. A low vitamin A status favours increased fat deposition (Bonet ML et al., 2003).²⁴ Vit. D. inhibits adipogenesis through VDR – dependent inhibition of c/EBP (CCAAT enhancer binding protein-alpha) and PPAR (Wood RJ. et al., 2008)²⁵ Vit. D deficiency and Vit D receptor polymorphism leads to obesity, through increased PPAR induced, Pre-adipocyte proliferation & differentiation.

Thermogenesis: Energy Expenditure

Regulation of body weight involves coordination of intake and phosphorylation in calories. Uncoupling of oxidation and phosphorylation in mitochondria via uncoupling proteins may act as energy buffers in humans. Uncoupling proteins provide new clues for causation of obesity (GURA T1998).²⁶

UCP-1 is expressed exclusively in brown adipose. Tissue (BAT). Transgenic mice with reduced BAT is abundant at birth but progressively disappears in adults. Recent availability of FDG PET /CT has demonstrated the presence of BAT in a substantial proportion of adult humans and is primarily located in supraclavicular and neck region (Fig.4.) BAT is seen in cancer patients undergoing FDG PET/CT. This BAT may contribute to cancer-induced cachexia. FDG uptake by BAT can be reduced pharmacologically using B blockers (propranolol), reserpine, benzodiazepine & fentanyl). The tumour uptake of FDG is not affected by such pre-medications. Role BAT in human obesity is discussed by Cinti (2006).²⁷

Tertaterol, a new 3 adrenoreceptor agonist increases mRNA of UCP-1, and down regulates PPAR γ and α 2 gene in adipose tissue thereby increasing thermogenesis. UCP-2, homology, of UCP-1 is expressed in numerous tissues including WAT, BAT and muscle. The UCP-2 locus on human chromosome 11

and mouse chromosome 7 is linked to obesity and hyperinsulinism (Fleury CV ET AL., 1997)²⁸ POSSIBLY, UCP-2 expression determines development of obesity. LEPTIN regulates UCP2 expression in adipose tissue.

UCP-3 is expressed in skeletal muscle (Kubota T et al., 1998).²⁹ Single nucleotide polymorphism in UCP-3 gene influences fat distribution in women of European & Asian origin (Bass et al., 1997)³⁰ (Cassell pg et al., 2000).³¹ Increased UCP2 and UCP3 mRNA expression occurs during fasting in obese and lean humans.

Increased UCP3 expression in skeletal muscles decrease muscle energy efficacy and affects thermoregulation and substrate oxidation (Klaus S et al., 2005).³²

UCP3 is the mediator of thermogenesis regulated by thyroid hormones, β adrenergic agonist and leptin (Gong DW et al., 1997).³³

Muscle as a Target of Insulin Resistance

Muscle is the largest tissue in the human body (less than 25% at birth more than 40% in young adults and about 30% in the aged). Skeletal muscle protein is the major non-fat store of energy. Prolonged caloric nutrition leads to large losses in muscle mass.

Insulin is anabolic for muscle, the mechanism of which has been studied by Chow et al.³⁴ One snag in the interpretation of BMI>25 as a measure of obesity is the assumption that the increase is mainly due to fat. Lele et al., (2007)³⁵ emphasized the importance of assessing the muscle component of BMI by simple somatoscopy or somatotyping. Unlike Western populations, only 25 percent of Indian T2DM have BMI>25, 75 percent of Indian T2DM have a normal or low BMI(<23) but they have increased visceral fat as indicated by increased waist girth (>90cm in adultmales,>85 cm in adult females). Strong muscle component in overweight females with T2DM and CAD has been shown (Goldberg & Gordon 1964)³⁶; (Lele RD 1965)³⁷.

Glucose transport via GLUT4 is critical insulin dependent rate controlling step for glucose uptake by muscle and insulin-stimulated glycogen synthesis in muscle. Glycogenin is a protein primer for glycogen synthesis and is a determinant of maximum glycogen storage capacity. InT2DM there is a marked decrease in muscle glycogen syntheses (as determined by C-13 MRS and C-13 glucose-1) this defect is also seen in first degree relatives and offsprings of T2DM patients. Increased intramyocellular lipid(MCL) is a feature of insulin resistance. This is seen also in lean healthy offsprings of T2DM.

Insulin stimulated rate of glucose uptake muscle is 60% lower on insulin resistance compared to normal. There is 80% increase intramyocellular lipid (MCL) and 30% reduction in mitochondrial oxidative phosphorylation, as assessed by P-31 MRS (acquisition time 120 minutes). Rate of ATP synthesis (ratio of inorganic phosphate to phosphocreatine in soleus muscle) is reduced by 20% which reflects a lower ratio of type 1 fibres (mostly oxidative) to type 2 fibres (mostly oxidative) in insulin resistance.

Increased number of type IIb muscle fibres in overweight, insulin resistant first degree relatives of T2DM patients with reduced mitochondrial content lean insulin-resistant offspring of T2DM patients also show impaired mitochondrial activity (Peter Kofey et al., 2004).³⁸ PGC1 (cold-inducible PPAR coactivator of nuclear receptors) has important role in mitochondrial biogenesis, thermogenesis and gluconeogenesis. Upregulation of PGC α converts WAT TO BAT. External physiological stimuli activate PGC which in turn activates NRF1 and NRF2 with increase in mt TFA-direct regulator of mt DNA replication / transcription.

Since skeletal is the primary site of insulin resistance, greater the muscle, greater the importance of physical exercise the muscle mass, greater the importance of physical exercise to insulin resistance and greater the importance dietary supplements of omega-3 PUFA to optimize the phospholipid composition of the muscle membrane (increasing residence of GLUT in plasma membrane).

Skeletal Muscle Membrane Phospholipids: Role of Dietary PUFA

The fatty acid composition of skeletal muscle membrane phospholipids is altered by n-3 PUFA (EPA and DHA), increasing the fluidity, thereby permitting prolonged residence of GLUT-4 in plasma membrane. Mothers with insulin resistance have children with less EPA and DHA in their muscle membrane and at increased risk for development of insulin resistance. (Baur et al., 1999)³⁹. Pima Indians have reduced capacity to incorporate n-3 PUFA into muscle membrane, EPA and DHA induce UCP2 and UCP3 expression which induce fatty acid oxidation in both liver and skeletal muscle, suppress hepatic lipogenesis, reduce hepatic triglyceride output. Peroxisomal fatty acid oxidation and mitochondrial uncoupling of oxidation & phosphorylation are both thermogenic.

Although the amount of peroxisomal fatty acid oxidation in skeletal muscle is unknown, the large size of muscle mass and a two fold increase in the peroxisomal oxidative capacity of skeletal muscle suggest that the peroxisomes could be a significant site of fatty acid oxidation and diet-induced thermogenesis. N3 PUFA in diet induces thermogenic pathways and reduce fat deposition by 25 percent. Transfat induces abdominal obesity and changes insulin sensitivity in monkeys. Interestingly enhancement of fatty acid

oxidation and thermogenesis by dietary PUFA is associated with an improvement in the glucose uptake and insulin sensitivity of muscles.

Ingestion of PPAR ligand is accompanied by an increase in expression of skeletal muscle UCP3 and decrease in hepatic expression of SREBP-1 and decrease in hepatic triglyceride synthesis.

AMPK: Cellular energy Sensor and Regulator

Regulating energy levels is fundamental process in every living organism. At a cellular level ATP must be maintained at relatively high levels (normally about ten-fold above the concentration of ADP) in order to drive essential metabolic processes. AMPK is activated in response to ATP depletion, which cause a concomitant increase in the AMP: ATP ratio. Activated AMPK cause switching off ATP-utilizing pathways (eg. Fatty acid synthesis) and switching on of ATP generating pathways eg. Fatty acid oxidation. AMPK is a sensor as well as regulator of cell energy status and plays a key role in maintenance of energy balance at the cellular as well as whole body level. (Towler and Hardie 2007).⁴⁰ SIRT1, activated by AMPK, plays an important role in metabolic function and longevity in mammals. Both act in concert with PGC - which interacts with transcription factors to stimulate mitochondrial capacity. Fibroblast Growth factor-21 regulates energy metabolism by activating AMPK-SIR-PGC1 pathway. In animal models of obesity FGF21 reduced abdominal fat by 50% (Chau SM et al., 2010).⁴⁴ Further research is needed to expand our understanding of the diagnostic relevance of FGF- dependent pathway in humans, and the potential to ameliorate both obesity and diabetes.

AMPK activity in the hypothalamus regulates feeding behavior ghrelin activates AMPK and NPY leading to increased food intake and decrease in energy expenditure. Leptin by suppressing AMPK & NPY leading to decreases food intake and increases energy expenditure in periphery. Lipoic acid, naturally occurring co-factor of mitochondrial dehydrogenases, inhibits AMPK in hypothalamus while activates AMPK in skeletal muscle (Kim MS et al., 2004)⁴¹ (Carling D 2005).⁴²

When nutrients are available, the Insulin/ IGF-1 signalling pathway is activated. When cells are starved of carbon source, the AMPK pathway is activated-glucose deprivation, ischemia, exercise activate AMPK which inhibits ACC and malonyl CoA decarboxylase as thereby inhibiting TG synthesis and simultaneously increasing FA oxidation in the mitochondria. AMPK is an important biogenesis, mediating its effects through MEF2 and CRFB mediated PGC α and PGC1 β . AMPK also increase expression of UCP2 in adipose tissue and ucp3 in skeletal muscle. AMPK activation of GLUT-4 in muscle is not suppressed by wortmannin (inhibitor of Insulin IRS-P13K) but by compound C, a selective inhibitor of AMPK. AMPK activation underlies many of

the health benefits of regular physical exercise, as well as beneficial effects of caloric restriction. In at least 3 animal models of resistance to diet induced obesity (USP-1, UCP-3 overexpression or mice with a knock out of stearoyl CoA desaturase 1), there is persistent activation of AMPK. Leptin, adiponectin and osmotin (plat homolog of adiponectin), AICAR, metformin and exercise all activate AMPK (Fig.5.) AMPK is a key player in the development of new treatments of obesity and metabolic syndrome (Lele RD2010).⁴³

Importance of Physical Exercise

Charaka states "Physical exercise increases the body's strength and firmness. It should be practiced regularly in the right measure. Lightness, capacity for work, firmness, tolerance to hardship, subsidence of humoral discordance and stimulation of gastric fire accrue from exercise". Fatigue, exhaustion, wasting thirst, asthma, cough, fever & vomiting result from over-exercise". A normal man at rest inhales between 6 and 8 liters of air per minute, from which about 0.3 litre of oxygen is transformed in the lung *aveli* to the blood. During maximal physical activity the same man takes in 100 litres of air per minute and extracts five litres of oxygen. Hill studied the effect of breathing pure oxygen during exercise. The immediate effect is to lower considerably the rate of ventilation. Athletes who have breathed oxygen enriched exercise reported a pronounced relief subjective distress and a decrease in ventilation. Oxygen breathing extended the work capacity of trained athletes. On the other hand the Mexico Olympic showed the adverse effects of high altitude and hypoxia on competitive athletics.

When the body is at rest, the muscle take up no more than about 20 per cent of the total oxygen consumption (60 to 70 ml of O₂ per minute out of 300ml per minute). During exercise, as in running or swimming the active needs about 3000 ml per minute or about 50 times their resting requirement.

Thanks to the presence of myoglobin the special oxygen store, the muscle cell is extraordinarily tolerant to a temporary shortage of oxygen supply. The amount of myoglobin in muscle tissue can be increased by physical training.

The increased requirements of exercising muscle (FFAs and glucose) are ensured by the production of 3 hormones noradrenaline, adrenaline and glucagon abetted by growth hormone and cortisol. Physical training results in improved myocardial performance, improved oxygen transport as well as increased oxygen extraction by muscle - the myoglobin levels are elevated, mitochondrial size and numbers increase so also their enzyme content and activity. Exercise fibrinolytic activity in plasma which is important in diabetic Patients.

Skeletal muscle contains 2 types of fibres: type 1 (slow twitch) fibres are red because they contain myoglobin (a reservoir of oxygen) and high number of

mitochondria. They maintain relatively sustained contraction (such as maintaining of posture) and their metabolism is aerobic.

Type ii (fast twitch) and have very few mitochondria, exhibit short duration of contraction and derive their energy from phosphor cratine and anaerobic glycolysis of glycogen.

Athlets training for marathons have increase in the number of type 1 fibres certain leg muscles, whereas 100 meter sprinters have a increased in number of type 2 fibres. Exercise increase GLUT-4 and hexokinase ii and glycogenin expression in human skeletal. (Kranion y et al., 2000).⁴⁵ In human skeletal muscle exercise results in increased mitogen-activated protein kinase (MAPK)activity and activation of down stream targets of MAPK. Impact of exercise training on insulin sensitivity and physical fitness and muscle oxidative capacity has been shown in healthy first degree relatives of TDM patients (Ostergard in healthy first degree relative of T2DM patients (Ostergard T et al., 2006).⁴⁶ Physical exercise is the most physiological wat to overcome insulin resistance in muscle.

Benefits of exercise have not only be show in metabolic syndrome but also in cancer. Female breast cancer patients who did regular physical exercise lived longer on chemotherapy compared to sedentary patients (Valenti M at al 2008).⁴⁷

Immunomodulatory effects of aerobic training in obesity have been demonstrated. Thomas Nickel et al., (2011)⁴⁸ have analyzed the effects of 10 week intensified exercise training (ET) in obese subjects. There was significant reduction in waist circumference and oxidized LDL level and increase in serum adiponectin level, and up-regulation of BDCA-1 dendrillic cells and (DCs) TLR-4 and TLR-7, indicating an enhance immunocompetence with higher antibacterial, antiviral and antitumor activity.

The traditional Indian practice of “Surya Namaskar” is an excellent combination of 12 Yogasanas (which maintain flexibility of all tendons and joints in the body) with dynamic aerobic exercise and deserve to be promoted universally.

The future

Effects of stress management training and dietary changes in treating ischaemic heart disease have been shown (Ornish DM et al., 1983).⁴⁹ Beneficial efforts of Yoga life style on reversibility of ischaemic heart disease have been documented in a prospective study of 80 patients with CAD (Yogendra J 2004).⁵⁰

To educate and motivate the general public to adopt a healthy lifestyle including diet (caloric restricted diet with 400g. Fruits & vegetables and essential fatty acids and avoidance of trans-fats), regular physical exercise, avoidance of tobacco and alcohol use and stress management, takes time and persistent effort. To educate and motivate the patient to implement the advice takes at least 10 minutes per visit, while it takes only ten second to write a drug prescription. There is a very powerful drug lobby but no lobby to promote nutrition exercise and stress control. The medical community should be reminded that the word "doctor" is derived from "docere"-to teach.

A unique feature of Ayurveda is emphasis on promotion of positive health, physical, mental and social and spiritual. "The wise man should control the impulses of greed, grief, fear, anger, vanity, impudence, malice and excessive attachment".

"He alone can remain healthy, who regulates his diet, exercise and recreation, who controls his sensual pleasures, who is just, generous, truthful and forgiving and who can get along with his kins".

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CLASSIFICATION - ANCIENT & MODERN

Introduction

Classification is defined as the ordering or arrangement of objects into groups or sets on the basis of their relationships. These relationships can be based on observed *or inferred* properties. Once classes are established, the allocation or assignment of unidentified objects to the correct class is "identification". Some philosophers, statisticians and mathematicians also employ the term classification for what is here called identification.

The term taxonomy (Greek *taxis* for arrangement or order, *nomos* for law) is used to indicate the theoretical study of classification, including its bases, principles, procedures and rules. This would include classification as well as identification. It is the science of 'how to classify and identify'.

The origin of the science of classification is generally traced back to the writings of ancient Greeks, not realising the tremendous contributions made by ancient Indians. The one thing that impressed me most during my study of Ayurveda is the tremendous flair of the ancient Indian Masters for classification, and their vast array of nomenclature.

Nomenclature is the naming of objects (in the context of medicine, naming of morbid conditions). Ayurveda has extensive nomenclature which covers many anatomical, pathological, clinical and therapeutic areas. The concepts of classification and nomenclature are closely related; the element of grouping distinguishes classification from nomenclature. Classification is an important aspect of most, sciences, and the subject of classification in Medicine continues to engage the minds of many thinking people. How do we classify and how *should* we classify? Classification is based on the recognition of similarities. What is similarity? How do human beings recognize similarity?

Impact of Computer on Taxonomy

The interface with the modern computer has forced clinicians to reexamine more critically their concepts of classification. Computers play a central role in modern classification for four reasons. Firstly they have helped to find solution to problems that were analytically intractable. Secondly, computers are able to carry out computations whose numerical solutions were known but exceedingly tedious. Also computers have been able to classify simultaneously for larger numbers of objects, using many more features of these objects, than any human taxonomists. Thirdly, algorithms of computer classification have led to *object wise* and *optimise* the classification process. Fourthly, because of the general development of pattern recognition and

perceptron technology, the availability of computers has given rise to fundamental investigations into how human beings perceive the world around them. In contemporary science, taxonomy has become an important creative intellectual discipline. If it is the purpose of science to discover the true nature of things then a classification should describe objects in such a way that their true relationships are displayed.

Disease classification— Nosology

As physicians we observe phenomena in the patient (symptoms and signs) and we develop ideas and theories to account for these observations. Hippocrates is given the credit for bringing medical observations alongside the observations of other natural phenomena such as the stars in astronomy. He states: "It is the business of the physician to know in the first place, things most important, most easily known, which are to be perceived by the sight, touch, hearing, smell and taste, and the understanding; things which are to be known by all the means by which we know all other things." Identical approach has been emphasised by Charaka and Sushruta.

In the ancient nosology, there were two steps in the classification process - the observational or *empiric approach*, the classified entity being a phenomenon that has actually been *witnessed*. An important intellectual step following observation is the process of *induction* to make *generalizations*. In the words of Hippocrates: "What escapes the eye is mastered by the eye of the mind; the attendant tries to track it by reasoning. Some symptoms indicate that a part is affected; others that a part may be affected thereafter. When this information is not afforded and Nature will yield nothing of her own accord, medicine has found methods of compelling Nature to give up her secrets".

In the *inferential* or *hypothetical approach*, the classified entity is a *deduction* or *speculation about the cause*. The Ayurvedic hypothesis of causation was based on "*Tridosha*"- *Vata*, *Pitta* & *Kapha*. It is important to make a distinction between *observed facts* (about which there can be no disagreement) and *concepts of their causation* (about which there can be genuine disagreement). Idealised conceptual classifications often relate to examination of an underlying hypothesis such as the concept of phylogeny implicit in botanical and zoological taxonomies. Problems in medicine are at once more changeable and immediate, and they relate to *processes* rather than to objects. Knowledge in medicine has not yet reached a stage that would permit development of so comprehensive a theoretical framework. The main thrust of the various chapters in this book is to indicate how far we have come from ancient *speculative concepts* like the "*Tridosha*", to the modern concepts based on *observations* and *experimental verification*. Today we have a much better understanding of causation of symptoms and signs and their underlying pathophysiology and their causative factors (etiology), than ever before.

Various Objectives of Classification of Diseases

It is axiomatic that classification is subordinate to a purpose. Thus to evaluate a classification one need consider its conformity to only a single criterion - that of *utility*. Does the taxonomy do what you want it to do? Any attempt to develop a classification should commence with a clear statement of its purpose. There are two main contexts in which the physician constructs conceptual taxonomies. First, he would need a scheme to interrelate biomedical phenomena in such a way as to enhance his *understanding* and to suggest avenues for further study and research. Secondly *clinical decision-making* will call for a rather simpler therapeutic scheme which will indicate, for instance, in the context of rheumatoid arthritis, that this is an "aspirin" patient and that is a "penicillamine" patient. Similarly in the context of fever, this is an "antibiotic" patient and that is an "aspirin" patient.

Take for instance this *binary* classification of Charaka: "Diseases are divided into two groups on the score of their *effects*: curable and incurable; on the score of their *intensity*; mild or severe; according to the *seat of affection*: mind or body; according to their *cause*: endogenous or exogenous".

For public health purposes and health service planning a more practically oriented classification like *causes of death* will suffice. William Farr (1807-1883) made the best possible use of the imperfect classification of diseases available in England during his time and utilised information by arranging it in five groups - epidemic diseases, constitutional (general) diseases, local diseases according to anatomical site, developmental diseases and diseases that are the direct result of violence.' Thus developed, the statistical classification of diseases, for purposes of prevention.

The International Classification of Diseases (ICD) was developed as a means of facilitating comparability in mortality studies. The ICD is subject to decennial revision under the aegis of WHO. Previous revisions have tended lack credibility with clinicians because the latter did not understand their limited purpose for public health measures. The 9th revision of ICD which came into use in 1979, offers options which in reality are two interdigitating but complementary classifications.

The scientific purist who will wait for medical statistics until they are nosologically exact is no wiser than Horace's rustic "waiting for the river to flow away". In selecting a classification scheme one has to make a choice, balancing gains and losses. The story of six blind men and the elephant is familiar to everyone; each observer perceived elements of the whole, but perception was selective. We are similarly selective in developing concepts and in integrating them into classification schemes.

Ayurvedic Classification of Diseases

Charaka Samhita has described over 200 diseases and over 150 pathological conditions and congenital defects. I have tried to arrange them under different systems as per WHO International Classification of Diseases (ICD)-(Table I). A recent WHO Reason-For-Encounter classification is discussed subsequently. It will be noticed from the list that many disease entities were descriptive of *topology* the sites of trouble, such as "*Karnaroga*" (diseases of the ear), "*Ardita*" (facial palsy). Some are descriptive of *symptoms*, such as "*jvara*" (fever), "*apasmara*" (epilepsy), "*Ardhavabheda*" (hemicrania). Some are descriptive of *physical appearance* - such as "*Shleepada*" (elephant leg). Many are *combinations of topology and pathology* - such as "*galaganda*" (tumour on the neck), "*Chhidrodar*" (perforation in abdomen) etc.

TABLE I

Clinical entities described in Charaka Samhita Systems arranged according to WHO classification (ICD)

I	Infections and Parasitic Diseases
	Sannipata jvara (typhoid fever) Su, 17, 41
	Visamajvara (recurrent fever) Ci, 3, 53
	Visuchika (Cholera) Vi, 2, 10
	Visarpa (acute spreading suppuration) Ci, 21, 29
	Krimi (parasitic infections) Su, 19, 4/9
	Shlipada (elephantiasis of leg) Ci, 12, 98
	Masurika (pox) Ci, 12, 93
	Kaksha (herpes) Su, 20, 14
	Dadru (ringworm) Ci, 7, 23
	Vicharchika (scabies) Ci, 7, 26
	Dhanustambha (Tetanus) Su, 20, 14
II	Neoplasms
	Arbuda (non-suppurative swelling) Ci, 12, 87
	Galaganda (tumour on the side of the neck) Ci, 12, 79
	Vradhna (permanent swelling) Ci, 12, 94 5 types
	Kakanaka (malignant growth) Ci, 7, 20
	Granthi (glandular swelling) Ci, 12, 81
	Vidardika (swelling in the groin) Ci, 12, 79
	Gulma (hard swelling) Ci, 5, 38
	Rakta granthi (tumour in bladder neck) Si, 9, 41
Vatasthila (hard tumour) Si, 9, 36	

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III	Endocrine, Metabolic, Nutritional & Immunological Disorders
	Atisthula (excessive obesity) Su, 21, 4
	Madhumeha (diabetes mellitus) Ni, 4, 44, Chi, 6, 55-56
	1. Pidaka (diabetic eruptions) Su, 17, 82
	2. Kacchapika (carbuncle single opening) Ci, 17, 85
	3. Jalini (carbuncle many openings) Ci, 17, 86
	4. Alaji (dry gangrene) Ci, 17, 88
	Shosha (wasting disease) Ni, 6, 11
Shotha (edema) Ni, 12, 1	
IV	Diseases of Blood and Blood-forming Organs
	Panduroga (haemolytic jaundice) Ci, 16, 7
	Halimaka (jaundice due to anaemia) Ci, 16, 132
	Shonitakleda (pernicious anaemia) Su, 20, 14
	Srotoroga (disease of body fluids) Vi, 5, 8 14 types
V	Mental Disorders
	Manovikara (mental disorders) Su, 1, 52
	Unmada (insanity) Ci, 9, 15 types described
	Durmanas (neurasthenia) Su, 17, 73
	Mada (intoxication) Su, 24, 27 7 types
VI	Nervous System and Sense Organs
	Anidra (insomnia) Ci, 28, 21
	Antarayam (stiff neck) Ci, 28, 43
	Apasmar (epilepsy) Ci, 10, 3
	Apatantraka (opisthotonus) Si, 9, 12
	Ardhavabheda (hemicrania) Si, 9, 74
	Ardita (facial palsy) Su, 20, 11
	Atatvabhinivesha (psychic epilepsy) Ci, 10, 52
	Dandaka (convulsions) Su, 24, 25
	Durmanas (neurasthenia) Su, 17, 73
	Ekangaroga (monoplegia) Su, 20, 11
	Gridhrasi (sciatica) Su, 20, 11
	Kampa (tremors) Su, 24, 15
	Khalli (neuralgia) Ci, 28, 57
	Khanjatva (lameness) Su, 20, 11
	Lalatabheda (frontal headache) Su, 20, 11
	Mada (intoxication) Su, 24, 27
	Moorchha (fainting) Su, 24, 35
	Mookatva (dumbness) Su, 20, 11
	Nidradhikya (hypersomnia) Su, 20, 17
Osha (heat stroke) Su, 20, 14	

CLASSIFICATION - ANCIENT & MODERN

	Pakshavadha (hemiplegia) Su, 20, 11
	Sankhabheda (migraine) Su 20, 1
	Sarvangaroga (general paralysis) Ci, 28, 29
	Shiroroga (diseases of the head) Su, 17, 6
	Shirastambha (cerebral thrombosis) Ci, 25, 29
	Suryavarta (recurrent neuralgic pain) Si, 9, 79
	Swarakshaya (aphonia) Su, 24, 15
	Tamas (asthenia) Su, 20, 11
	Tamotidarshana (repeated fainting fits) Su, 24, 15
	Tandratiyoga (drowsiness) Su, 24, 25
	Timira (paralysis of vision) Su, 20, 11
	Urustambha (paralysis of thigh)
	Vakbhanga (failing speech) Su, 20, 21
Special Senses	
Ear	Karnaroga (diseases of ear) Ci, 26, 127
	Karnabadhira (deafness) Ci, 26, 128
	Karnashopha (inflammatory swelling of ear) Ci, 29, 127
	Karna Srava (pus discharge from ear) Ci, 26, 127
	Putishravana (suppuration of middle ear) Ci, 26, 127
Eye	Aksipaka (ophthalmitis) Su, 20, 14
	Aksiroga (eye affections) Ci, 26, 130 96 varieties mentioned
	Aksibheda (squint eye) Su, 20, 1
Nose	Nasaroga (diseases of the nose) Ci, Chapter 26
	Dushtapratishyaya (pernicious rhinitis) Ci, 26, 10
	Ghranapaka (anosmia) Ci, 26, 115
	Nasarshas (polypus in nose) Ci, 14, 6
	Nasarbuda (tumour in nose) Ci, 26, 116
	Nasa Srava (nasal catarrh) Ci, 26, 111
	Nasashosha (atrophy of sense of smell) Ci, 26, 111
	Pinasa (acute rhinitis) Ci, 26, 114
	Pratinaha (obstruction to nasal passage) Ci, 26, 112
VII	Diseases of Circulatory System
	Hridrava (tachycardia) Su, 20, 11
	Hridroga (heart disease) Su, 20, 11
	Hridmoha (heart block) Su, 20, 11
	Parshvavimarda (painful spasm in chest with dyspnoea) Su, 20, 11
	Udaraveshta (cardiac pain referred to stomach) Su, 20, 11
	Dhamani pratichaya (dilation of arteries) Su, 20, 177

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VIII	Diseases of Respiratory System
	Kasa (chronic cough) Ci, 18
	Rajayakshma (pulmonary tuberculosis) Ci, 8, 14
	Shvasa (asthma) Ci, 17, 46 5 types according to symptoms
	Chhinna Shvasa (interrupted breathing) Ci, 11, 54
	Galagraha (acute swelling inside throat) Su, 18, 22
	Galapaka (suppuration in throat) Su, 20, 14
	Galashundika (tonsillitis) Su, 18, 20
IX	Diseases of the Digestive System
	Adhijihva (abscess under the tongue) Ci, 12, 77
	Agnimandya (dyspepsia) Su, 20, 17
	Ajatodaka (dehydration) Ci, 13, 58
	Ajeerna (indigestion) Ci, 15, 42
	Amadosha (disorder of chyme formation) Ci, 2, 10
	Amapitta (biliousness) Ci, 8, 60
	Amatisara (dysentery with mucus) Ci, 19, 5
	Amlapitta (acid-dyspepsia) Ci, 15, 47
	Anaha (acute constipation) Ci, 28, 20
	Annapanavidah (intestinal inflammation) Su, 24, 14
	Antravidhhi (hernia) Ci, 12, 94
	Arochak (anorexia) Ci, 26, 124
	Arsha (haemorrhoids) Ci, 14, 7
	Aruchi (distaste for food) Ci, 8, 60
	Asyavipaka (stomatitis) Su, 20, 14
	Atisara (dysentery), Ci, 19, 4
	Atripiti (morbid hunger) Su, 20, 14
	Baddhagudodar (peritonitis) Ci, 13, 39
	Bhagandara (anal fistula) Ci, 12, 96
	Chhidrodar (perforation-peritonitis) Ci, 13, 42
	Grahanidosha (diarrhoea) Ci, 15, 51
	Gudabhramsa (prolapsed anus) Su, 20, 11
	Gudapaka (proctitis) Su, 20, 14
	Jalodara (ascites) Ci, 13, 45
	Jatharagnivikara (morbid appetite) Vi, 6, 12
	Kaamala (jaundice) Ci, 16, 34 3 types
	Kumbhakaamala (malignant jaundice) Ci, 26, 36
	Mukharoga (oral disease) Ci, 26, 119
	Raktatisara (dysentery with blood) Ci, 19, 70
	Udararoga (acute abdomen) Ci, 13, 9
	Udavarta (paralysis of intestines) Ci, 26, 6

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X	Diseases of Genito-urinary System
	Ashmari (urinary calculus) Ci, 26, 36 - 2 types according to etiology
	Ikshuvalikarasameha (glycosuria) Ni, 4, 10
	Medhrapaka (urethritis) Su, 20, 14
	Mutrajathara (retention of urine causing abdominal distension) Si, 9, 30
	Mutrakrcchra (dysuria) Ci, 26, 32 8 types according to etiology
	Mutraksaya (oliguria, anuria) Si, 9, 34
	Mutratita (polyuria) Si, 9, 35
	Mutrotsanga (bloody urine) Si, 9, 34
	Prameha (urinary disorders) Ni, 4, 8 20 different varieties
	Raktagrathi (tumour in bladder neck) Si, 9, 41
	Svetamutravarcastva (white urine) Su, 20, 17
	Vatasthila (hard tumour in urinary passage) Ci, 29, 36
XI	Complication of Pregnancy, Childbirth & Puerperium
	Garbhiniroga (diseases of pregnancy) Sa, 8, 26
	Kshiradosa (disorders of lactation) Ci, 30, 237
	Mritagarbha (abortion) Sa 8, 30
	Yoniroga (diseases of the vagina) Ci, 20
XII	Diseases of Skin and Subcutaneous Tissue
	Alasaka (itching red papules) Ci, 1, 23
	Charmadala (bursting eruption) Ci, 7, 24
	Charmakushtha (eczema with thickened dermis) Ci, 1, 21
	Ekakushtha (localized eczema) Ci, 7, 21
	Kandu (pruritus) Ci, 29, 17
	Khalitva (baldness) Su, 5, 30
	Kapala (erythema) Ci, 7, 14
	Kitibha (hard, rough, discoloured dermatosis) Ci, 7, 22
	Kustha (chronic skin disease) Ci, 7
	Mandala (urticarial dermatosis) Ci, 1, 16
	Pama (mild leprosy) Ci, 7, 25
	Pundarika (ulcerated dermatosis) Ci, 7, 18
	Rsyajivhaka (suppurated dermatosis) Ci, 7, 18
	Raktapitta (purpuric eruptions) Ci, 4, 11 7 types according to etiology
	Romantika (small eruptions over entire skin) Ci, 12, 92
	Sataru (leprous sore) Ci, 7, 26
	Sidhma (psoriasis) Ci, 1, 19
	Svitra (patchy dermatosis) Ci, 1, 173
	Tvagraidarana (scaly skin) Su, 20, 14

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	Udarda (urticaria) Su, 20, 17
	Viloma (alopecia) Ci, 25, 118
	Vipadika (dermatosis with fissures in extremities) Ci, 7, 22
	Visphotaka (boils) Ci, 7
XIII	Diseases of the Musculoskeletal System and Connective Tissue
	Asthibhanga (fracture of bone) Ci, 25, 68
	Asthikshaya (atrophy of bones) Su, 17, 67
	Chyutasandhi (dislocation of joints) Ci, 25, 68
	Gulphagraha (sprained ankle) Su, 20, 11
	Hanubheda (dislocation of jaw) Su, 20, 11
	Janubheda (bow legs) Su, 20, 11
	Januvislesa (knock knees) Su, 20, 11
	Kubjatva (hunch back) Su, 20, 11
	Kotha (localised thickening of muscle) Su, 24, 16
	Mamsadaha (painful muscles) Su, 20, 14
	Mamsakleda (softening of muscle tissue) Su, 20, 19
	Padabhramsa (flat foot) Su, 20, 11
	Pangulya (deformed foot) Su, 20, 11
	Prstagraha (stiff back) Su, 20, 11
	Urusada (atrophy of thigh muscles) Su, 20, 11
	Vatabalasa (rheumatism), Ci, 29, 11 3 types
XIV	Congenital Anomalies
	Oshthabheda (Hare-lip) Su, 20, 11
	Vamanata (dwarfism) Su, 20, 11
XV	Certain Conditions Originating in the Perinatal Period
	Nadiroga (diseases of new born babies) Sa, 8, 45
XVI	Symptoms and Signs and Ill-defined Conditions

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CLASSIFICATION OF DISEASES

Syndromes

Semiology or classification of diseases based on symptoms and signs were in vogue for many centuries. One of the most creative acts in Medicine has been the *detection of association of symptoms and signs* and developing them into *syndromes*. For instance Sushruta recognised the syndrome of diabetes mellitus or "*Madhumeha*" wherein he correlated the appearance of sugar in the urine (from which the disease derived its name) with the clinical symptomatology as well as causative factors:

"A person who is habituated to pampering his belly even if a previous meal has not been thoroughly digested, who is addicted to a habit of sleeping in the day or leading a sedentary life, who is averse to taking any kind of physical exercise, develops such symptoms like thirst, ravenous appetite, perspiration, fetid odours in the body, shortness of breath, dullness and heaviness in the body, inert feelings in the limbs he suffers from obstruction of the internal channels with deposits of fat. Hence all things or conditions which foster the growth of excessive fat should be carefully avoided." All this knowledge was based on observations, without any knowledge of underlying pathology.

Thomas Sydenham (1624 -1699) was a great English clinician in the tradition of Charaka and Sushruta and Hippocrates. He paid great attention to the observation of signs and symptoms of disease; he studied the time-course (temporal profile) of diseases and lumped associated symptoms and signs into syndromes. He emphasised that '*natural history*' of the disease and not just isolated clinical manifestations, should be used in establishing diagnostic entities. Thus the concept of *cluster* and *temporal correlation* improved the then-existing nosology. Sydenham kept clear of theories and philosophical speculations and relied mainly on observations, including response to specific therapy, such as response to cinchona bark in identification of malaria, response to colchicine in identification of gout, and response to mercury in the identification of a syphilitic lesion. By considering the temporal profile and natural history, Sydenham descriptively separated gout from rheumatism, and the cluster of measles and scarletina from other exanthemata. He identified several other clusters like "Sydenham's chorea" or Saint Vitus' dance, and quartan malaria. Relying on clinical manifestations alone, Sydenham's successors in the 18th Century developed elaborate nosologies to classify "disease" according to arbitrary clusters of symptoms and signs.

Carl Linnaeus (1707-1788) was a Swedish doctor and professor of medicine, but his versatility extended to many other branches of natural science.

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such as botany, zoology, geology and mineralogy. His publication "*Systema Naturae*" in 1735 created a new era in the history of natural sciences. Linnaeus was a great classifier. In both his famous works, *Systema Naturae* and *Species Plantarum*, he introduced the binomial system of nomenclature for plants and animals. He gave each species name consisting of two words, a generic name and a specific name which represented a major simplification and precision in terminology. After creating an effective observational taxonomy for botany and zoology, Linnaeus produced a medical classification system that had 1 major category and 325 subdivisions of clinical "diseases". One of his treatises was entitled *General Morborum*. Francis Boissier de Lacroix (1706 -1777), better known as Sauvage: used similar approach to attempt a classification of disease systematically. His comprehensive treatise was published under the title: *Nosologia Methodica*. It contained 10 major classes, subdivided into 44 orders, 315 genera and 2400 species, all based on signs and symptoms.

William Cullen (1710-1790) of Edinburgh, published a classification of diseases in 1785 under the title *Synopsis Nosologiae Methodicae*. Cullen tried to simplify clinical nosologies by giving greater attention to internal logic in selecting categories and by making a Sydenham-like attempt to distinguish individual symptoms and signs from "diseases".

The main defect of the 18th Century nosology was that it was an intellectual construction that depended on clusters but not on correlations, either in time-course or underlying morbid anatomy and pathology.

The Impact of Anatomy on Classification

The Renaissance Period in Europe (1500-1700) witnessed an extraordinary flowering of intellectual activity. The period was characterised by the liberation of the intellect from the shackles of traditional dogma and established authority. The past was no longer supreme and truth was not necessarily all that was given in the ancient books, but something which should be ascertained by direct observation and experiment. Unquestioning acceptance of authority gave way to criticism and experimental enquiry.

In the same year (1543) that Copernicus made his revolutionary observations in astronomy, Andreas Vesalius (1514 -1564) published "*Fabrica Humani Corporis*" or Structure of the Human Body. Sir William Osier in this Century described it as the greatest book ever printed from which modern medicine dates. Vesalius was interested in anatomy, and while still young dissected animals like mice, rats, cats and dogs. He wrote: "My study of anatomy would never have succeeded had I, when working at medicine at Paris, been willing that the human viscera should be merely shown to me and to my fellow students at one or another public dissection by wholly unskilled barbers, and that too in the most superficial way. I had to put my hands to the business".

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In 1537 Vesalius was appointed Professor of Anatomy and Surgery at the University of Padua. He did dissections with his own hands and taught only what he could observe himself in the structures of the human body, and not what Galen had written in the first century A.D. Thus Vesalius ushered the era of medical science based on observation of facts rather than traditional descriptions, based on speculations.

Concept of Morbid Anatomy

Leonardo da Vinci (1452-1519) was a multifaceted genius, an artist, sculptor, scientist, architect, geologist, physicist, mechanical engineer and a biologist, all in one. Leonardo performed many dissections on the human body with a marvellous anatomic technique. He used injections into veins, liquid wax in arteries, and made gross serial sections to study structures of the body and drew beautiful diagrams of the appearances he observed. He studied muscles and bones, made sections of the brain, traced the cerebral veins and studied many other aspects of anatomy. Although his work did not attract much attention at the time, the following passage shows his seminal contribution in extending medical thought. He wrote: "And this old man, a few hours before his death told me that he had lived a hundred years and that he did not feel any bodily ailment other than weakness. And thus while sitting upon a bed without any movement or sign of anything amiss he passed away from this life. I made an autopsy in order to ascertain the cause of so peaceful a death, and found it proceeded from weakness through failure of blood and of the artery that feeds the heart".

The correlation of morbid anatomy with the understanding of disease was a major step in the history of medicine. Because of the lack of appreciation of the relation of anatomy to pathology the ancient Greek physician Philinus of Cos, a pupil of Herophilus, a follower of the Hippocratic school lamented: "All the anatomical knowledge have derived from Herophilus has been useless to me in treating the sick".

Clinico-Pathological Correlation

Giovanni Battista Morgagni's (1682-1771) magnum opus, "On the sites and Origins of Disease", published in 1761, was a landmark in the history of medicine and an important step ahead in the classification of diseases. Morgagni was by no means the first to make morbid anatomical observations, but he was the first to make systematic and meticulous *correlations of symptoms and clinical findings* in 640 case records, *with the morbid anatomic findings at autopsy*. From now on, clinical records took new meaning by being linked with the knowledge (and therefore prediction from symptoms during life) of abnormal appearances in the viscera. Moreover, since Morgagni wrote as a clinician, and headed each of his letters by symptoms rather than morbid anatomy, his work was easily appreciated by the clinicians.

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In a letter, "which treats of epilepsy", he describes a fellow citizen, a grave and worthy priest in his 68th year, "who was seized with an epilepsy which left behind it the greatest slowness of the pulse". Morgagni had the intellectual honesty and courage to confess that he could find no satisfactory morbid anatomical cause for the symptoms. In the latter part of the 20th Century, the patient would be recognized as suffering from "sick sinus syndrome", with extreme bradycardia and cerebral ischaemia causing the convulsions, and would be put on a permanent pace-maker.

From Morgagni's days onwards, the word diagnosis took on a new meaning; the location of the site of origin of the patient's symptoms became an essential part of the diagnostic concept. Thus the site and size of the thoracic and abdominal viscera, both in health and in illness, became of prime importance to the clinician. No longer could the clinician claim that anatomical knowledge was useless in the management of the sick people. Furthermore, the search for clinical methods of examining the body which might give information about the state of the thoracic viscera was begun by Leopold Auenbrugger in 1761, the same year as Morgagni's publication. Auenbrugger wrote: "I here present the reader with a new sign which I have discovered for detecting diseases of the chest. This consists in percussion of the human thorax, whereby according to the character of the particular sounds thence elicited, an opinion is formed of the internal state of that cavity". Sound, he revealed, could bring information of parts which could not be reached by sight of the eye, for example the thoracic cavity.

Auenbrugger's work was neglected during his time but revived in 1808 by Corvisart, Napoleon's physician. Corvisart, founder of the Parisian School of Morbid Anatomical Medicine, applied Morgagni's method to diseases of the heart. He differentiated various valvular lesions, made a distinction between hypertrophy and dilatation, and distinguished hydrothorax consequent on heart failure from primary pleural effusion. He wrote: "It is clear that the majority of the individuals reputed to have died of anasarca and particularly of hydrothorax, and of various species of asthmas and singular dyspnoeas, may have perished from diseases of the heart."

Laennec in 1819 introduced the method of mediate auscultation. It was purely a chance discovery, in no way an outcome of the knowledge of the physical laws of sound, nor for many years were the findings of auscultation satisfactorily explained in terms of physics. But Laennec made anatomic sense of sounds, correlating the auscultatory findings in the chest with disease of the underlying lung. He recognised tuberculosis as a single disease, and identified the abnormal liver anatomy of cirrhosis.

Adams, Cheyne, Corrigan, Graves, Parkinson, Stokes were the other great Irish and British patho-clinicians who joined the French, German, Viennese and

other European patho-clinicians who provided clinico-pathological correlations for nosology.

Bichat (1771 -1802) extended the organ concept of disease to the tissue level. Pinnel and Bichat, the two Frenchmen began a consistent system of anatomic correlation for "disease". A diagnostic nomenclature based on correlation with pathologic anatomy immediately removed two of the many obvious scientific disadvantages of the preceding clinical and etiologic classifications. The "etiologic" concepts of classification were speculative (for instance "excess" of Vata, or "decrease" of Kapha), unaccompanied by verifiable, observable evidence. The "clinical" concepts were based on observation, and often consisted of only a patient's subjective feelings. Anatomic pathology provided correlation with what was observed clinically. The very word "disease" which had originated as an expression of the patient's abnormal sensations, now often was used to designate an abnormality of gross or microscopic structure. Until that moment in the history of science, astronomers were the only few scientists who could confirm their experimental reasoning merely by observing nature. Now, after observing the symptoms and signs at the bedside the clinician too could make a scientific prediction (diagnosis) during life, of what the pathologist would find post mortem in the organs, tissues or cells.

Concept of Patho-physiology

During the time of Vesalius, Padua was an enlightened seat of learning and it was here that Galileo Galilei (1564-1642) designed and worked with his telescope and laid the foundation of a new era of experimental scientific studies. Although he studied medicine for some time at Pisa, Galileo was essentially a mathematician and laid great stress on exact measurement. The experimental spirit of Galileo greatly impressed the Englishman William Harvey (1578-1657) who studied medicine in Padua in 1602. Harvey demonstrated that blood circulates in the body, thereby ushering the era of experimental method in medicine. In his famous book "Exercitatio Anatomic de Motu Cordis et Sanguinis in Animalis", he wrote: "I frequently and seriously thought, what might be the quantity of blood which was transmitted, in how short a time its passage might be effected, and the like; and not finding it possible that this could be supplied by the juices of the ingested aliment without the veins on the one hand becoming drained, and the arteries on the other hand becoming ruptured through the excessive charges of blood, unless the blood should somehow find its way from the arteries into the veins and so return to the right side of the heart; I began to think whether there might not be a motion, as it were, in a circle. Now this I afterwards found to be true and I finally saw, that the blood forced by the action of the left ventricle into the arteries was distributed to the body at large and its several parts, in the same manner as it is sent through the veins and along the vena cava, and so round to the left ventricle in the manner already indicated, which motion we may be allowed to call circular".

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“Since all things, both arguments and ocular demonstration, show that the blood passes throughout the lungs and heart by the action of the ventricles, and is sent for distribution to all parts of the body it is absolutely necessary to conclude that the blood of the animals is impelled in a circle and is in a state of ceaseless motion, that this is the act or function which the heart performs by means of its pulse; and that it is the sole and only end of the motion and contraction of the heart”.

To us it is perhaps surprising that Harvey did not attempt to define the clinical effects of the heart's failure as a pump, but he justified his reluctance to enlarge on all such matters, even the function of circulation, by the remark: “Our first duty is to inquire whether the thing be or not, before asking wherefore it is”. Harvey did however, in fact give a good account of left and right ventricular failure in his friend Sir Robert Darcy, who, “when he had reached the middle period of life made frequent complaint of a certain distressing pain in the chest so that dreading at one time syncope, at another time suffocation in his attacks, he led an unquiet and anxious life. The disease, going on from bad to worse, he by and by became cachectic and dropsical and died in one of his paroxysms. In the body of this gentleman we found the wall of the left ventricle of the heart ruptured”.

Wunderlich and other Germans urged that *pathological physiology* be the true basis of medical science. One group of pathologic physiologists, led by Rudolph Virchow, concentrated on delineating causes and mechanisms of disease at the *cellular level*— cellular pathology.

Another group of pathologic physiologists, led by Claude Bernard concentrated on function. Before the end of the 19th Century Bernard and many others had begun to reject the nosology of morbid anatomy for its failure to identify abnormal function. With the advances in biochemistry it became evident that biochemical lesions preceded structural changes and hence may not be detected by morbid anatomy alone (See chapter on “Nutrition”). The increasing array of modern laboratory tests have identified physiologic and biochemical disorders, etiologic agents and many other aspects of disease that cannot be detected from observations of morbid anatomy. Clinical chemistry is a new medical specialty for dealing with many of these tests.

In a pioneering effort to improve clinical diagnostic nomenclature the New York Heart Association in 1965 established a system for classifying etiology, anatomy, physiologic function, and clinical consequences, in the diagnosis of heart disease. As an illustration, let us follow the intellectual process of a Cardiologist when he examines a patient with the symptoms of shortness of breath or angina pectoris. The *sensation* described by the patient is the actual phenomenon perceived by the patient himself, such as discomfort in the chest. By clinical interrogation the cardiologist provides *specification*, that is, adds further characteristics such as substernal location, aggravated by

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exertion, relieved by rest; The next intellectual step is *designation*—the cardiologist gives a name to the specified sensation—angina pectoris. The next intellectual step is to make an inference about the underlying structural abnormality—Coronary artery atherosclerosis.

Similarly the *first order* classification of the *symptom* such as dyspnoea on exertion, is developed into a *second order* of classification, a *syndrome* of congestive failure by clustering all symptoms and signs such as pulmonary basal crepitations and swelling of the feet; and then into a *third order* of classification—*inference* about the *underlying structural abnormality* responsible for the congestive heart failure, such as mitral stenosis, or congenital heart disease; the *fourth order* of classification is an *inference* about the *etiology*: rheumatic valvular disease or maternal rubella infection. The fifth *order* of classification is the *functional status* of the patient—based on observed effort tolerance.

It is worth noting that all the *inferences* are based on verifiable evidence and not on philosophic speculations.

The clinician of today is fortunate in having detailed information about altered anatomy, physiology and biochemistry in the patient through clinical chemistry, endoscopy, radiology, electrophysiology (ECG, EEG, EMG), ultrasonography, gamma scintigraphy, computerised X-ray tomography and NMR imaging. He can thus correlate and integrate the signs and symptoms with altered anatomy, physiology and biochemistry and pathology.

In the absence of such an integration, the present day practitioners of Ayurveda or Homoeopathy must find themselves in the same predicament that Philinus of Cos was in, two thousand years ago.

Problems in Disease Classification

The American College of Pathologists has presented a nomenclature and classification of diseases on the basis of four modalities; topology, morphology, etiology and function. The main defects of the pathologists' taxonomy are its omissions, not its contents. For example, gout, syphilis, haemophilia, diabetes mellitus, systemic lupus erythematosus are examples of *non-topographic, non-morphologic* diagnosis involving *multiple organs or systems*, with multiple clinical syndromes, and the diagnosis is based on laboratory support. Myasthenia gravis is the name of a symptom; erythema nodosum and hypertension are names of physical findings; some of the non-morphologic diagnoses represent a straight-forward classification of observed Para-clinical evidence, for example porphyria, hyperglycaemia, hypertriglyceridemia, or proteinuria; or the physiological diagnosis of paroxysmal atrial tachycardia with 3:1 block, or "sick sinus syndrome". Chronic alcoholism

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and drug addictions are names of habits; renal failure, hepatic failure, "irritable bowel", imply physiologic dysfunction resulting from diverse etiological factors.

Disorders of the Cell

Since the cell is the functioning unit of life, all disease is the result of damage, disablement and malfunction of the cells and tissues of the body. According to our current understanding, disorders of the cell can arise from genetically determined defects, lack of essential nutrients, adverse physical environment, harmful substances or living agents causing injury. The various mechanisms whereby injury could be caused are listed in Table II.

TABLE II
Disorders of the Cell

I.	Genetically determined defects
	Point mutations - defects in proteins & enzymes
	Visible changes in Karyotype
II.	Lack of essential nutrients
	Poverty of diet
	Defective absorption of nutrients
	Deficiency of internal secretions
	Interruption or retarded supply of blood - ischaemia, infarction
	Defective penetration of nutrients into cells
III.	Adverse Physical Environment
	Trauma
	Heat
	Cold
	Ionizing radiation
	Electrical shock
IV.	Harmful Substances
	Direct action on cell architecture
	Interference with enzyme action
	Lethal synthesis
	Carcinogenesis
	Antigenic action
V.	Living Agents
A.	Injury by cells of the body itself
	Depriving other cells of essential nutrients
	Liberating or forming harmful substances

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	Forming antibodies or sensitizing cells that subsequently cause damage by reacting with antigen
B.	Injury by parasitic cells
	Depriving other cells of nutrients
	Liberating harmful substances, exotoxins, endotoxins Harmful antigenic actions - lymphokines
	Intracellular growth.

Molecular Disease

The conceptual union of genetics and metabolism is perhaps the most fruitful development in biologic science of the past decades. Sir Archibald Garrod's monograph "Inborn Errors of Metabolism" published in 1909 marked the beginning of the era of biochemical genetics, and the concept of biochemical lesions. Direct evidence that human mutations actually produce an alteration in the primary structure of proteins was first obtained in 1949 by Linus Pauling and his associates, by their studies on sickle cell haemoglobin. The subsequent study of Ingram established that the electrophoretic abnormality arose because HbS had a valine substitute for glutamic acid residue at Humber 6 position in the amino-acid sequence. Thus the fact was established that inborn errors of metabolism were caused by mutant genes that produced abnormal proteins whose functional activities were altered.

Biochemical Lesions

All injuries, whether mild or lethal, ultimately occur at a biochemical level beyond our present range of detection. Four intracellular systems are thought to be particularly vulnerable: (1) aerobic respiration involving oxidative phosphorylation and production ATP, (2) Synthesis of enzymic and structural proteins, (3) maintenance of the integrity of cellular membranes on which the ionic and osmotic homeostasis of the cell and its organelles are dependent, and (4) preservation of the integrity of the cells genetic apparatus.

Whatever the precise point of attack, injury at one locus leads to wide-ranging secondary effects. Because maintenance of the ionic and fluid balance of the cell is energy-dependent, impairment of aerobic respiration and the synthesis of ATP soon lead to profound alterations in the intracellular content of ions and water. Loss of aerobic respiration is usually followed by reversion to anaerobic glycolysis with the production of excessive amount of lactic acid. The falling pH has secondary effects on enzyme systems and biochemical reactions. Protein synthesis is impaired, preservation of membrane integrity hampered, and progressive cellular dysfunction ensues. Such a sequence of biochemical events does not occur instantaneously. It is a dynamic process which evolves over a period of time from minutes to hours. The precise time span involved depends on the particular characteristic of the injured cell, such as its metabolic activity and vulnerability to a specific lesion as well as the

defensive mechanisms of the organism as a whole. Morphologic changes become apparent only after some critical biochemical system within the cell has been deranged for some time.

The Full Circle

The searching human mind has always tried to delve deeply into the “whys” and “wherefores” of disease. The search for causes and mechanisms is continuous, for therein lie the origins of the pathophysiology of disease and the implications to the patient and the physician. In the 20th Century the focus is on biomolecular and ultra-structural origins of disease and the evolution of the cellular and tissue alterations from their incipency to their full-blown stages of development. In this way diseases are presented as dynamic processes changing with time, modified by therapy and by host and invader adaptive responses all having effect on the ultimate clinical manifestations.

It must be accepted with humility that there are gaps in our knowledge and much is still unknown, hence the search for greater understanding is unending.

It is interesting to see the full circle that medical science has taken in 2000 years. Conceptually, Charaka and Sushruta thought of disease as disequilibrium of normal body constituents (of the three *doshas*) and restoration of that equilibrium as the objective of medicine. Although their thinking was purely intuitive and speculative, they dealt with health and disease at a molecular level. In the reductionist approach of experimental medicine, we went from the whole person to the level of individual organs and tissues and looked for specific causes. When we reached the level of the cell and subcellular organelles the doctrine of specific causes becomes blurred, because various types of insults may produce the same result in terms of biochemical lesions. In future classification of disease we might emphasize what underlying disturbance of control mechanism we are treating rather than treating a given disease.

Holistic Approach and Disease Classification

Another criticism of the reductionist biological approach to disease classification is becoming more and more vociferous in the rising tide of “holistic medicine”. Doctors primarily deal with patients as *persons* while the medical taxonomy classifies them into diseases. It has been well said, “There are no diseases, there are only sick persons”. Feins-tein has in recent years written extensively to advocate the need for a *clinical taxonomy* as distinct from the taxonomy of morbid anatomy, that was initiated 200 years ago. He says, “In preserving the diagnostic nomenclature of pathological anatomy as the main contemporary system of identifying human ailments, clinicians perpetuate a mode of thinking that classifies disease but not people or illness; and that

classifies clinical inferences, but not clinical observations". A clinician's nomenclature must classify a *host*, and an *illness* and a *disease*. A clinician must have a language that will categorize the variations in human clinical behaviour, and the nuances of human response to sickness and to therapy.

The WHO Reason-for-Encounter Classification

Most classifications are designed to classify the interpretation, by the healthcare provider, of a patient's illness, disease or injury. In 1978 a working party of experts, both in primary healthcare and in classification systems met in Geneva. After several years' work they produced a Reason-For-Encounter Classification (RFE-C), which classifies the reasons for seeking healthcare from the perspective of the patient. The reasons for the encounter are those given by the patient before the physician or other health worker makes any judgment as to their validity or accuracy. It is thus patient-oriented rather than disease or provider oriented. The classification is designed along two axes:

Chapters and components:

Most chapters cover the body systems; others are non-anatomical and are entitled "general", "psychological" and "social". Infectious diseases, neoplasms, injuries and congenital anomalies do not form separate chapters as they do in the International Classification of Diseases, 9th revision (ICD-9), but rather are represented in the diagnosis/disease component of each chapter. Each chapter is subdivided into the same seven components:

1. Symptoms and complaints.
2. Diagnosis, screening and preventive procedures.
3. Treatment procedures and medications.
4. Test results.
5. Administrative.
6. Others.
7. Diagnoses and diseases.

The use of one and the same classification first to identify patient demand and then to classify the result of the health care providers' interpretation and intervention could significantly improve the quality of information available concerning the use and appropriateness of health care services at the primary level.

In India there are 200,000 practitioners of modern medicine and more than 500,000 practitioners of Ayurveda and Homoeopathy. All of them can use the "reason for encounter" classification, which will give health planners in India a useful data base essential to the planning, implementation and evaluation of

services for the prevention and treatment of disease and to the setting up of priorities among these services. It may result in a more intelligent structuring of the primary health care.

Classification of Human Types

Attempts to classify people according to their physical and mental attributes are quite ancient. Ayurveda classifies human constitution into three types, namely the *Vata Prakriti*, the *Pitta Prakriti* and the *Kapha Prakriti*. No true *mono-doshic* individual exists. Therefore it is the general predominance of the activity of a particular dosha in an individual that decides his type and not the absence of the other *doshas*. The *doshic* manifestations themselves are twofold, healthy and unhealthy. Enthusiasm and fear, courage and anger, cheerfulness and dullness exemplify the respective healthy and unhealthy manifestations of the three *doshas*, *Vata*, *Pitta* and *Kapha*, on the psychic plane. Similarly physical agility respectively and lightness of the limbs on the one hand, and pains and aches in the body on the other, are both *Vata* characteristics.

Hippocrates described the habitus phthicus and habitus aploecticus. Kretschmer described the pyknic or athletic and asthenic types. In the 19th Century "Vagotonic" and "Sympathotonic" types of personalities were described and in the 20th Century we talk of "Type A" and "Type B" personalities. In the 20th Century systematic, objective and reproducible measurements of the human physique have been made by Sheldon, Draper, Tanner and Dupertuis; somatotyping as the science is called, has demonstrated interesting relationships between somatotype and disease, both physical and mental. Tuberculosis is more common in "ectomorphs" while cancer seems to spare high ectomorphs.

Somatotyping

Somatotyping is an estimate of body build or physique. The physique is measured in terms of its shape and the relative preponderance of structures developed from the three layers of the germinal plate—the endoderm, the mesoderm and the ectoderm which form its three basic components. The guts and the viscera are developed from the endoderm and predominate in those with dominant endomorphy, the muscles and bones are developed from the mesoderm and predominate in mesomorphy, the skin and nervous system are ectodermal structures and are well developed in the predominant ectomorph.

Somatotyping recognises the continuous variation in the degree of development of these three components in different persons, and in different regions of the same body. Each component, endomorphy, mesomorphy and ectomorphy is graded from 1 to 7 in a seven-point scale. Each physique consists

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of some degree of each component and 1 represents the minimum development, 7 the maximum and 4 the midposition of each component. Sheldon has found that in the natural distribution of human physique the sum of the three component numerals varies from 9 to 12, and there are more 10's and 11's than 12's and 9's. If a physique has 7 in one component, it cannot have more than 4 in any other; if one has 6 in one, not more than 5 in another and even rating of 5 in two of the components is very rare in natural distribution of men. In terms of one rating as a unit there are 88 known somatotypes. If VI rating is used as a unit in a scale of 1 to 13, then there are more than 400 somatotypes (Fig. 4.1).

Somatotyping of 5 regions head and neck, thorax, upper limbs, abdomen, lower limbs may show varying degrees of dysplasia or disproportionate development.

In terms of maleness or femaleness, a rating of 1 to 7 can be given with android and gynoid types at extreme ends (Fig. 4.2).

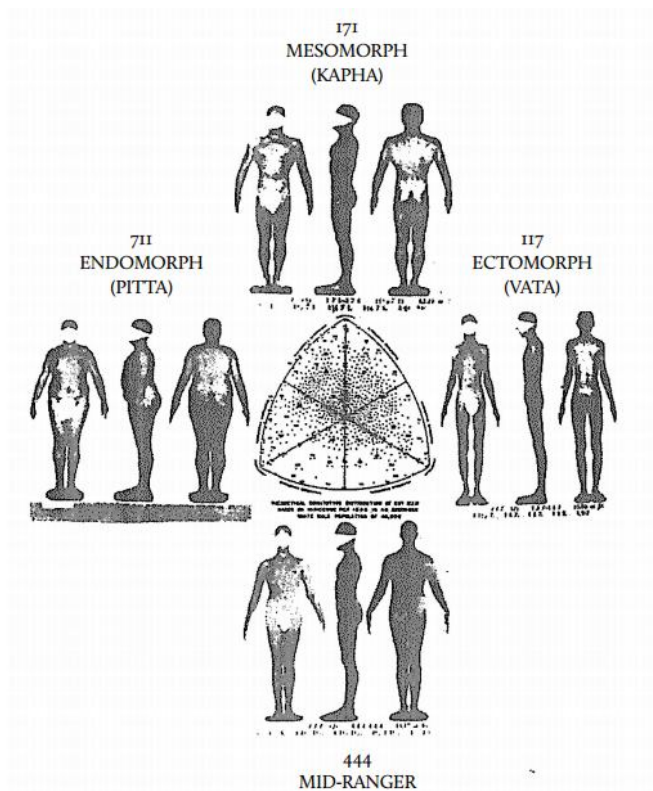


Fig. 4.1 Examples of extreme ECTOMORPH (117), MESOMORPH (171) and ENDOMORPH (711) Most physiques fall in MID-RANGER (444) as shown in the Scatter diagram.

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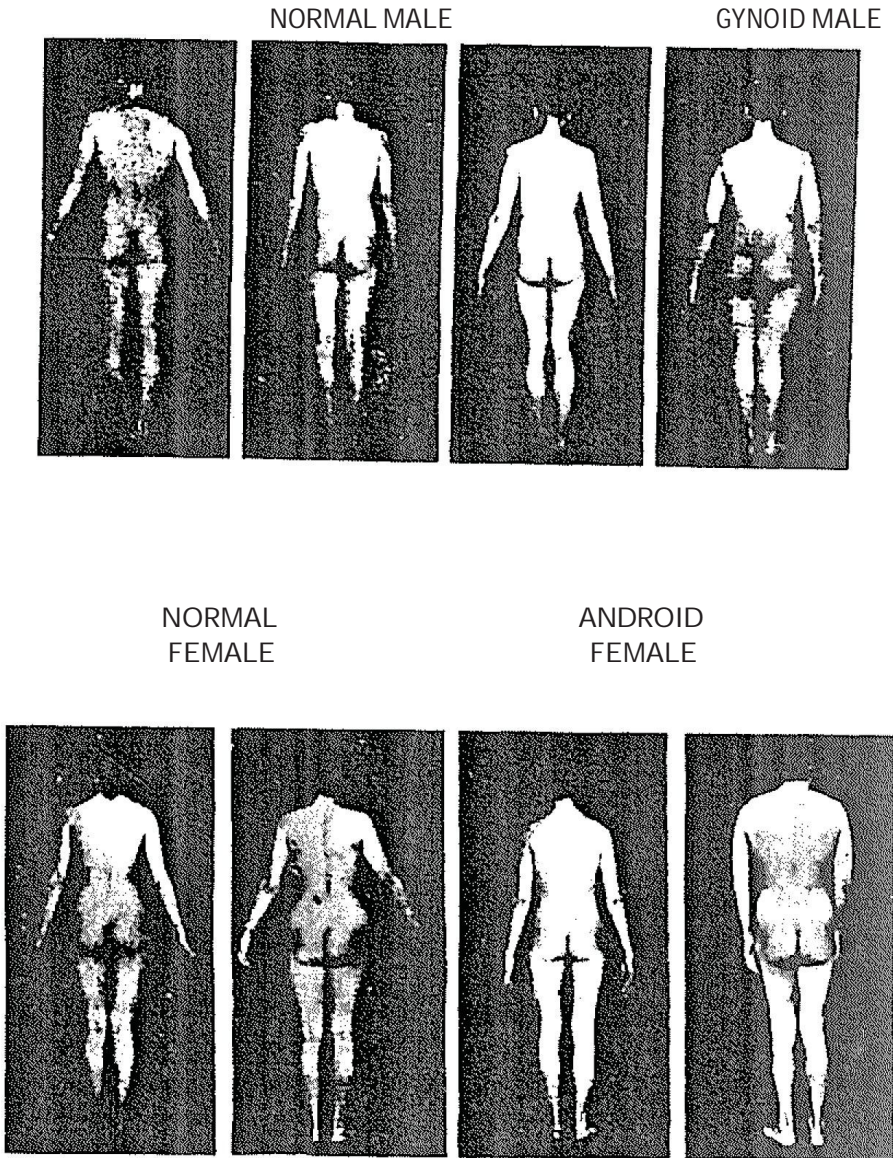


Fig. 4.2 Showing examples of NORMAL MALES and GYNOID MALES (upper row), and NORMAL FEMALES and ANDROID FEMALES (lower row)

Somatotype is estimated from carefully posed, full-length photographs in 3 views—anterior, posterior and left lateral, taken in the nude or near nude and from estimating the ponderal index from the height/Cuberoot of weight. Tanner

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has shown that with some training, observer error between two observers and in the same observer at different times, is not more than half a rating in 90% of the cases.

In a recent study of 800 patients at the Cleveland Clinic in USA, who had recovered from "heart attack" (myocardial infarction), Dr. Wesley Dupurtuys noted a striking predominance in endomorphic mesomorphs— as shown in Fig. 4.3. Some examples of physiques more prone to "heart attacks" are given in Fig. 4.4.

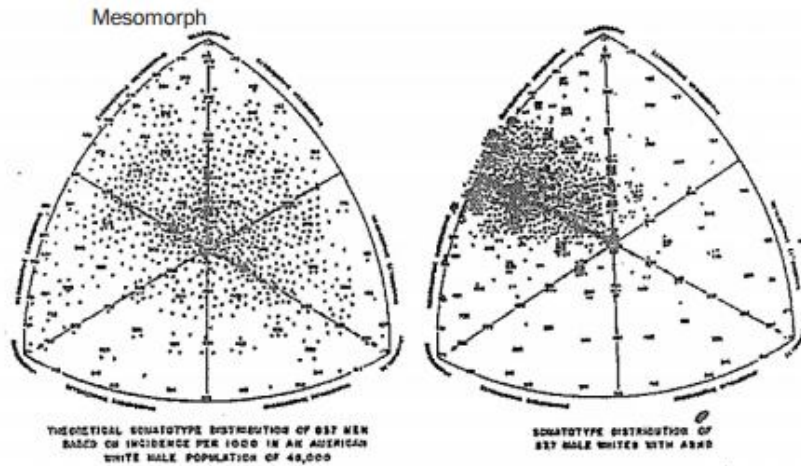


Fig.4.3 Comparison of NORMAL POPULATION (left) with patients of MYOCARDIAL INFARCTION (right) showing predominance of endomorphic mesomorphism

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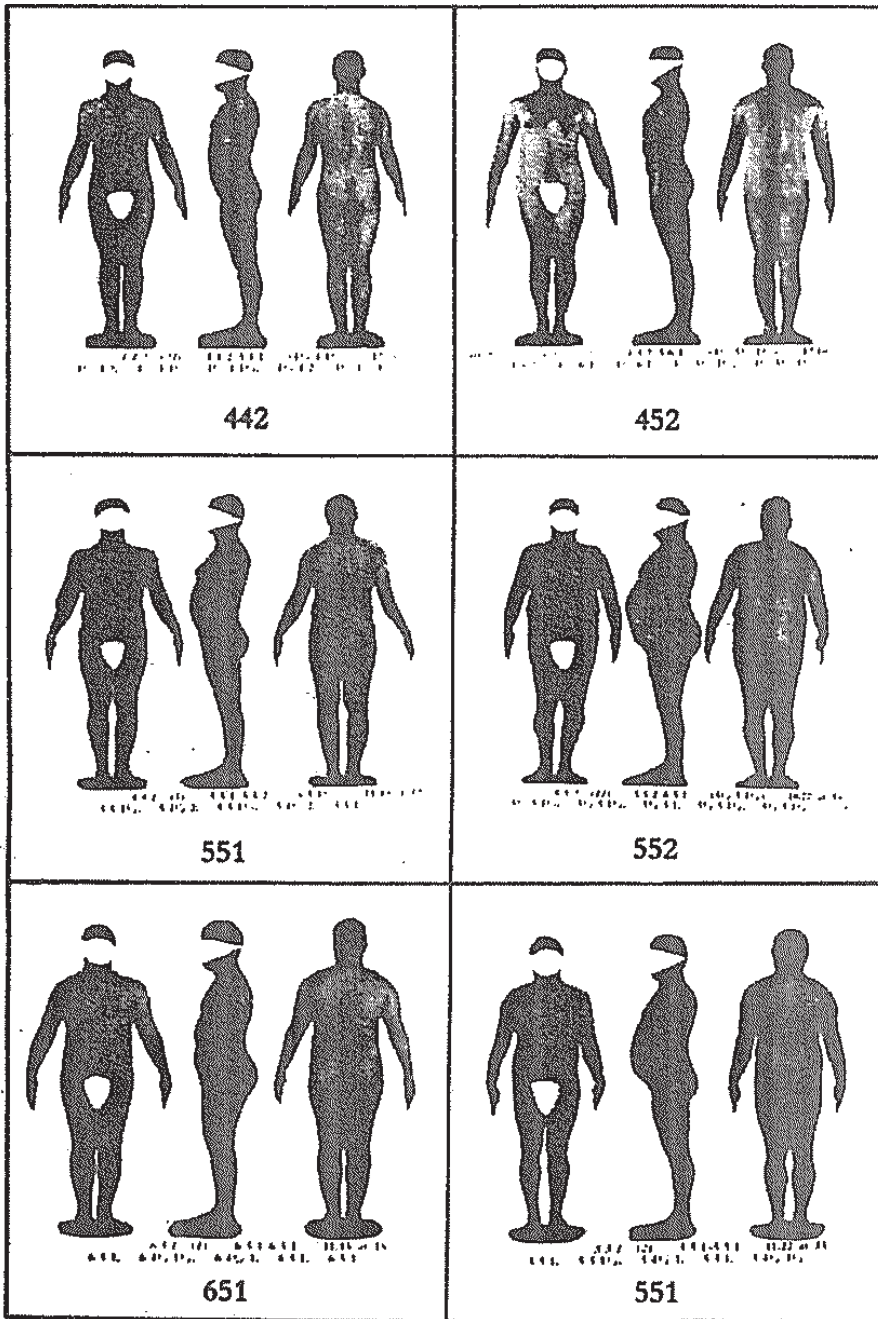


Fig. 4.4 Showing the examples of physiques prone to HEART ATTACKS

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The nude or near nude and from estimating the ponderal index from the height/Cuberoot of weight. Tanner has shown that with some training, observer error between two observers and in the same observer at different times, is not more than half a rating in 90% of the cases.

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The extreme endomorph 711 is rounded and shows the maximum mass for minimum surface area. His head and trunk are rounded, the trunk, abdomen and pelvis have the maximum mass, the limbs are heavy proximally and taper peripherally into small hands and feet. Bones and muscles are poorly developed and all contours are mounded by abundant fat. The skin is soft and delicate. The viscera are large and weigh more than in the other types.

The extreme mesomorph 171 shows the greatest development in muscles and bones. The head is square shaped and massive, the neck is thick, the chest broad and square shaped, the abdomen and pelvis comparatively small, the limbs are heavy and large throughout and end in massive hands and feet. Muscular contours stand out throughout; the skin is thick and firm.

The extreme ectomorph 117 is thin and fragile and has maximum surface area for minimum mass. The body is linear, the limbs long and thin, right upto the hands and feet, the chest and abdomen are thin and flat, the shoulders are rounded, the scapular stand out of the neck just forward to support the head, the face is triangular.

The somatotype is genetically determined, though its full manifestation occurs only after puberty which is the proper time to assess the type. Different races show predominance of one or the other component. On the whole, in cold climates there is higher mesomorphy though some of the Polynesians show high mesomorphy. Exercise cannot increase the mesomorphy though the estimate may be improved by half a rating and wasting due to malnutrition cannot convert an en-domorph or a mesomorph into an ectomorph as it is still possible to detect the basic physique. Women are on the whole more endomorphic and will rarely show extremes of mesomorphy or ectomorphy met with in men.

There is little information on the biochemical counterparts and determinants of the somatotypes. For every degree of rise in endomorphy, there is an average increase in serum cholesterol by 11 mg %. Persons with effort syndrome show blood lactate levels higher than normal males. Women have higher blood lactate

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levels after exercise than males, significantly effort syndrome is common in gynandromorphic males.

Sheldon and his colleagues have observed a close relationship between physique and temperament. The viscerotonic temperament loves comfort and relaxation, eating and sleeping, is tolerant and complacent, craves for affection and approval and needs people when troubled. This is seen in dominant endomorphy.

The *somatotonic* temperament is assertive, energetic, forthright and unrestrained.

The *Cerebrotonic* temperament is restrained, sociophobic, loves privacy, sensitive of feeling, needs solitude when troubled; this is seen predominantly in ectomorphs.

Paranoid schizophrenia tends to occur in mesomorphs and hebephrenic schizophrenia in high ectomorphs. Dysplasia and gynandromorphy are high in schizophrenics.

It is perfectly feasible to judge by inspection (somatoscopy) the predominant primary component and the secondary component. In clinical examination ten types can be commonly used to describe patients: (1) *ectomorph*, (2) *mesomorph* and (3) *endomorph* can be used to describe those in whom the other two components do not each exceed an estimated rating of 2, (4) *endomorph mesomorph*, (5) *ectomorph mesomorph* (6) *ectomorph endomorph*, (7) *mesomorph endomorph*, (8) *mesomorph ectomorph*, (9) *endomorph ectomorph*—in these the main component has a rating of 5 or 6 and the secondary component 3 or 4 and (10) *Midranger* in whom all the three components lie between 3 and 4. Along with height and weight it will give the requisite information about physique. This should replace the current height, weight and "ideal weight" tables.

Recent Advances in Taxonomy

Charaka states: "A classifier may classify a subject admitting of classification in one particular way. Reclassifying his subject over and over again with reference to other differentiating factors, he is able to achieve a fresh classification each time. A subsequent classification does not repudiate the validity of the previous one".

In the above statement of Charaka, we find a profound basic truth about classification theory, the distinction between *monothetic* and *polythetic* classification, clearly enunciated in modern times by Beckner.

Monothetic classifications are those in which the classes established differ by at least one invariant property which is uniform among the members

CLASSIFICATION OF DISEASES

of each class. Such classifications are especially useful in setting up taxonomic keys and certain types of reference and filing systems. Polythetic classifications are those in which the taxa are groups of individuals or objects that share a large proportion of their properties but do not necessarily agree in any one property. No single uniform property is required for the definition of a given group nor will any combination of characteristics necessarily define it. This somewhat disturbing concept is readily apparent when almost any class of objects is examined, including human beings.

A corollary of polythetic classification is the requirement that many properties (characters or indicants) be used to classify objects. This is true of almost any type of objects being classified. Once a classification has been established, few characters are generally necessary to allocate objects to the proper taxa, or identification. Initial classifications based on few characters usually have to be modified once information on additional characteristics was acquired. Diseases not differentiated in earlier times now represent separate clinical entities with the accumulation of new knowledge.

A convenient way of developing classifications is to compute functions that yield similarities or dissimilarities (distances) between all objects taken two at a time. A symmetric matrix of such similarity or dissimilarity coefficient is then analysed to represent their relationships as clusters. Much recent progress in classification has consisted of devising methods of clustering. Properties of clusters include their location in an "n" dimensional space (some measure of central tendency), their dispersion, their shapes, their connectivity and the magnitude of gap between clusters. Clustering algorithms can be agglomerative or divisive. In most clustering techniques especially in polythetic methods, the agglomerative approach is preferred for practical reason in devising a workable computer algorithm.

The whole idea of hierarchic, non-overlapping (mutually exclusive) classification which has been so attractive to the human mind is currently undergoing re-examination. The acceptance of polythetic taxa is a major conceptual advance. Computer techniques of cluster analysis and ordination have been successfully applied to a broad range of disciplines, and it is very desirable that it should be extensively applied in Medicine.

Analysis of Integrative Medical Databases Employing Machine Learning Algorithm for Health Assessment

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1. The whole idea of hierarchic, non-overlapping (mutually exclusive) classification which has been so attractive to the human mind is currently undergoing re-examination. The acceptance of polythetic taxa is a major conceptual advance. Computer techniques of cluster analysis and ordination have been successfully applied to a broad range of disciplines, and it is very desirable that it should be extensively applied in Medicine.
2. A convenient way of developing classifications is to compute functions that yield similarities or dissimilarities (distances) between all objects taken two at a time. A symmetric matrix of such similarity or dissimilarity coefficient is then analysed to represent their relationships as clusters. Much recent progress in classification has consisted of devising methods of clustering. Properties of clusters include their location in an "n" dimensional space (some measure of central tendency), their dispersion, their shapes, their connectivity and the magnitude of gap between clusters. Clustering algorithms can be agglomerative or divisive. In most clustering techniques especially in polythetic methods, the agglomerative approach is preferred for practical reason in devising a workable computer algorithm.
3. Prakriti assessment is one of the key concepts of Indian system of medicine (Ayurveda), which assists in understanding the healthy status of a person. This is highly important while defining preventive and curative treatment modality of a healthy or unhealthy person. However Prakriti assessment process consists of ample imprecise environment, imbedded with inherent subjectivity in defining Prakriti class. Hence precision is completely depend upon expertise of a physician. In recent years, different theories have been postulated to address diverse uncertainties in engineering, economics, environment and medical sciences. We conducted extensive literature review to understand experimental approaches to handle uncertainty in medical data. However as per the reported publications, researchers have not attempted to deal with the vagueness and subjective attributes of Prakriti assessment, which is being practiced since thousands of years in India. It is challenging for Ayurveda expert to apply their wisdom in creating distinct rules, which can be uniformly repeated and equally acceptable across scientific fraternity. In a Prakriti assessment method, we attempted to deal with lack of expert knowledge in the design of the uniform Prakriti classifier.
4. In the proposed research work we are trying to devise a mechanism based on computation model to identify specific set of Prakriti characteristics as per the Prakriti class. There are comprehensive characteristics described in Ayurveda classical texts, which are used to define 7 Prakriti classes. However considering current contemporary lifestyle and modern era, many of the characteristics seems to be

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impractical or not significantly contributing in defining specific class of Prakriti. These parameters are ranging from anatomical characteristics like size of forehead to highly subjective or perception based descriptive parameters like type of dream, politeness etc. We also tried to find association between Ayurveda Prakriti class and Sheldon's body categories.

Ayurveda Prakriti Types

There are distinct attributes described in Ayurveda for each Prakriti class

Attributes	Vata	Pitta	Kapha
Physique	Thin	Medium	Plump
Built	Weakly	Medium	Well developed
Skin	Dry and rough	Soft thin, tendency of mole, acne	Smooth and confirm
Hair	Dry thin, brittle, tendency to split	Thin, soft, oily, early graying	Thick and soft
Complexion	Dark	Fair	Whitish
Appetite	Sometimes good, sometimes weak	Good	Low
Bowel movements	Frequent, irregular	Regular	Regular
Food habits	Irregular	Higher food & water intake	Stable food intake
Physical movements	Quick & excessive	Moderate & precise	Less mobile
Climate resistance	Cold intolerant	Heat intolerant	Tolerance to both
Speech	Talkative	Sharpe , analytical capability	Less vocal with good communication
Initiative	Quick response	Quick	Sluggish
Memory	Quick at grasping & poor recall	Moderate grasping & recall	Slow grasping and good recall
Liking for taste	Sweet, Sour, Salty	Sweet	Pungent , Astringent, Bitter
Graying of hairs	Slow	Fast	Slow

Sheldon's Personality theory

William Herbert Sheldon categorized human body types into three categories termed as somatotypes. Sheldon has described typologies for these somatotypes (ectomorph, mesomorph, and endomorph).

Personality traits as per Sheldon's theory

Sheldon's Somatotypes	Traits	Body frame
Endomorph	relaxed, sociable, tolerant, comfort-loving, peaceful	plump, developed structure, buxom, visceral
Mesomorph	active, assertive, vigorous, combative	muscular
Ectomorph	quiet, fragile, restrained, non-assertive, sensitive	lean, delicate, poor muscles

Methodology

Data collection: Prakriti data of 500 healthy individuals has been collected from Clinics & medical colleges in Pune.

Data preprocessing:

Prakriti data set was preprocess considering following aspects of data

- Incomplete: shortage of attribute values or certain other attributes.
- Noisy: contains error or outlier values that deviate from the expected
- Missing values are identified and corrected using domain insight
- Inconsistent: discrepancies in the use of the code or name. Here good data quality based on the good decisions and data warehouse integration requires consistent data quality.

Feature engineering

The most of the variables in the Prakriti data set are categorical variables. Features engineering methods specific to categorical variables have been applied to create new features from existing feature set to improve model performance. We explored different machine learning techniques to classify Prakriti characteristics as per Prakriti class.

Feature selection

We have used following techniques to identify feature set as per the Prakriti class Random forest, Decision Tree, Genetic Fuzzy approach, ANN

Results

- We observed that Random Forest algorithm gives better accuracy as compare to other methods. Classification accuracy perceived 86 %
- We found association between Prakriti types and Sheldon's somatotype. We observed most associated groups of Vata Prakriti and Ectomorph, Pitta Prakriti & Mesomorph, Kapha Prakriti & Endomorph,
- We also observed the combinations of Sheldon's personality types and its association with Ayurveda Prakriti types
- Vata Pitta Prakriti type and Ectomorph & Mesomorph personality types
- Pitta Kapha Prakriti and Mesomorph & Endomorph personality types
- Kapha Vata and Endomorph & Ectomorph personality types

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HEALTH RELATED BEHAVIOUR

Alcohol in Ayurveda & Modern Medicine

Introduction

It is difficult to say if it was a fortunate or unfortunate accident when man first discovered that the juice of grape, if allowed to ferment, becomes wine. Alcoholic beverages have been used since the dawn of history. Charaka has praised wine as "the destroyer of sorrow, unhappiness, fear and distress". In addition to its beneficial effects as an appetite stimulant, tonic, tranquillizer and anaesthetic, wine was used by the ancient physicians as a vehicle for active therapeutic agents derived from plants. When the Arabs introduced the then new science of distillation into Europe in the middle ages, the alchemists believed that alcohol was the long sought elixir of life. Alcohol was therefore held to be a remedy for practically all diseases as indicated by the term "Whisky" which in Gaelic means "water of life".

Intemperance in the use of alcohol creates many problems — psychological, medical and sociological. All over the world one can witness the immense toll attributable to overuse of alcoholic drinks, in terms of illness, disability and death, decreased productivity, accidents, crime, family disruption and economic and psychologic hardship in all classes of society. It is impossible to quantify human misery and human suffering, but the havoc wrought by alcohol is underestimated rather than overestimated.

Effects of Alcoholic Drinks

The pleasurable as well as the harmful effects of alcohol have been known since antiquity.

Charaka Samhita contains a most balanced and objective evaluation of the merits and demerits of alcohol, which appeals to the contemporary reader.

"Wine is prepared from various substances and possesses various qualities. It has various actions on the body. It is intoxicating in nature. Hence it should be viewed from the point of both its good as well as evil effects".

"If a person takes it in right manner, in right dose, in right time and along with wholesome food, in keeping with his vitality and with a cheerful mind, to him wine is like ambrosia".

"While to a person who drinks whatever kind comes in hand to him, and whenever he gets an opportunity and whose body is dry due to constant exertion, that very wine acts as a poison."

"In the first stage of intoxication, the mind becomes stimulated. In the second stage the vital essence is slightly affected and in the third stage, it is completely affected".

"When the brain is affected by the action of alcohol there will result exhilaration, ardent desire, exultation, sense of happiness and various kinds of changes according to the psychic make up of the person and according to its *Rajasic* or *Tamasic* qualities. It promotes sound sleep and happy awakening. This is the first and happy stage of alcoholic effects."

"Fitful recollection, fitful forgetfulness, indistinct, thick and laryngeal speech, indiscriminate talk, unsteady gait, impropriety in sitting, drinking, eating and conversation— these are to be known as the symptoms of the second stage of alcoholic effects".

"After transcending the second stage and before reaching the last stage, there is no impropriety which persons of the *Rajasic* or *Tamasic* nature will not commit".

"Which wise man would ever wish to be intoxicated to an extent which is as frightful as insanity, even as no traveller would select a road which leads to an unhappy end and which is beset with many troubles?"

"Having reached the third stage of intoxication, he becomes paralysed like a felled tree, with his mind submerged in intoxication and stupor, and though alive, he resembles a dead man".

"He does not discriminate between, or recognize the qualities of things or his friends. He does not possess even a sense of his own happiness for the very sake of which alcohol is drunk".

"Which wise man would like to attain that state in which he cannot discriminate between what ought to be done and what ought not to be done, between pleasure and pain, and between what is good and what is evil in the world?"

"On account of his addiction, he is condemned and censured by all people and is regarded an unworthy man by them. He gradually develops painful diseases as a result of his addiction."

"For all men, all that which contributes to wellbeing in this life and in the other, and happiness in that higher life of liberation, is established in the perfect tranquility of the mind".

"Wine causes great agitation to such a tranquil mind, like the strong wind that shakes the trees on the bank".

"Ignorant men, who are addicted to and are blinded by intoxication and overcome by passion and ignorance, consider the intoxicated state which is a greatly morbid and diseased condition, to be a state of happiness. These men, enslaved and blinded by alcoholism, are deprived of wisdom and 'Satvic' qualities and are lost to all goodness".

"Wine is also the cause of great delusion, fear, grief, anger and death as well as of insanity, toxicosis, fainting, epilepsy and convulsions".

"When a man is deprived of his very memory, then everything that follows upon it, is necessarily evil. Thus those who know the evils of drink, condemn the drink habit strongly. True and undoubted indeed are these great evil effects described about wine, if it is taken in excess or taken in disregard of the prescribed regulations".

"Wine by nature is regarded as similar to food in its effects. It is productive of disease if taken in improper manner, but is like ambrosia if taken in proper manner. Even food, which is the life of living creatures, if taken in improper manner, destroys life, while poison, which by nature is destructive of life, if taken in proper manner, acts as an elixir."

Merits of Measured Drinking

"Wine taken in proper manner soon induces exhilaration, courage, delight, strength, health, great manliness and joyous intoxication. It is an appetiser, digestive stimulant, cordial, promoter of voice and complexion, and is nourishing, roborant and strengthening. It relieves fear, grief and fatigue. It acts as a soporific to those suffering from insomnia and as a stimulant of speech in reticent people. It renders the mind unconscious of the pain of trauma, ligature and other kinds of pain and suffering. It increases the enjoyment of sense-pleasures and the desire for the continuance of such pleasures. Even to the very aged, alcohol gives elation and delight. There is nothing comparable on earth to the delight derived during the first stage of alcoholic effects".

"The wise man who abstains from all kinds of intoxicating drink and who has his senses under control is not afflicted with any disorder due to alcohol, either somatic or psychic."

Proper Company at Drinking:

"The men of excellent character, those that are pleasant of speech, that are amiable in expression, that are applauded by the good, that are versed in the arts, that are clean of heart and quick in the grasp of things, those that are mutually helpful and whose coming together is out of sincere friendship, who enhance the pleasure of drinking by their joy, affection and sweetness of

manner and the sight of whom causes mutual increase of joyous spirits, such men indeed make happy companions at drink, for by drinking in their company, one enjoys delight".

Pharmacology & Metabolism of Alcohol:

Ethyl alcohol or ethanol is the active ingredient in beer, wine, whisky, gin, brandy and other less common alcoholic beverages. In addition, the stronger spirits contain enanthic ethers, which give the flavour but have no important pharmacologic properties.

Alcohol is absorbed unaltered from the stomach and the small intestine. Its presence may be detected in the blood within five minutes after ingestion, and the maximum concentration is reached in 30 to 90 minutes. The ingestion of milk and fatty foods impedes the absorption of alcohol and water facilitates it.

After entering the blood stream, alcohol enters the various organs of the body, as well as the cerebrospinal fluid, urine and pulmonary alveolar air, in concentrations which bear a constant relationship to that in the blood. It is eliminated chiefly by oxidation to carbon dioxide less than 10 percent being excreted chemically unchanged in the urine, sweat and breath. The energy liberated by the oxidation of alcohol is equivalent to 7 KCal/g.

The metabolism of alcohol takes place mainly in the liver, where several enzyme systems can independently oxidize alcohol to acetaldehyde. The most important of the enzymes is alcohol dehydrogenase. Another enzyme acetaldehyde dehydrogenase converts acetaldehyde to acetyl co-enzyme A and acetate, and the latter are metabolized further through well-established pathways to yield carbon dioxide and water.

Ethyl alcohol is oxidized at a constant rate independent of its blood concentration; about 1 oz 90 proof whisky or 10-12 oz beer per hour. Chronic alcoholics metabolize alcohol somewhat faster than normal individuals. Amino-acids, especially alanine, insulin and fructose enhance ethanol metabolism. It is interesting to note that Charaka recommends "to eat, while drinking, salted fragrant flesh and fried flesh of many kinds of creatures of the land, water and air".

A scale relating to the various degrees of clinical intoxication to the blood alcohol levels in non-habituated persons has been constructed by Miles. At blood alcohol levels of 30 mg/dl (0.03 percent) a mild euphoria is detectable, and at 50 mg/dl, a mild incoordination. At 100 mg/dl ataxia is obvious. At 200 mg/dl the subjects are drowsy and confused. At 300 mg/dl they are stuporous; a level of 400 mg/dl is accompanied by deep anaesthesia and may prove fatal. Such a scale has little pertinence to the chronic alcoholic patient whose liver increases the alcohol metabolic rate and who has developed tolerance to alcohol.

If the alcohol concentration in the blood is raised very slowly, few symptoms appear even at quite high levels. On the contrary, when the blood alcohol level peaks rapidly, the degree of intoxication is severe.

The most important action of alcohol is on the nervous system. It is not a stimulant, but a depressant of the central nervous system. The hyperactivity that is seen is due to removal of the inhibitory effects of the highest brain. The first functions to be lost are the finer grades of judgement, reflection, observation and attention, the faculties largely Acquired through education which constitute the elements of restraint and prudence that man usually imposes on his action.

There is a common belief that alcohol is an aphrodisiac, but the reality is very well expressed by William Shakespeare, "It provokes the desire but it takes away the performance". Performance in other forms of athletics is also impaired by alcohol, hence managers of cricket teams are wise to keep a close vigil on this score.

In general, efficiency, both mental and physical, is reduced by alcohol in any amounts worth taking for social purposes. There is an important exception; the person, who is so disabled by anxiety or nervous tension that his performance is gravely impaired, may improve with the correct dose of alcohol.

The effects of alcohol become of crucial importance in case of pilots or car or truck drivers. In Britain, a blood concentration exceeding 80 mg alcohol per 100 ml blood while in charge of a car is a statutory offence. At this concentration the liability to accident is twice normal. Other countries set other concentration limits, some lower, some higher, but even for experienced professional drivers there is no "safe" blood alcohol level below which it is certain that judgement would not be impaired. The danger remains even after alcohol has left the blood, during the hang-over period, due to irritability, fatigue or hypoglycaemia (low blood sugar). All-over the world the adolescents and adults who drive after drinking are a grave menace to public safety.

Causation of Alcoholism:

Alcoholism has been defined both as a chronic disease and a disorder of behaviour, characterized in either context by drinking of alcohol to an extent that interferes with the drinker's health, interpersonal relationship and/or means of earning a livelihood. In pharmacological terms, it is addiction to alcohol.

The important question is why individuals drink excessively, often with full knowledge that such action will result in physical injury to themselves and irreparable harm to their families.

There is probably a genetic influence in the development of alcoholism. It has been shown that the concordance rate for alcoholism in identical twins is 55 percent or higher and for fraternal twins of the same sex, 28 percent. The incidence of alcoholism is 4 to 5 times higher in the biological offsprings of alcoholic parents. Thus, it appears that genetic factors are important, in addition to psychological and social and cultural ones.

Alcoholism should be taken as a symptom or manifestation of maladaptation to many social or environmental stresses or psychological difficulties which the person has been unable to handle. Psychological characteristics associated with alcoholism may provide useful clues for management. These include a low frustration threshold, excessive dependency needs, underlying feeling of inferiority, inadequacy or self-doubt. Many alcoholics are sensitive to rejection and have difficulty in entering into close social relationships. They may reveal recurrent themes of depression, emptiness and loneliness. Alcoholism is commonly rooted in family and marital problems, which may need help by specialised agencies like marriage counsellors.

Very often it is not the patient but the wife or close relatives who can see more clearly how seriously his life is being interfered with by his alcoholic addiction. These unwilling patients are particularly difficult to treat. But the prospect is very different when the patient himself is distressed by his dependence on alcohol and is anxious for a change.

The problem of excessive drinking is formidable but not necessarily hopeless. A useful point at which to undertake this task is during convalescence from a serious medical or neurological complication of alcoholism or in relation to loss of employment, arrest or threatened divorce. Such crisis may help convince the patient, better than any argument presented by the family or physician, that the drinking problem has reached serious proportions.

The following is a list of alcohol-induced diseases with which the patient may present himself.

Alcohol-induced Diseases

Gastrointestinal System

Alcoholic gastritis—morning nausea & vomiting. Peptic ulcer (higher incidence). Mallory-Weiss Syndrome (due to persistent vomiting).

Liver

Fatty liver (reversible on abstinence), Alcoholic hepatitis. Alcoholic cirrhosis. Hepatic coma. Chronic hepatocerebral degeneration.

Pancreas

Pancreatitis, Steatorrhoea due to deficient exocrine pancreatic function.

Haemopoietic System

Bone marrow depression, Anaemia with macrocytosis, Leucopenia, Thrombocytopenia.

Nervous System

Alcohol intoxication

Withdrawal syndrome—delirium tremens Nutritional deficiency secondary to alcoholism:

- a. Wernicke-Kor sakoff syndrome
- b. Polyneuropathy
- c. Cerebellar degeneration
- d. Optic neuropathy
- e. Pellagra.

Uncertain pathogenesis, associated with alcoholism

- a. Pontine and extrapontine myelinolysis
- b. Marchiafava-Bignami disease
- c. Alcoholic dementia
- d. Alcoholic central atrophy
- e. Fetal alcohol syndrome

Cardiac & Skeletal Muscle

Alcoholic cardiomyopathy, Alcoholic myopathy

Ayurvedic Treatment of Alcoholism

The prescription for the “Vata type” of alcoholism (hiccup, dyspnoea, tremors, insomnia, excessive garrulity) makes interesting reading. “Various kinds of confections and various appetisers, meat preparations, dry massage, hot baths, affectionate embraces of women’s bodies full of the warmth of youth, by the arm clasp of their waists, thighs, and full-grown breasts, by the warmth of the bed and the cover and the warmth of happiness and cheer of the interior apartments subdue alcoholism by the vata type”.

The same therapy is recommended for two complications of alcoholism called "Dhwamsaka".

Modern Treatment of Alcoholic Addiction

The requisite for successful treatment is total abstinence from alcohol, and this represents the only permanent solution.

The doctor, the therapeutic team, the family and friends have to accept the alcoholic as a sick person needing help. It does not help to adopt a sermonising, moralising, judging or condemning attitude towards him. A rigid and punitive attitude may be counterproductive. The physician, family and friends should enhance motivation not to drink by caring about what happens to him being reasonably optimistic about the outcome, showing him feasible ways to begin to deal with his problems rather than evade them or drown them in alcohol. Helping the patient to explore his capacity for alternative modes of adaptation to his life situations and to arouse and to develop the patient's own adaptive potentialities will be necessary. It is worthwhile assuming that the patient would not be alcoholic if such alternatives were easily available and readily apparent to him.

Alcoholism has to be considered essentially a relapsing disorder. A relapse is to be taken as a challenge to try again and not to throw up arms because of a feeling of personal failure or affront. No treatment can succeed with an alcoholic without his motivation and cooperation. Treatment of alcoholic addiction initially consists of "drying out" which often calls for hospital admission. Sudden withdrawal of a sustained high uptake of alcohol may result in the onset of delirium tremens, characterised by gross tremors of the hands, great restlessness, misidentification of persons and places, and delusional ideas which may be terrifying—these withdrawal symptoms can be well controlled by drugs like phenothiazines, diazepam, haloperidol or chlormethiazol. The next phase of treatment once the patient is abstinent is to explore with him by means of a series of interviews his personal and other problems which require attention. The abstinent alcoholic can ensure against the temptation of another drink by taking "antabuse" drugs like disulfiram or citrate calcium carbimide. When on those drugs, the patient will have a very unpleasant reaction after taking even a small amount of alcohol. Metronidazole, a drug commonly used to treat amoebic infections, and oral antidiabetic drugs, also cause a similar antabuse effect.

Disulfiram interferes with the metabolism of alcohol so that patients who take both alcohol and disulfiram accumulate an inordinate amount of acetaldehyde in the tissues, resulting in nausea, vomiting, and hypotension.

The experience is so nasty that the patient does not like to repeat it. The patient taking disulfiram, aware of the danger of mixing liquor and the

drug, is protected against the impulse to drink, and this protection may be renewed every 24 hours by the simple expedient of taking a pill. Compliance can be checked by measuring disulfiram levels in the blood. The willingness with which the patient accepts this form of treatment is an index of his motivation.

Alcoholics Anonymous (AA), a worldwide movement (including India) whose members are ex-alcoholics, is a great help in rehabilitation of alcoholic patients. Group discussions help patients to gain insights into their problems and personality difficulties, so that they learn to cope, with inner tensions and environmental stresses in a more mature and less destructive manner than by seeking oblivion in alcohol.

Tobacco Smoking and Health

Introduction

Charaka Samhita contains a detailed discussion on medicinal smoking. Medicinal smoking can be defined as inhaling smoke of medicines through the nose or the mouth. Smoking of tobacco or ganja (hash hash) should not be considered as medicinal smoking, since there are no medicinal benefits.

Charaka classifies smoking according to its uses, under:

- A. "*Prayogika*": It is advised for regular use by persons of "sama" and "kapha" constitution. The medicines commonly used — harenuka, priyangu, prithvika, keshar and nakha.
- B. "*Snigdha*": Smoking with oily medicines such as ghee, wax, animal fat, jeevaka and rishabhaka.
- C. "*Vairechanika*": Smoking of strong types used for its cleansing action on air passages. Medicines commonly used are shveta, jyotismati, haritala, manashila, and leaves of agaru, turmeric and castor roots.
- D. "*Kasaghna*": Smoking to relieve cough, with medicines like glycerrhiza, ajamoda, jeevanti, agaru, sarjaka, roots of castor plants, vacha, asafoetida, bhurja granthi, and ghee prepared on silk cloth.

For patients with asthma, a "*Shvasaghna*" smoking is prescribed with various ingredients.

For patients with ulcers in the mouth, pharynx, trachea and air passages, a "*Vranadhoopana*" smoking is prescribed, using java, shriveshtaka, sarja rasa and ghee.

A medicated cigarette is prepared from grass sticks and put in a smoking tube or pipe, the dimensions of which are prescribed according to the types of smoking as described earlier.

Charaka gives a list of persons in whom smoking is contraindicated, such as children under the age of 18, pregnant women, persons with head injuries, eye diseases etc. Various benefits of medicinal smoking are claimed, I am not aware of any scientific studies to validate those claims. Moreover, medicinal smoking does not appear to be widely employed by Ayurvedic practitioners.

Tobacco Smoking

Tobacco smoking and its ill effects are not mentioned in Ayurveda. It is not clear when the practice of tobacco smoking was started in India. Tobacco smoking is perhaps the world's most accepted vice. Those who have never smoked a cigarette in their life may consider the topic of smoking, with its alleged pleasures, addiction and miseries, with a sense of calm detachment. Recent research has revealed that non-smokers in a smoky atmosphere are also prone to disease as much as the smokers, which makes the smokers' an enviable lot — they get both the pleasure and the cancer while the non-smokers may get only the cancer! How do people start smoking? When you are young you take to your first cigarette imitating others — mainly because your friends are smoking and you feel a bit left out — or you want to prove your manhood or grownupness. Although the initial experience is often quite unpleasant, many continue to smoke for self-esteem or status need. The films or advertisements show every smoker as a handsome, young, healthy, wealthy and relaxed man with a pretty girl admiringly watching him light his cigarette; hence the impressionable youth identify smoking with manhood, success and happiness.

Psychoanalysts suggest that getting something orally is the first great libidinous experience in life; first the breast, then the bottle, then the comforter, then food and finally the cigarette. The common sight of a pipe smoker with an empty or unlit pipe in his mouth would seem to lend support to this.

The reasons people habitually smoke tobacco are certainly complex and it is no easy matter to reach a simple and reasonable conclusion concerning the mental health aspects of smoking. Some people smoke purely for pleasure when resting, reading or watching television. Others smoke out of sheer boredom. For some it reduces fatigue in monotonous or demanding tasks. Most people smoke more when under tension because they find that smoking relieves their tensions. There is no clear-cut personality difference between smokers and non-smokers. Cigarette smokers tend to be more extroverted, less rigid and perhaps more neurotic than non-smokers. Pipe smokers are notably introverted.

Social environment plays a large part in determining smoking, and the offering and acceptance of cigarettes is important in the development of

personal relations in business and in private life. What is it that gives satisfaction to the tobacco smoker?

Action of Nicotine:

The sole physiologically active ingredient of tobacco smoke is nicotine. Although cigar and pipe tobacco contain considerably larger quantities of nicotine than does cigarette tobacco, their heavy alkaline smoke is intensely irritating to the respiratory tract and is not usually inhaled. On the other hand, the light, bland smokey cigarette with practice is readily tolerated by the bronchial tree.

Accordingly, nicotine is rapidly and completely absorbed in the lungs of the cigarette smoker.

The novice smoker commonly experiences the toxic effects of nicotine; giddiness, nausea and vomiting, abdominal cramps, cold sweat and even collapse with a fall of blood pressure. These symptoms, when unusually severe, may deter formation of the smoking habit. The veteran smoker does not acquire tolerance to nicotine, inasmuch as all measurable circulatory responses persist without attenuation, but he learns to manipulate time-dosage factors so as to avoid poisonous effect.

A standard cigarette contains about 20 mg. nicotine. Considerable amounts of nicotine are destroyed by heat or dispersed in the sidestream smoke, so that the average inhaling cigarette smoker absorbs about 2 mg. of nicotine. This amount causes small but consistent increases in heart rate, in systolic and diastolic blood pressure, in the work of the heart. Blood flow to the skin and temperature of the skin are sharply reduced. All these effects are similar to those produced by the hormones adrenaline and noradrenaline, and in fact in human subject the urinary excretion of adrenaline metabolites may increase upto 50 percent after heavy cigarette smoking. Adrenaline and noradrenaline are the body's emergency hormones, produced by strong emotions like sudden rage or fear and prepare the body for fight or flight. The heart rate speeds up, the arteries tighten to raise blood pressure, digestion comes to a halt, and sugar from the liver and free fatty acids from the fat stores are mobilized into the blood stream to provide more fuel for the muscles. Platelet stickiness is enhanced and clotting capability of blood is quickened, in case of injury. By smoking continuously the smoker is perpetuating this state of emergency, which nature designed only for short periods of time. The price paid for this artificial thrill of 'living dangerously' is in the form of heart attacks. Smoking twenty cigarettes or more daily is associated with a hazard of heart attack three times greater than in non-smokers or in cigar or pipe smokers. Angina pectoris or chest pain due to less blood supply to the heart is often precipitated or aggravated by smoking, suggesting that the effects of cigarette smoking are acute as well as chronic. Cigarette smoking makes the heart patient more liable to a dangerous and life-threatening complication, namely ventricular fibrillation.

Action of Other Ingredients

Apart from nicotine, it seems increasingly probable that carbon monoxide is the chief toxic constituent of cigarette smoke in relation to cardiovascular complications. Heavy cigarette smokers have carboxy haemoglobin concentrations of 2-15 percent. Even at low levels, carbon monoxide causes hindrance to the smooth transfer of oxygen from the oxygen-carrying red blood cells to the tissues where it is needed. Normally this is achieved by the red pigment oxy-haemoglobin which transfers oxygen readily. Carboxy Hb does not give up its oxygen readily. This is a particularly serious handicap to the patient whose coronary arteries are already narrowed, hence his increased oxygen requirements on exertion cannot be met by increase in blood flow.

When carboxy haemoglobin reaches 20 percent it inhibits oxygen utilisation by cells of the vessel walls and favours the formation of atheroma, or thickening of arteries.

Cigarette smoking harms the heart patient in yet another way. The normal air passage is lined by cells with microscopic hair or cilia which wave to and fro like wheat in the wind, about 12 times a second. Their upward thrust does an important cleaning job by bringing up trapped dust particles in sticky mucus. Cigarette smoke or badly contaminated air paralyse the cilia; if the irritation continues the cilia wither and die, never to be replaced. Now the only mechanism left for cleaning the airway is the noisy, inefficient smoker's cough which has replaced the quiet efficiency of the cilia. Cigarette smoking is the most important cause of chronic bronchitis and is significantly related to another lung disease namely emphysema. Both bronchitis and emphysema aggravate heart disease of any type.

Smoking should be prohibited for the heart patient. The patient with angina pectoris should not smoke. A well-known cardiac surgeon said recently that he refuses to do coronary bypass surgery on any patient who refuses to stop smoking. "If a man thinks smoking is more important to him than his heart, then I will have nothing to do with him".

The simultaneous presence of several risk factors is more than merely additive. If the patient is a male, above 45 years of age, has a blood cholesterol level over 250 mg. per 100 ml, has a diastolic blood pressure over 90 mm Hg, is overweight and is a smoker, his risk of a heart attack is 44% as against 9% if none of these factors were present.

Almost all patients of Buerger's disease (thromboangiitis obliterans) are male tobacco smokers. If the patient stops smoking completely, arrest of the disease is usual.

If he continues to smoke, progression of this disease is almost a certainty.

If the cigar and pipe smokers, after reading this tirade against cigarettes, are getting a feeling of security and comfort about their choice, there is bad news for them. Excessive smoking of strong pipe tobacco may cause damage to the nerve of the eye-optic neuritis. Tobacco smoke contains cyanide which experimentally has been shown to cause demyelination. Hydroxycobalamin, derived from Vitamin B12 plays an important part in the detoxication of cyanide. If the intake of Vitamin B12 is low and cyanide ingestion is high, demyelination of the optic nerve is likely to occur. A typical history is that there is a growing inability to see colours of small objects. A mist obscures the central field of vision and gradually becomes so intense that it becomes impossible to recognize acquaintances. There is usually no pain.

Smoking and Lung Cancer:

The most dreaded and most publicised complication of cigarette smoking is of course lung cancer. In the 1940's there was a growing impression that environmental factors are responsible for most human cancers and a relationship between cigarette smoking and bronchogenic cancer emerged as an important link. Doll and Hill in England in 1951 chose doctors on the medical register in Britain and asked them to record their smoking habits at that time. They then recorded the deaths that occurred in the next few years and calculated the death rates from lung cancer. Their results were very striking indeed: as against 7 deaths per 100,000 in non-smokers, there were 47 in light smokers, 86 in moderate smokers and 166 in heavy smokers. Doctors are a particularly suitable population for prospective study because they are comparatively easy to follow up and when sick, usually choose leading physicians to care for them. Their death certificates are therefore more than usually reliable. Hence the conclusion, based on the study of almost 60,000 doctors in England, can be accepted that heavy smokers (more than 20 cigarettes per day) have death rates from lung cancer 23 times greater than non-smokers.

The tar component of cigarette smoke contains a cancer producing chemical called benzopyrene. It is also likely that alpha radiation is another contributing factor in tobacco-related cancer. The alpha emitters, polonium-210 and lead 210 are highly concentrated in tobacco trichomes. The major source of polonium is phosphate fertilizer which is used in growing tobacco. In a person smoking 30 cigarettes a day the radiation dose to the lining of the airway is 8000 millirontgens per year. The alpha particles have a high mutagenic potential.

It must be appreciated that environmental factors alone cannot explain the range of susceptibility of individuals in a population exposed to the same or similar carcinogenic agents. Clearly genetic influences are at work. But since

genetic factors are beyond our control, we concentrate on what can be controlled. In the United States of America, there is a group called Seventh Day Adventists, whose religious faith prohibits smoking. They have 1/8 incidence of lung cancer compared to the non-members. In respect of cancer of other body sites there is no difference between the groups, so that the Seventh Day Adventists have evidently no genetic immunity from cancer.

The "bidi" is a typical Indian product consisting of strong powdered tobacco wrapped in dried "tendu" leaf grown extensively in Andhra Pradesh and Orissa. It is essentially a poor man's smoke, and an estimated 100 million bidies are smoked daily in India. Out of every eleven Indian smokers, ten are bidi smokers.

When the cigarette smoking public in the Western Countries was warned about the harmful effects of cigarette smoking, a large number turned to bidi smoking in the belief that it was less harmful than cigarettes. A comparative chemical analysis of Indian Bidi and American Cigarette smoke was published a few years back in the International Journal of Cancer. A single bidi delivers about one-and-a half times the carcinogenic hydrocarbons delivered by a single cigarette. Phenol, a cancer promoting agent, is also found in larger amounts in bidi smoke than in cigarette smoke. Thus the bidi, if anything, is more dangerous.

Since the appearance of the Surgeon General's report in U.S.A. in 1964, there have been marked changes in the cigarette smoking habits of Americans. By 1975, the proportion of men smoking cigarettes had declined by 25 percent, from 53 percent in 1964 to 39 percent in 1975. There has been increased use of filter-tip cigarettes which contain less tobacco than regular cigarettes.

Recently, the Ministry of Health and Family Welfare, Government of India, New Delhi wrote to State Governments about getting the health warning printed on bidi bundles. Some states have expressed doubt about the effectiveness of this action, for a large number of bidi smokers are illiterate. Besides, experience all over the world has shown that the statutory health warnings on cigarette packs have been of little help in dissuading people from smoking, especially women and teenagers.

Women have taken to smoking in Western cultures in larger numbers than ever before and they have also started paying the price for it. Women who smoke during pregnancy have a higher incidence of abortion, babies 170 gm. Lighter and a fetal and neonatal mortality rate 28 percent higher than non-smokers and retarded, later development of the babies. Facial wrinkles above age 30 years correlate with the number of cigarettes smoked.

Benefits of Stopping Smoking

Despite all the knowledge about the harmful effects of tobacco smoking, health education, and the statutory warning about harmful effects of smoking, the sales of cigarettes have increased in the past few years. What are the reasons? Many smokers believe that after some years of smoking it is useless to give up because the damage is done already. This is not true. Stopping has been shown to reduce the mortality from lung cancer as well as from sudden cardiac deaths. Abstention from cigarettes may improve longevity, since morbidity data indicate that former cigarette smokers are at little if any greater risk than non-smokers, for cardiac deaths. Stopping smoking accelerates the healing of gastric ulcers. Stopping smoking completely arrests the progress of the peripheral vascular narrowing in Buerger's disease.

The primary motivation for giving up smoking is the risk of ill health and death. Many people do in fact give up smoking following a heart attack. But prevention must start much earlier. Less than 20 percent of smokers become non-smokers at present.

According to Mark Twain it is very easy to stop smoking. "I ought to know", he said, "because I have stopped smoking a thousand times!"

For the moderate smokers (less than 20 cigarettes per day) who really are motivated to give up smoking and who cannot do it in a single shot, here are some ways to begin "Nicking the habit".

1. Choose a cigarette with less tar and nicotine.
2. Smoke only the first half of the cigarette.
3. Reduce the number of times a puff is taken.
4. Reduce the depth of inhalation.
5. Smoke fewer than 3 cigarettes a day.
6. Exercise more.
7. Pursue other hobbies and interests.
8. Find a safe substitute for handling cigarettes like a lucky coin, pen or pencil.

The list of tips to stop smoking is endless and challenges the creative ability of the doctor to adapt and personalise the patient's management. People who smoke more than 20 cigarettes a day are exceedingly more difficult to motivate. Stronger encouragement, guidance and support are required. Anti-smoking group sessions, on the lines of Alcoholics Anonymous, may prove to be of added value. The health and life of patients is the first concern of the doctor. The World Health Organisation in 1970 condemned the use of tobacco smoking on account of its consequences for health. The medical profession should therefore be in the forefront in the efforts to

persuade their patients to adopt a more healthy way of life, to dissuade the young from beginning to smoke and to persuade the smoker to stop smoking.

Psychotropic Drugs

Introduction

In earlier sections I discussed the health hazards of alcohol and tobacco smoking. Western society is presently concerned greatly with the use and misuse of psychotropic and recreational drugs particularly by the younger generation. Society has accepted alcohol and tobacco smoking as "legal" while the psychotropic drugs are considered "illegal". Far too often the legal drugs alcohol and tobacco are treated as if they are much safer than, and altogether different from, illegal drugs. Scientific opinion stresses the common ground between the two; many different types of drug-related behaviour can be considered in general terms. The evidence about why people use drugs and what happens to those people, is strikingly similar in relation to both legal and illegal drugs. In addition, ideas about what constitutes addiction or drug dependence, and conclusions about what becomes of dependent individuals also appear similar in relation to legal and illegal drugs. It is very essential that society develops a proper perspective.

Drug use in some form or other is virtually universal. From time immemorial, people have sought a change of consciousness with the aid of whatever appropriate vegetation or other source was available. Alcohol, man's oldest drug, is the most widely used because it can be produced from the fermentation of so many types of plant products.

Great Social Problem

During the 20th Century "drug misuse" has become widely regarded as one of the world's great social problems. The complexity of the situation has been perceptively described by Professor Griffith Edwards:

"If you fly over any part of the earth's land surface, you would have a fair chance of seeing below you some process of drug cultivation. You would see vineyards, coffee plantations, tea plantations, tobacco crops, Fields of opium poppy and patches of lank Indian hemp flowering even on vacant city lots: the coca plant grows on the slopes of the Andes, so that six million peasants shall obtain their cocaine. Even the desert has the peyote cactus. As you look down on the great industrial countries, the factories will catch your attention, which spill out the tranquillizers, stimulants, analgesics, sedatives and antidepressants, by the billions, and the chemist much improves on cactus and mushroom. The money at stake is immense and countries might fill their treasuries to a large extent from drug revenues. Conflicts of opinion are violent, the state's response to impermitted use Draconian."

Popular Misconceptions

Public thinking about the drug problem is highly coloured by lurid media coverage which has often exaggerated and sensationalised both the scale and meaning of various forms of drug abuse. A great deal of propaganda is designed to frighten people away from experimenting with illegal substances such as *Cannabis indica* ("bhang", "charas", "ganja"). Society generally acknowledges that drinkers vary enormously and that most do not appear to suffer from ill effects as a result of their alcohol consumption. Similar conclusions are as valid for cannabis. Those who panic about smoking "grass", conveniently forget that 25,000 people are dying each year in Britain alone from the direct effects of tobacco smoking and that over 226,000 drunkenness convictions, 18,000 hospital admissions for alcoholism occur in that country every year. And yet an energetic vendor of alcohol or tobacco, especially an exporter of these things, might justifiably expect his efforts to be rewarded by a State Award, while an energetic trader in Cannabis will be lucky to escape a long prison sentence. This is the paradox in an intelligent society. Like alcohol any psychotropic drug is likely to be used unwisely, harmfully and excessively by some people. The more widely a drug is used, the greater is the risk of some form of harm or misuse in relation to it.

Effects of Psychotropic Drugs: Cannabis

Cannabis (marijuana), derived from the plant *Cannabis sativa*, occurs in two varieties, the hemp type and the drug type. These differ in relation to the amount of the main psychoactive ingredient, delta 9-tetrahydro cannabinol (THC) that they contain. The hemp type (used for rope making) contains relatively little of the intoxicating substance, while the drug type contains far greater levels of THC. Cannabis has been used for thousands of years, in China, India, and subsequently in Middle East and North Africa. Cannabis was adopted by Western Medical Practice during the 19th Century. The introduction of much more effective and useful drugs has long since removed the use of cannabis from medical practice. Its use on a large scale has been for recreational purposes by Western Youth.

Marijuana consists of the flowering and fruiting tops and leaves of the plant. Very often seeds, stems and other parts of the plant are also included.

Cannabis resin (hashish, Charas) is the dried caked resin derived from the tops and leaves of the female plant. Because of its higher THC content it is more potent than marijuana. Cannabis oil, a ruddy brown extract from the resin or the plant, is known by a variety of names, including "hash oil" or "liquid hash". This is the most potent form of cannabis apart from pure THC. Hash Oil may contain a THC concentration of 25 to 60 percent. Cannabis is normally smoked, although it may also be chewed or ingested as an ingredient in

food or drinks. A typical marijuana cigarette contains 0.5 to 1 g. of plant material.

Cannabis, like alcohol, is a depressant drug on the central nervous system, slows reaction time, impairs co-ordination and may induce drowsiness. The desired short-term reaction is a "high" or euphoria similar to mild alcoholic intoxication. This may be followed by a quieter, passive phase which in turn is followed by sleep. Reddened eyes and increased pulse rate are also commonplace, short-term effects. Experienced users report that they achieve the greatest effects by inhaling the smoke and holding it in their lungs.

Tolerance may develop very rapidly with cannabis, so that users sometimes need to smoke steadily increasing amounts to recapture the original effects of the drug. THC potentiates with alcohol, amphetamine and tobacco. Consequently, their combined use magnifies the effects. Some cannabis users certainly become psychologically dependent on the drug. Derivatives of cannabis accumulate in the tissues of the brain, lungs and the sex glands. Prolonged and heavy cannabis use has been found to cause damage to the blood cells and spermatozoa.

Animal studies have shown that cannabis use in pregnant mammals increases the incidence of fetal damage and death. There is abundant evidence to support the view that prolonged heavy cannabis use is physically damaging (particularly lung function) and is likely to lead to loss of motivation, apathy and passivity. To some extent the motivational syndrome may be attributable to the ideology and life-style of the drug scene rather than the chemistry of cannabis.

Large numbers of cannabis smokers use the drug only intermittently and they do so without harm. Even so the potential dangers of the regular cannabis use make it a health hazard, like alcohol and tobacco smoking.

Lysergic Acid Diethylamide— LSD

LSD is possibly the most dramatic of the psychotropic drugs. Its characteristic effect is to distort the way its user sees and senses the world.

Many hallucinogenic drugs (sometimes called psychedelics) occur naturally and have long been used in South, Central and North America for recreational purposes or in conjunction with religious ceremonies. The substances include peyote (a cactus) and mescaline (a mushroom).

LSD is by far the most potent of the commonly available hallucinogens. It was first produced in 1938, and its hallucinogenic effects were noted in 1943 and since then it has been used experimentally in psychiatry, although its use for such purposes is now almost non-existent. The subjective effects of

LSD have been vividly described in Aldous Huxley's "The Doors of Perception". It has been hailed by some as mind-expanding, a key to self-enlightenment. LSD is an incredibly potent drug. Tiny amounts are sufficient to trigger off a "trip" or experience which may well be psychologically overwhelming and routinely lasts for as long as seven hours. The drug is available in many forms: capsules, microdots or as a liquid. It is usually prepared as a tartrate salt that is water-soluble. It is easily carried or smuggled and is often soaked in sugar or blotting paper. It is usually swallowed, but may also be sniffed or injected. The effects normally begin an hour or so after ingestion and reach their peak two to three hours later. The effects do not directly depend on dose and as little as 30 or 40 micrograms are sufficient to produce the desired effect. LSD accentuates and distorts the users' antecedent mental and emotional state. LSD often causes profound changes in perception and mood. These may be extremely pleasant or devastatingly horrifying. High blood pressure, rapid pulse rate, rapid respiration, nausea, weakness, convulsions and depression may also occur.

Flash-backs, or recurrences of the effects experienced during an LSD trip have been widely reported by users even months after experimentation. Sometimes such flash-backs occur at dangerous or at least embarrassing times.

There certainly have been fatal accidents and suicides attributable to LSD, although extremely rare. While LSD does sometimes produce extremely interesting and enjoyable effects, those cannot be relied upon and users participate in a hazardous game of Russian roulette.

Heroin & Other Opiates

The juice of the oriental poppy (*Papaver somniferum*) has been used for pleasure and medical use for thousands of years. The practice of using opium for diarrhoea and for making children quiet was wide-spread all over the world till the 1920's.

Morphine, the active alkaloid of the opium poppy was isolated in the mid-nineteenth century, and since it was available as a solution for injection, became popular as a potent pain-killer. Heroin (diacetyl morphine) was derived in 1898, ironically, as a result of a quest for safer, less addictive morphine derivatives. Subsequently other similar drugs, synthetic or semisynthetic opiates have been produced. All have been shown to produce *drug-dependence and addiction*. The number of heroin addicts in USA alone is estimated to be about 500,000. The cost to the nation, of heroin abuse alone is about six billion dollars a year.

Morphine and heroin are mainly injected, but may also be eaten, smoked or sniffed. All opiates produce tolerance if used regularly and abrupt cessation of regular use may produce withdrawal symptoms. Heroin withdrawal symptoms usually occur six to twelve hours after the last dose. They range from minor

discomfort, similar to that from a cold, to cramps, nausea, sweating, dilated pupils, diarrhoea, headache and insomnia. Usually withdrawal passes its worst within two to three days and recovery generally takes no more than a week, although it often takes longer for sleep patterns to return to normal.

Heroin users often use syringes and needles which are unsterile, or share them with other users, thereby spreading viral hepatitis and syphilis. Sometimes heroin bought on the black market contains highly dangerous substances such as caustic soda added to increase the weight and thereby the vendor's profit.

Babies born to addicted females are also physically dependent and might die unless this condition is detected and treated.

A number of factors, socio-economic, psychological and pharmacological, all contribute to the genesis of opium and heroin addiction. The most susceptible are young men or delinquent youths living in the economically depressed areas of large cities. Group pressure and peer pressure are very potent factors for initiation of addiction in the youth, mostly under age 21.

Cocaine

Cocaine is derived from the coca plant (*Erythroxylon coca*) which grows in South America, South-East Asia, Africa and the West Indies. Coca has been used for centuries in South America as a cure for a variety of ailments such as rheumatism, and as a stimulant. The Incas regarded Coca as a divine plant with magical properties. The active alkaloid cocaine was isolated in the mid-nineteenth century, and it is far more powerful and potentially dangerous than the mild coca leaves which contain 1 to 1.5 percent cocaine.

Cocaine is a stimulant and as such may be broadly compared with the amphetamines.

Cocaine is a white crystalline powder, usually sniffed when used recreationally. The drug is rapidly absorbed from the nasal mucosa and produces a brief, dose-related stimulation and enhancement of mood. It induces alertness and energy. Sniffing cocaine is a potentially very dangerous practice, which can erode through the septum of the nose.

Although it has been assumed that use of cocaine is relatively safe, death caused by respiratory depression and cardiovascular collapse has been documented after cocaine "snorting" (inhalation) and after intravenous administration. Protracted cocaine abuse may induce paranoid ideation and visual and auditory hallucinations.

Cocaine is very expensive in comparison to other illicit drugs and has attained the reputation of a “status” drug in western industrialised societies.

Amphetamines

Three categories of this group, amphetamine (benzedrine), dextro amphetamine (dexedrine) and methyl amphetamine (methedrine) have been widely available, and hence used recreationally on an un-precedented scale. Amphetamine misuse reached its peak in Japan where it was estimated that half a million people were using it non-medically in 1954. During the Viet Nam war American soldiers used 225 million amphetamine tablets. Amphetamines are stimulants which produce feelings of energy and confidence. They increase heart rate, blood pressure and blood sugar. The pupils are dilated and appetite is suppressed. They enable users to remain awake for longer periods. For these reasons they have been used illegally to stay awake at parties, dances and concerts, or simply to generate a feeling of energy and euphoria. In many ways the effects of amphetamines resemble those of adrenaline. Excessive amphetamine use has, rarely, led to fatalities due to burst blood vessels in the brain, and heart failure.

While the effects of moderate doses of amphetamine may be pleasant, it often produces restlessness, anxiety and overconfidence. Amphetamine does not create energy, it simply uses it up so that fatigue invariably follows stimulation, often combined with irregular sleep pattern. This is known as the amphetamine “crash”.

Phencyclidine (PCP) “Angel Dust”

One of the nastiest and most dangerous substances to be used recreationally during recent years is “angel dust”—phencyclidine hydrochloride. This substance, also colloquially known as PCP, crystal, super grass, goon, scuffle etc. was first produced over twenty years ago as an anaesthetic. During the 1960's it was used by youthful drug takers in USA and its excessive misuse has recently caused considerable public concern.

PCP is a hallucinogen. It is available either as “Angel Dust” in crystalline form, or may be easily dissolved in water, for ingestion or injection. The usual or desired effects of PCP are a “high” accompanied by a feeling of detachment, dreaminess or pleasant or exciting hallucinations. The effects may be dramatically unpleasant and may cause depression, panic and psychosis, and self-destructive behaviour. Thus PCP is a major health hazard.

Sedative-Hypnotic Drugs

The barbiturates, and the benzodiazepines are the most commonly prescribed sedative drugs today. More than 1.4 billion prescriptions for these drugs are filled each year.

Despite the steadily diminishing medical use of barbiturates (being displaced by benzodiazepines), the high incidence of addiction, suicides and accidental deaths attributable to the improper use of these drugs is a matter of continuing concern. The Domestic Council Drug Abuse Task Force (1975) in USA estimated the total number of regular users of barbiturates who were "in trouble" (suicidal and accidental overdoses and medical complications of barbiturate abuse) to be 300,000.

Chronic barbiturate addiction, like other addictions, tends to develop on a background of some psychiatric disorder, most commonly depression or psychoneurosis with symptoms of anxiety and insomnia.

As the desired effects of the drug are lost by continuous use (tolerance), the patient increases the dose gradually until he or she is taking an amount sufficient to produce symptoms when it is withdrawn. Alcoholics find that barbiturates effectively relieve their nervousness and tremor; then they may continue to take both alcohol and barbiturates. Heroin and morphine addicts may turn to barbiturates when they are unable to obtain opiates. As with other addicting drugs, the incidence of barbiturate addiction is particularly high in individuals with ready access to drugs such as doctors, nurses and pharmacists.

The benzodiazepines, librium and valium have been used extensively to control anxiety, and over-activity. While comparatively safe in the recommended doses, they are far from ideal. They frequently cause unsteadiness of gait and drowsiness and at times hypotension and syncope, particularly in the elderly.

The carbonic acid derivatives, exemplified by meprobamate, have a modest sedative action and can relieve mild degrees of nervousness, anxiety and muscle tension. Addiction to meprobamate can occur, and if four or five times the daily recommended dose is taken over a period of weeks to months, withdrawal symptoms, including convulsions, may appear, resembling those which follow chronic barbiturate intoxication. There have been occasional reports of death following the withdrawal of meprobamate and diazepam in persons who had been taking large doses of these drugs for protracted periods. In view of these observations, extreme caution must be exercised in prescribing new sedative drugs which are continually being introduced and which are said to possess no addicting or habit-forming properties.

Why People Use Drugs?

Three general types of theories have been suggested to explain drug addiction. These are constitutional, individual and environmental.

Animal research has shown that sometimes there is a genetic predisposition to use specific drugs. During recent years considerable interest and excitement have been aroused by the discovery-that the body produces its own opium-like substances, endorphins. The human brain has specific receptors for opiates, and these are concentrated in the pathways of the brain that are concerned with the perception of pain. It is speculated that opiate dependence in some people may be due to a genetically determined endogenous opioid deficiency.

It has been widely noted that most drug use is not attributable to any personality abnormalities. There is no unique "alcohol-dependent or heroin-dependent personality".

Drug-takers vary a great deal in their intelligence and there is little support for the view that drug use is caused in many cases by lack of intelligence. Evidence shows that drug takers are of average or above average intelligence.

Drug dependents in treatment institutions are often psychiatrically disturbed. It is possible that drug-taking satisfies disturbed psychological needs. It is possible that both psychiatric disturbance and drug taking may be caused by some other factor.

Most of the drugs that are used or misused have definite and usually relaxing effects. People who have high anxiety levels or other strong psychological needs find that drugs help them to adjust their unsatisfactory mental states to a more acceptable and bearable condition.

Many drug users certainly report that they do use drugs "to get high", "to feel relaxed", "for the experience". Often this motivation appears to be (quite casual. Drugs can be fun, and often a reliable means of obtaining enjoyable experience. Many autobiographical accounts of drug use have described and emphasized the important appeal of these pleasant effects. Most drug use is indulged in as a facet of other leisure pursuits which are themselves widely considered a source of pleasure. Clearly, these people are not psychologically disturbed. They have only to be reminded that exhilaration and pleasure can be obtained by alternative methods like music, sports or mountaineering.

Why do people continue to take drugs in spite of the realisation of immense harm being done by them? The theory of self-destruction is offered; people have poor self-images and strong feelings of hostility directed at themselves.

Youthful illegal drug use is often a *symbolic gesture of defiance* against parental or authority values. Family disturbances, broken homes, loveless homes or excessive protection by parents, educational disturbance, social deprivation are all important environmental factors.

Youthful curiosity and peer pressure are the most important factors in the initiation and perpetuation of drug use. Most youthful drugtakers are introduced to drug use by friends of their own age and background, particularly those staying away from their parental homes in flats or hostels. Peer pressure generates strong social endorsement for using cannabis, LSD or even heroin, especially on impressionable youths. It is clear that people will normally only be influenced by those whom they regard as acceptable, if not exemplars; people whom they like and wish to be accepted by.

The emergence of a distinctive youthful drug culture during the 1950's and 1960's probably occurred for a variety of reasons. The use of cannabis received a certain amount of encouragement by North American musicians. Rock music, permissiveness and Hippie culture arrived in the 1960's with a heavy emphasis of rebellion against established conventional values and practices, and an increasing alienation or anomie. The music of the period was also explicitly drug-oriented ("psychedelic music") and further fostered the integration of drug use with the general youth culture. Instead of fitting into the rat-race of straight society with its long-term planning and deferment of gratification, the drug culture permitted instant enjoyment.

Education—the Way Out of the Tunnel

The scale of drug problem is enormous and apparently on the increase. It is very important therefore to consider what can be done to prevent such problems arising. Health education should begin by parents themselves following healthy living practices which their children can imitate. A father who smokes or drinks alcohol is hardly the right person to teach his teenager son not to try "smoking grass".

The impact of health education is effectively nullified by commercial advertisements of alcohol, tobacco and tranquillizers. It has been suggested that there should be a total ban on advertising tobacco and alcohol. It is doubtful if such steps would produce any dramatic results.

Education is defined as an activity that modifies attitudes and behaviour. Attitudes to alcohol, tobacco and illicit drugs have taken decades, if not centuries to develop. It may take as long to change or improve these attitudes. We need a revival of the Ayurvedic emphasis on healthy living practices which ensure a *happy* life as well as a *good* life (*Swastha Vritta* and *Sad Vritta*).

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PHYSICAL EXERCISE IN HEALTH AND DISEASE

Introduction

The importance of physical exercise for the maintenance of positive health has been appreciated since ancient times. The following passage from *Charaka Samhita* sums up the subject very well:

"That activity of the body, which is meant to increase its strength and firmness is regarded as physical exercise. It should be practiced regularly in the right measure. Lightness, capacity for work, firmness, tolerance to hardship, subsidence of humoral discordance and stimulation of the gastric function accrue from exercise."

"Fatigue, exhaustion, wasting, thirst, asthma, cough, fever and vomiting result from over-exercise".

An important undesirable characteristic of modern life that distinguishes it from the past is the *low level of physical activity*. Epidemiological studies have suggested sedentary life style and associated overweight as important contributory factors in two very important diseases, diabetes mellitus and atherosclerotic arterial disease. The co-existence of the two diseases is common, and a major cause of mortality and morbidity in diabetes mellitus is cardiovascular complications. The purpose of this chapter is to review the physiology of exercise and the evidence in favour of the role of exercise in the prevention and treatment of these two important diseases, and to raise the important question are the two terms "physical exercise" and "Yogasanas" equivalent and interchangeable?

The Physiology of Exercise

The detailed study of muscular exercise began in the 18th Century when Antoine Laurent Lavoisier and Pierre Simon de Laplace discovered that the process consumes oxygen and produces carbon dioxide. As investigation progressed it became clear that exercise involves not only the muscles but also many other tissues; indeed, it involves an extraordinary coordination of the respiratory, circulatory and nervous systems, all working together under highly integrated controls. During the 19th Century almost every front-rank physiologist worked on muscular exercise at one time or the other. In the 20th Century, A. V. Hill of Britain, August Krogh of Denmark and Otto Meyerhof of Germany have received Nobel Prizes largely for work relating to muscle or muscular exercise. In the years before World War II the Fatigue Laboratory at Harvard University became a world centre for the experimental study of muscular exercise.

A normal man at rest inhales between six and eight litres of air per minute, from which about 0.3 litre of oxygen is transferred in the lung alveoli to the blood. Simultaneously carbon dioxide is given off by the blood and exhaled. When the same man is engaged in maximal muscular activity he may take in 100 litres of air per minute and extract five litres of oxygen. The term "maximal oxygen intake" introduced by Hill in 1924 characterizes the upper limit of performance of an individual in a remarkably predictable way and has proved to be an extremely useful physiological tool. The maximal oxygen intake in the normal individual, however, has to do not with the capacity of the lungs for ventilation or diffusion but with the maximal pumping capacity of the heart. Maximal oxygen intake is therefore a fair index to circulatory capacity, given normal lung function.

In 1905 John Scott Haldane (father of the late J. B. S. Haldane) and John G. Priestley showed experimentally that lung ventilation can be doubled by increasing the amount of carbon dioxide in the inspired air from the usual negligible amounts to about 3 percent. They postulated that the respiratory centre in the brain is primarily subject to the influence of carbon dioxide in the arterial blood flowing into it. More refined studies later showed that Haldane's chemical control theory was an over-simplification. Whatever its exact modus operandi, the respiratory control mechanism ordinarily prevents carbon dioxide from accumulating in any significant degree and virtually assures an adequate supply of oxygen over a range extending from rest to maximal exercise.

Hill studied the effects of breathing pure oxygen during exercise. The immediate effect of switching during steady exercise from ordinary air to air enriched with oxygen is to lower considerably the rate of ventilation. Athletes who have breathed oxygen-enriched air during exercise have reported a pronounced relief of subjective distress and have evinced a decrease in ventilation. Oxygen breathing extended the work capacity of trained athletes. On the other hand the Mexico Olympics showed the adverse effect of high altitude and hypoxia (deficient oxygen) on competitive athletics.

Oxygen Debt

An important mechanism employed by the body when it is under fairly severe stress from exercise is its ability to incur an oxygen debt. Dr. Roger Bannister of England in 1954 (as a medical student) ran a mile in 4 minutes. Later, Peter Snell of New Zealand ran the mile in 3 minutes 54.4 seconds. Such amazing feats are possible because the body mechanisms enable the exercising body to live temporarily beyond its capacity for transporting oxygen to active muscles and to compensate for doing so during rest after the exercise. Ventilation and oxygen intake continue to remain higher than normal for some time after vigorous exercise stops. The term "steady state" is used by exercise physiologists to define a rate of work that can be performed for

considerable periods of time without oxygen debt. During continuous activity such as walking steadily at three miles an hour for several hours, oxygen debt is built up rapidly at first and then levels off. Thereafter it may remain virtually unchanged for some hours. During violent activity it builds up rapidly and continuously until the activity ceases.

Normally arterial blood contains about 18 percent oxygen by volume (carried by the haemoglobin of red blood cells), breathing pure oxygen raises this figure to 18.5 percent. When a person is at rest, the tissues absorb oxygen at a rate that reduces the 18 percent oxygen content of the arterial blood to about 12 percent in the venous blood. The drop is known as the arterio-venous oxygen difference.

During exercise, on the other hand, the blood may have to give the tissues as much as 15 out of its 18 percent of oxygen, about 2/3 times more than at rest. The biological properties of haemoglobin play a very important role in enabling the body to adapt to exercise.

In a young man the heart can increase its output from about 5.5 litres of blood per minute at rest to nearly five times that figure during maximal exertion. At peak demand for oxygen the heart increases its output both by speeding up its rate of beating and by increasing the volume of blood pumped at each stroke. The pulse rate may double or triple, the stroke volume may go up from 60-80 millilitres per beat at rest, to as high as 120 millilitres per beat during exercise. Under moderate stress the heart may increase either its pulse rate or stroke volume, depending upon the individual's physical training and perhaps on other factors. The heart of a trained Athlete increases its stroke volume more readily than that of a sedentary person. Under the stress of emotions such as fear and anger the heart increases its output almost entirely by speeding up its rate of beating. If the nerves controlling the pulse rate are blocked experimentally by drugs, however, the heart will expand its stroke volume. The increase in cardiac output during emotional stress is considerably less than it is under physical stress, not more than a third over the normal output at rest.

Redistribution of blood flow

The heart's capacity for increasing its output five-fold is not enough even allowing for the ability of haemoglobin to give up oxygen more freely, to account for the muscles' consumption of oxygen during violent exercise. An extra margin is provided by a change in the pattern of blood flow. During heavy exercise most of the arterial blood is diverted to the active muscles where the need for oxygen is most acute.

When the body is at rest, the muscles take up no more than about 20 percent of the total body oxygen consumption; substantial amounts of oxygen go

to the brain, the heart, the skin, the kidneys and other organs. If the muscles' share of the oxygen is about 20 percent, they use at rest only 60 to 70 millilitres of oxygen (the body's total oxygen consumption at rest being 300 millilitres per minute). During exercise, as in running or swimming, the active muscles need about 3000 millilitres per minute, or about 50 times their resting requirements. The other body organs do not need anything like this increase of oxygen; in fact most of them actually use substantially less oxygen during maximal exertion. By adaptive mechanisms, all but a relatively small portion of the increased cardiac output can go to the active muscles.

The muscle cell is extraordinarily tolerant to a temporary shortage in oxygen supply, thanks to the presence in these cells of myoglobin/ this substance, like haemoglobin carries oxygen but it surrenders its oxygen much less readily than haemoglobin, and serves as a special oxygen store for the muscle cell. An intermittently contracting muscle cell might recharge its myoglobin during the resting phase and then, during a succeeding contraction call on myoglobin oxygen stores. Short periods of work alternating with short periods of rest seem to be more efficient metabolically as well as in work accomplished than long work periods followed by long rest periods. The amount of myoglobin in muscle tissue can be increased by physical training.

Research on the physiology of exercise has important practical objectives, particularly with respect to what can be accomplished by physical training. The training methods of athletes, from the time of the Greeks to the present, have been largely empirical. With methods based rationally on fuller physiological knowledge there is room for improvement of human physical achievement, well within the bounds of safety.

Exercise and Diabetes Mellitus

An early as 600 BC Sushruta advised the affluent diabetic to indulge in vigorous physical exercise (such as walking twenty "yojanas", or digging a well). At the same time Sushruta exhorted the thin diabetic not to exert too much.

After the discovery of insulin, Joslin and Katsch in particular emphasized the importance of physical exercise as one of the three basic principles in the management of diabetic patients. The advent of oral hypoglycaemic drugs in the 1950's contributed to a slackening in the attitude of both physicians and patients towards the basic principles. Diet control, exercise and weight reduction needed sustained effort on the part of the patient, which in turn required strong motivation and constant vigilance. Swallowing a pill or two every day was so much more comfortable, and if it reduced the blood sugar, then why bother about physical exercise? Manufacturers of drugs would ensure drug promotion. Who would promote physical exercise and weight reduction?

The results of a ten-year prospective multicentric randomized clinical study by the University Group Diabetic Programme (UGDP) comparing different treatment regimens gave a big jolt to everybody in the 1970's. The suggestion that a relationship existed between higher cardiovascular mortality and use of oral sulphonyl urea drugs was, to say the least, disquieting to both physicians and patients. The results have been subject of great controversy but the one good thing that has emerged from it is the *re-emphasis* on physical exercise and weight reduction as a primary modality of treatment in the maturity onset diabetes. A good physician today will give neither insulin nor oral drugs initially to asymptomatic diabetics in whom a diet and exercise regimen has not been first pursued sincerely. He will emphasize the need and method of regular physical exercise and weight reduction more aggressively than before.

What are the effects of exercise on diabetes? In 1887 it was discovered that the rate of glucose uptake is enhanced in the working muscles. Allen in 1919 demonstrated that exercise induces a fall in blood sugar and that it may improve acutely the tolerance to a carbohydrate load in the diabetic patient. On the other hand it was also appreciated that in poorly controlled ketotic diabetics, exercise may have deleterious effects. During the insulin era it was shown by Lawrence that exercise enhances the hypoglycaemic effects of subcutaneously injected insulin. When exercising and non-exercising children in juvenile diabetic summer camps were compared it was found that insulin requirements decrease on exercise. Goldstein et al., described a muscular activity factor (MAF) released by exercising muscles which apparently stimulated glucose uptake even in non-contractile muscles. Subsequent studies however, could not confirm the MAF hypothesis. Stimulation of glucose uptake during muscular exercise might depend upon increased binding of insulin to its receptors in muscle cells, resulting in *enhanced insulin sensitivity* even for the very small amount of insulin that may be present.

The increased fuel requirements of exercising muscles (free fatty acids, glucose) are met basically by increased production of three hormones, noradrenaline, adrenaline and glucagon, abetted by growth hormone and cortisol. Noradrenaline increases the rate of lipolysis and release of FFA from fat depot. Adrenaline increases muscle glycogenolysis upto six-fold during exercise and also mobilizes liver glycogen; it stimulates glucagon and inhibits insulin secretion. Glucagon plays a central role in the exercise-induced increase of hepatic glucose output.

Physical training results in improved myocardial performance, improved oxygen transport as well as increased oxygen extraction by the muscles; the myoglobin levels are elevated; mitochondrial size and number increase, so also their enzyme content and activity. Hence for the same amount of oxygen extraction there is less metabolic and circulatory demand. There is decreased catecholamine activity in the trained subject. Exercise increases fibrinolytic

activity of plasma, which is important since in diabetes, there is significant reduction in plasma fibrinolysis and a primary fibrinopathy may precede the metabolic and vascular abnormalities.

Currently there is wide-spread enthusiasm for *yogasanas* in diabetes. Compared to the exuberance of the enthusiasm for Yoga there, is a remarkable paucity of hard data on the physiological effects of *yogasanas*, on the various circulatory and hormonal parameters, to compare with data derived from treadmill or supine bicycle exercise. The need for such studies cannot be too strongly emphasized. The type of exercise recommended by Sushruta (long walks, digging a well, wrestling, horse riding) is similar to the treadmill exercise which has been extensively studied. It may be erroneous to consider that type of exercise and *Yogasans* as interchangeable. In fact *Yogasans* may be acting in an entirely different manner.

The emphasis of Yoga is on mind control. One of the modern methods advocated for the control of blood sugar is by *bio-feedback mechanism*. In this technique muscular relaxation is obtained by the help of electromyograph. The idea behind this is that stress causes rise in blood sugar (through neuro-endocrine mechanisms), relaxation techniques would lower the same. Other data show that meditation helps to change the metabolic pattern from type A (overdrive of sympathetic nervous system) to type B (predominance of parasympathetic). Adrenergic drive is essential for competitive sports, and *yogasanas* for Indian Olympic athletes might have actually reduced their performance (personal communication from Dr. Bhole of Kaivalyadham, Lonavala). The point to appreciate is that physical exercise and *yogasanas* are not interchangeable terms and the benefits derived from either of them may be mediated via entirely different mechanisms.

Exercise and Coronary Artery Disease

Atherosclerotic coronary artery disease has a multifactorial origin, of which each of physical activity and overweight (which are closely correlated) emerge as important contributory factors. Community settlements in Israel have an identical diet and life style for all inhabitants; those who have sedentary habits have shown two to four times higher incidence of coronary heart disease as compared to more active people. The Framingham studies in USA have shown that physical activity increases HDL (high density lipoproteins) which have a *protective role* against development of atherosclerotic lesions. It has been found that HDL levels of less than 30 mg/ dl are associated with twice as much risk of myocardial infarction as those with HDL over 60 mg/dl,. Vigorous exercise like jogging raises HDL to the desirable range. Several reports have indicated that increased physical activity, both at work and at leisure, is associated with diminished risk of myocardial infarction (heart attack). More and more people are therefore now engaging in such physical activities as jogging, golfing, swimming etc. as part of their health programme.

Not many years back, patients of myocardial infarction were advised prolonged rest and a somewhat resigned life. Today the pendulum has swung to the opposite side. Early ambulation and high levels of physical activity are now widely recommended in many patients who have recovered from myocardial infarction. Participation of such patients in marathon races (which perhaps represent the ultimate in physical exertion and endurance) is a testimony to what aggressive rehabilitation under supervision can be achieved. On the other hand non-supervised indulgence in jogging by enthusiasts has led to some sudden deaths. Hence it is worth examining critically the exact contribution of exercise in coronary patients. Eckstein in 1957 produced ischaemia in dogs experimentally by ligating their coronary arteries. In one set of dogs, after 48 hours the animals were put on a treadmill; many developed ventricular aneurysms; another set of dogs was rested for seven days after ligation and then put on a treadmill for exercise; they demonstrated development of collateral circulation. This attractive idea that exercise induces development of collaterals has strongly motivated physicians and patients to take up enthusiastically to physical exercise. It must be stated however, that similar experiments in rats foiled to confirm this. Gregg in 1974 observed that there is really no experimental evidence that physical exertion improves the collateral circulation in the normal heart.

However, evidence that human coronary artery disease can *regress* has been provided in studies on swine and primates and in serial human coronary angiographies. Exercise by inducing higher levels of HDL probably contributes to this regression. Control of high blood pressure and complete stoppage of cigarette smoking are the other two contributory factors aiding the regression or non-progression of lesions. But it is worth noting that the *type* of exercise that is considered essential is *dynamic* muscular exercise of sufficient *magnitude and duration*: it should raise the pulse rate to at least 70 percent of the maximum attainable for the age and sex (say over 120 per minute for a man of 55), which should be sustained for at least 30 minutes, at least 3 days in a week preferably on non-successive days. Fast walking, jogging, bicycling, swimming are the examples of dynamic muscular exercise. During the last ten years I have done executive health check-up of over 5000 middle aged healthy individuals and a routine question regarding physical exercise elicits from many persons a reply: "I do Yoga for 10 minutes every day". Here again physicians as well as patients seem to use the two terms as if they are interchangeable. The haemodynamic and metabolic changes associated with 45 minutes of vigorous dynamic muscular exercise will probably be entirely different from the "ten minute yoga". I am looking for hard data on metabolic, hormonal and haemodynamic effects of Yogasanas, to match the claims made and enthusiasm shown by their adherents. The sophisticated methods are now available to us to substantiate and validate the beneficial effects if any. On the other hand yoga might be producing its benefits by an entirely different mechanism from that discussed under dynamic muscular exercise. The

conversion of Type A coronary prone personality to Type B has been discussed earlier. Increased adrenergic activity is an important contributory factor, especially in the onset of dangerous arrhythmias. Reduction of adrenergic activity by means of beta-blockers or by yoga and meditation would be beneficial. The motivation and attitude towards health-related behaviour (refraining from smoking, control of caloric intake, a more relaxed attitude by practising "Shavasan") of the health conscious individual may be important contributory factors, irrespective of the direct contribution of exercise and yogasanas. The scientific method demands validation of any proposition. Uncritical acceptance and uncritical rejection are both equally inimical to the spirit of science. Open-minded curiosity about any claims of benefit by any mode of therapy or procedure, and healthy scepticism about claims till validation is established; make an ideal blend in a scientific mind. This way one would safeguard against missed opportunities and false hopes about Yogasanas end up by making a plea for an increasing network of play grounds, gymnasiums and sporting facilities of all sorts, and promoting their full utilization as a means of promotion of positive health.

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PHARMACOLOGY- ANCIENT AND MODERN

Introduction

Ancient Indian Medicine had attained a very high degree of sophistication in its consideration of drugs and their classification according to their conceived modes of action. Considering that the main intellectual tool at their disposal was empiric observation, one marvels at the great width and depth of their conceptual thinking about drugs. In addition, one finds appreciation of certain basic principles in therapeutics which are valid even today. Examples:

"Medicine is of two kinds — one kind is promotive of vigour in the healthy; the other, destructive of disease in the ailing".

"The opposite of medicine is also of two kinds — one causing immediate disorders and the other causing remote ill effects".

"He is the best physician who knows the science of the administration of drugs with due reference to the clime and season, and who applies it only after examining each and every patient individually".

"A drug while inducing therapeutic effect should not evoke untoward effects".

"A drug that is not understood perfectly is comparable to poison, weapon, fire and the thunderbolt; while the perfectly understood drug is comparable to ambrosia".

"The drug whose name, form and properties are not known, or the drug which though known, is not properly administered, will cause disaster".

"The art of prescription depends upon the knowledge of dosage and time and on this art depends success. Hence the skilful physician stands even superior to those possessing merely a theoretical knowledge of drugs".

"The physician, endowed with a good memory, well-versed in diagnosis and the application of therapeutic agents, self-controlled and prompt in taking right decisions, is entitled to undertake treatment by prescribing these drugs".

Ayurvedic Material Medica

Drugs are derived from vegetable, animal and mineral origin. Sushruta has classified drugs according to their properties into 37 "*ganās*" (groups).

Charaka Samhita describes 600 purgative preparations and 500 decoctions classified into 50 principal groups according to their action (Table I). Some common constituent detectives keep recurring in these principal groups, the reasons for which are explained thus: "A single drug may have many appellations owing to its diverse actions. A man is able to perform various actions. He is given that particular appellation which is characteristic of the action which he does, either as an agent or instrument or doer. The same thing is observed in the case of drugs".

It is interesting to see how the ancient physicians classified substances according to the concepts then prevalent, and how their mind worked in making working hypotheses, which look so far removed and irrelevant in today's thinking.

"Substances that are heavy, rough, hard, slow, stable, clear, dense and gross and abounding in the quality of *odour*, pertain to the protoelement *earth*. They promote compactness, plumpness, heaviness and stability".

"Substances that are fluid, unctuous, cold, slow, soft and slimy and abounding in the quality of *taste*, pertain to the proto-element *water*. They produce moisture, unctuousness, union, liquefaction, softness and delight".

"Substances that are hot, acute, subtle, light, dry and clear and abounding in the quality of *form* pertain to the proto-element *fire*. They produce burning, digestion, radiance, lustre and colour".

"Substances that are light, cold, dry, rough, clear and subtle and abounding in the quality of *touch*, pertain to the proto-element *air*. They produce dryness, depression, clearness and lightness".

"Substances that are soft, light, subtle, smooth and abounding in the quality of *sound*, pertain to the proto-element *ether*. They produce softness, porousness and lightness.

"In the light of this knowledge there is *in* the world no substance that may not be used as medicine in this or that manner, for this or that purpose".

"Whatever therefore substances do, whether by virtue of their nature as substances, or by virtue of their qualities, or by virtue of both their substantive and qualitative nature, in any given time, at any given place, having been administered in a given mode with a given result in view — all that is their *action*. Whereby they act is the *potency*. Wherein they act is the *place*. When they act is the *time*. How they act is the *mode*. What they achieve is the *result*". "Heavy things increase and light things decrease by the repeated use of heavy and light articles".

"Substances are divided into 63 groups according to the distribution of tastes. This number of 63 swells into an incomputable figure if the after tastes are taken into count".

"The sweet taste is born of the preponderance of the water element, the sour taste is born of the preponderance of the earth and fire elements, the salt taste are born of the preponderance of water and fire elements, the pungent taste are born of the preponderance of the air and fire elements. The bitter taste is born of the preponderance of the air and ether elements; and the astringent taste is born of the preponderance of the air and earth elements".

"Among these, the tastes which are of the nature of fire and air have, for the most part, a tendency to go upwards by virtue of the light and soaring quality of air and the propensity of fire to flame upwards".

"Whereas tastes which are of the nature of water and earth have, for the most part, a tendency to go downwards by virtue of the heavy nature of earth and the propensity of water to flow downwards, the tastes of a mixed nature evince both these tendencies".

The Qualities and Actions of Each Taste

"*Sweet taste* increases the body nutrient fluid, blood, flesh, fat, bone, bone marrow, vital essence and semen, prolongs life, clarifies the sense organs, imparts vigour and complexion, *alleviates pitta, toxicosis* and *vata*, and allays thirst and burning sensation. It promotes cheerfulness, vitality, allays fainting". At this juncture it is tempting to speculate that the above hypothesis was built on the basis of observing the effects of sugar on hypoglycaemia brought on by exertion, and the effect of sweet eatables on the healthy people.

"*The salt taste* is diffusive; it is liquefacient, digestive, and curative of *vata* stiffness, obstruction and accumulations. It gives relish to food and is always used in food".

Here again one could speculate that the hypothesis could have been built on the basis of observing effects of common salt on salt-depleted or heat-exhausted subjects (abdominal pain and cramps in the legs attributed to "vata", relieved by taking salt) and the effect of potassium salts in paralytic ileus ("curative of obstruction and accumulations".)

"*The bitter taste*, though in appetitive, is yet appetising in action. It is *antidotal to poison*, vermicidal, curative of fainting, burning, itching, dermatosis and thirst. It is *febrifuge*, digestive stimulant, depletive and desiccant of moisture".

Primitive man discovered plant poisons (alkaloids and glycosides) through their bitter taste. He also observed animals vomiting bitter herbs and getting well. By accident he found the willow bark and the cinchona bark reducing fever.

The Nature of Specific Action

“Where there exists similarity in taste, potency and post-digestive changes and yet a difference in action is observed, such special difference in action is called the *specific action of the substance*. For example, white flowered leadwort is pungent in taste and hot in potency. Red physic nut is similar to it in all respects and yet by reason of its specific action it acts as a purgative when administered to man”.

Here is an instance of intuitive wisdom which conceived a *specific effect of a drug*, which would become the dominant theme of 20th Century pharmacology.

Ayurvedic physicians considered the *Kala* (duration of action), *Karma* (action), *Veeryaus* (potency), *Adhikaranam* (site of action), *Upaya* (mode of action) and *Phalam* (therapeutic effects) of a drug.

Since the pathogenesis of disease centered on food and digestion, and accumulation of toxic substances in the alimentary tract, the major emphasis was on *emetics* and *purgatives*, a wide variety of which was used. There was also a remarkable preoccupation with cleansing procedures comprising five procedures, “*panch karma*”, those including emesis, purgation, enema. Since the concepts about pathology and pathogenesis have now changed considerably, much of the ancient pharmacopoeia has become irrelevant in the present context. It is interesting to note, however, that iatrogenic illness is not a new phenomenon in the practice of medicine, since Charaka describes twelve complications of improper use of enema (inadequate action, overaction, exhaustion, distension of abdomen, hiccup, cardiac disorder, diarrhoea, headache, bodyache, griping pain and excessive discharge).

Further Additions to Ayurvedic Pharmacopoeia

It is notable that opium does not figure in the Ayurvedic pharmacopoeia. It was probably added in the 8th Century after contact with the Arabic physicians. “*Rasachikitsa*” was added in the 10th Century and conceptually it comes closer to modern chemotherapy.

Rise of Modern Pharmacology

The Science of Pharmacology is concerned with the action of drugs or chemicals on the living systems. Today's pharmacology borrows heavily from its sister disciplines such as biochemistry and physiology. Pharmacologists and physiologists speak the same language.

Our understanding of how drugs act depends upon our concepts of how the normal body works. For instance, Ayurveda formed the concept of *Vata* to explain observed phenomena — normal and abnormal. Normal *vata* was responsible for locomotion, speech, sense perception, gastrointestinal mobility, respiration, circulation, and so on. They sought to explain observed abnormal phenomena in terms of disturbed *Vata* — paralysis, tremors, hiccup, vomiting, pain and so on. The effect of drugs was necessarily studied by empiric observations on a large number of patients and beneficial effects, when noticed, were attributed to their qualities in normalising the vitiated *Vata*. The same logic applied to the concept of *pitta* and *kapha*. The Arabs, best exemplified by Avicenna (980-1037 A.D.) made important contributions to the corpus of empiric knowledge about crude herbal drug preparations. Arabic pharmacologists developed Galen's physiology to provide explanations of how the combinations of four qualities of a drug — i.e., hot, cold, moist and dry, could affect the four humours of the body, blood, phlegm, black bile and yellow bile, the Greek humoral concepts similar to Ayurveda. For many centuries this was the language of the pharmacologists. Twentieth Century biology has brought us a far better understanding of how the normal body works. Today we understand the nature of drug action a lot better than ever before in the history of medicine. As new mechanisms of life processes are elucidated by advances in 20th Century biology, today's attempts to understand drug action are made in terms of cell membrane receptors, activation of membrane-bound adenylate cyclase and cyclic AMP, enzyme activation or inhibition, neurotransmission and ion fluxes especially of sodium, potassium and calcium, and cell structure as revealed by electron microscopy. Today, in effect a new pharmacology is being mapped out within the interior of the cell. The DNA and RNA, ribosomes, mitochondria, lysosomes, storage granules, micro-tubes are all known sites of drug action. For instance, alkylating agents damage chromosomes and produce mutations by their action on DNA. Streptomycin interferes with normal transcription via messenger RNA; Chloramphenicol binds to ribosomes and inhibits protein synthesis; barbiturates act on mitochondria and inhibit respiration; Corticosteroids protect lysosomal membranes; Colchicin acts on micro tubes and stops mitosis at spindle stage. As in all biological sciences, there is now a tendency to deal with drug effects on a molecular basis. It is interesting to note that conceptually the Ayurvedic physicians were also thinking at a molecular level, so were the Chinese physicians in their concept of *yang* and *yin* which is so similar to current day Cyclic AMP and Cyclic GMP. It is highly rewarding intellectually to follow the march of science from the ancient intuitive

approach to the modern experimental approach, a long march spread over 3,000 years. Today's concepts are based on objective documentation of events revealed by, for instance, electron microscopy and auto radiography, and what is more important, they lend themselves to experimental verification and stand the scrutiny of science as enunciated by Karl Popper — testability, verifiability, reproducibility and falsifiability. This is why modern medical science is intellectually more satisfying.

Rise of Chemical Knowledge

In relation to medicine, little knowledge recognizable as chemistry existed prior to the 15th Century. With the rise of alchemy during this period, a limited number of simple and useful chemical compounds became known, for instance, the use of sodium sulphate as a purgative by Johann Rudolph Glauber (1604-1688). Paracelsus (1493-1541), an unusual and gifted physician popularised the use of tinctures of salts of potassium, iron and arsenic. His greater contribution was his iconoclastic attitude towards the then prevalent classical Galenical doctrines, which spurred independent thinking.

The first great chemical advance was the isolation in relatively pure chemical form of the active ingredients of crude extracts of plant origin. Friedrich W. Serturner isolated *morphine* from opium in 1806. It took mankind 5,000 years to make this all-important advance. The exact chemical structure of morphine was arrived at in 1923. And the complete synthesis, as a conclusive proof of structure, was achieved in 1950. Today hundreds of synthetic and some semi-synthetic morphine congeners adorn the shelves of organic chemists.

Francois Magendie (1783-1855) was able to publish in 1821, a medical formulary made up entirely of purified chemical agents. In it were such alkaloids as emetine from ipecacuanha, quinine from cinchona bark and strychnine from nux vomica.

The industrial revolution of the 19th Century which gave birth to synthetic organic chemistry for industrial use, established the type of knowledge necessary for the synthesis of new drugs. The new chemical industry produced general anaesthetics, disinfectants, antipyretics and hypnotics. Emil Fischer (1852 - 1919) was the great genius of organic synthesis. He collaborated with Joseph von Mering in 1903 in the synthesis of barbital, the first barbiturate. This opened the way for other investigators to synthesize thousands of similar structures. The synthesis of rubber, plastics, commercial solvents, industrial enzymes and synthetic fibres, to mention only a few, have all aided in the eternal quest of new drugs. During the last 25

years, more new drugs have been introduced than all the drugs already existent in the pharmacopoeia put together. Not only are drugs being discovered at an ever increasing rate, but the quantity manufactured and deployed for various purposes is also increasing enormously.

Drugs and Cell Membrane

The use of ether as a general anaesthetic started with the dramatic demonstration given by William Morton, while he was still a medical student at Massachusetts General Hospital in Boston, USA, in 1846. General anaesthesia, which radically altered the surgical scene was a major landmark in the history of medicine.

Sir James Young Simpson and his colleagues in England introduced chloroform in 1847, just twelve months after Morton's use of ether in America.

Although nitrous oxide was prepared in 1772 by Joseph Priestley one year after his discovery of oxygen in Britain, the use of nitrous oxide along with oxygen was introduced by Edmund W. Andrews, a surgeon in Chicago in 1868, in surgery and dentistry.

The understanding about the mode of action of these compounds came much later. In 1899, the German pharmacologists Overton and Meyer observed independently that substances which were common nutrients (such as sugars and amino-acids) did not penetrate readily into cells whereas alcohols, ethers, amides, ketones and various hydrocarbons entered rapidly and produced a narcotic effect (Greek narcosis means numbness). Cells that were active and motile rapidly became inactive on exposure to these agents; when they were removed, the cells promptly recovered. In seeking an explanation for this unexpected difference in the penetration of molecules, Overton suggested that entry of foreign molecules depends on a *physical property* which was common to them all, namely *solubility in lipids*, and that the entry of nutrient molecules required the cells to perform work as in glandular secretion.

The work of Overton and Meyer had important consequences. It led to the view, first, that lipids might be constituents of cell membranes, and second, that the entry of nutrient molecules depended on some form of *active transport*; third, that lipid-solubility was a clue to the mode of action of narcosis-producing drugs.

Recently it has been suggested that narcosis occurs when a constant fraction of a highly polar non-aqueous phase of the cell is occupied by molecules of the narcotic. The greater potency of halothane (CF₃CHClBr) as compared to chloroform (CHCl₃) may be due to its greater volume and mass.

Such molecules might, by obstructing aqueous channels in the membrane, interfere with the movements of sodium ions.

The action of polar narcotics (soluble in water as well as in lipids) such as ethyl alcohol which are *metabolized* by the cell is different from the inert gases and the non-polar narcotics such as ether and chloroform which leave the cell unchanged. Probably the action of the latter is readily explicable in *biophysical* terms. There is no evidence so far of their combining with any receptors or inhibiting any enzyme systems.

The Concept of Specific Receptors

In the early years of the 20th Century, a number of synthetic drugs became available for the treatment of some infections, notably syphilis and trypanosomiasis. Paul Ehrlich (1854 - 1915) developed the concept that the specific effects of a drug could be explained by the reaction between the drug and a particular chemical group in the cell or tissue, a *specific receptor*. That drugs may work upon only one organ system or may have a highly selective site of action was known to Ayurvedic physicians as shown earlier in this Chapter.

Felice Fontana (1720-1805) in 1765 made an exhaustive study of snake venoms and other toxic substances and concluded that drugs act preferentially on one type of body tissue.

James Black (1815-1893) using mainly inorganic compounds, established that drugs are active only when they reach a responsive tissue. Comparable studies were made later by A. Crum Brown (1838 - 1923) and T.R. Fraser (1841 - 1920) on organic compounds. Ehrlich's concept of specific receptors had far reaching consequences, as we shall see later. Receptor theory is an important part of present day pharmacology. It is particularly applicable to drugs which modify behaviour of excitable tissues.

Pharmacodynamics

During the early decades of the 19th Century, in France, physiology first developed its scientific identity as an autonomous discipline. Francois Magendie (1783-1855) was the pioneer in the development of experimental physiology and the beginnings of experimental pharmacology.

Towards the end of the 19th Century, as the young field of physiology began to emerge, the newly discovered mechanisms of bodily function lent themselves admirably to the description and elucidation of the mode of action of drugs on living organisms. In fact, it is fair to state that the fathers of modern pharmacology were

trained primarily in physiology. Rudolf Buchheim (1820 -1879) was such a physiologist who became the first recognized professor of pharmacology in 1846. He made many contributions to the study of drug action especially concerning atropine and ergot.

Among the pupils of Buchheim was Oswald Schmiederberg (1838 - 1921) who was destined to establish a long lineage of pharmacologists.

For centuries it was known that eating *ergot*, a fungus infecting rye grains, caused abortion and it was used for inducing labour, it was also known that eating bread made of infected rye for any considerable time could produce severe gangrene of the limbs. Henry Dale (1875 - 1968), a young man freshly trained by the great physiologists of the day at Cambridge in England brought modern pharmacological science to ergot at the beginning of the 20th Century, with extraordinary success. In 1906, Dale discovered that ergot extract could annul the blood-pressure-raising effect of adrenaline. Dale found that his ergot extract was a partial or selective antagonist to adrenaline; the *excitatory actions* (faster heart rate, higher blood pressure) were reduced but the *inhibitory actions* (bowel, bladder muscle inhibited into quiescence) were left untouched. Dale went on to look at the chemical nature of his ergot extract. Ergotoxine was the name given to the "pure" substance found in it. *Ergotoxine* is now known to be a mixture of three different but closely related substances, all derivatives of lysergic acid. But the sympatholytic actions, mentioned above, were not the basis of ergot's stimulant action on the uterus. Dale had to wait nearly thirty years to see the agent responsible for this effect, another related derivative of lysergic acid, *ergometrine* (ergonovine) to be extracted from ergot.

Dale discovered two other substances which led to a revolution in pharmacology. Unlike the ergot alkaloids which are complex chemicals, these new substances, *histamine* and *acetylcholine* were very simple substances. Dale showed that histamine acted on tissues and organs throughout the body to produce a picture almost identical with what clinicians later recognized as anaphylactic shock. Histamine opens up millions of pores in the blood capillary walls to flood the area with plasma proteins and blood cells, esigned to repel foreign invaders, but as in every war, there are innocent victims: in this case there is also stimulation of the secretions in eyes and nose, contraction of muscles in the bronchi, narrowing the airway, and dilation of blood vessels leading to fall of blood pressure and shock. The whole reaction can be unpleasant, dangerous or even fatal.

The understanding of the pathology produced by histamine led to the development of anti-histaminic drugs in much the same way as ergotoxine blocked some of the effects of adrenaline.

Dale discovered that acetylcholine had two distinct types of action. One type was capable of being blocked by atropine and the other type by nicotine. Indeed, Dale had a central role in establishing the chemical theory of transmission of the nerve impulse. When impulses travel along the nerve fibres which pass between the brain and the muscles, they release at the nerve endings, the contents of millions of tiny vesicles, each of them containing a few thousand molecules of acetylcholine. These molecules of acetylcholine convey the information from nerve-endings to muscle fibre and initiate its contraction. Drugs having actions like nicotine, including the arrow poison curare, can annul this action of acetylcholine and produce muscle paralysis. However, when acetylcholine is released at nerve endings in certain organs such as the heart and blood vessels, atropine, but not curare, is able to block this action.

How does it come about that drugs can pick and choose in this way? How is it that foreign substances can produce such selective actions? Twentieth Century molecular biology has given answers to these questions in terms of cell membrane receptors, enzymes and activated proteins.

Drugs and Enzymes

The discovery that enzymes were sensitive to drugs marked the beginning of biochemical pharmacology. In receptor theory the interaction between drug and receptor is analogous to that between substrate and enzyme.

Acetylcholine is an ester which can be rapidly broken down to acetic acid and choline by the catalytic enzyme cholinesterase. At the nerve-muscle junction, as soon as the muscle is stimulated by acetylcholine, the enzyme cholinesterase rapidly destroys it. If the enzyme is inhibited, the effects of the nerve impulses become greatly exaggerated and the muscles are thrown into irregular twitching and spasm.

Physostigmine (Eserine), an alkaloid extracted from the calabar bean, an ordeal poison once used by witch doctors in West Africa, inhibits cholinesterase — a classical example on an enzyme inhibitor. Eserine was the first drug to be used as a biochemical tool for the identification of a substrate (acetylcholine) which would otherwise have been destroyed instantly. But for eserine, the theory of neuro-chemical transmission of nerve impulse might have remained untested by experiment. The so-called nerve gases (contemplated in warfare) are capable of forming irreversible chemical bonds with cholinesterase. Other cholinesterase inhibitors like malathion are used as insecticides.

Myasthenia gravis is a disease in which the patient suffers from muscle weakness which is often severe. The muscles behave as though there was not enough acetylcholine to stimulate them. When cholinesterase is *reversibly*

inhibited by a drug like neostigmine (which is in the same category as physostigmine) muscle power returns dramatically because acetylcholine now stays around longer to give stimulation to the muscles.

Many useful drugs are enzyme inhibitors. Allopurinol (zyloric) is chemically almost similar to the substrate hypoxanthine, which is acted upon by xanthine oxidase, an enzyme which helps to add an oxygen molecule to hypoxanthine to produce uric acid. Allopurinol has affinity for the active site of xanthine oxidase, and thus causes *enzyme blockade*, thereby preventing the rise of uric acid and an attack of gout. The unoxidised precursors xanthine and hypoxanthine now accumulate in the tissues and blood but they are readily eliminated by the kidneys into urine.

Drugs can be used to play tricks on enzymes. The enzyme is offered a drug which closely resembles the substrate (which it unites or divides), and the enzyme can be persuaded to make *counterfeit molecules*. For example noradrenaline, the transmitter at the sympathetic nerve endings, is synthesized from an earlier amino-acid precursor, DOPA. The enzyme DOPA oxidase can also act on administered methyl DOPA to produce methyl noradrenaline which has been described as a *false transmitter* because it is far less effective than the normal neuro transmitter. Methyl DOPA is therefore successful in reducing high blood pressure by decreasing the normal vasoconstrictive effect of noradrenaline.

Cell-Membrane Bound Enzymes and Drugs

Most enzymes are not found free in cell fluid but are firmly fixed to cell membranes. There may be several ranks of enzymes so arranged that the products of one reaction immediately become the substrate for the next. Cell membranes are highly specialized structures made of a mosaic of proteins and fats (lipoproteins) and the movement of molecules and ions across the membrane is strictly regulated. Impedance to the flow of ions gives cell membranes a static charge like an electrified perimeter fence which can be switched on and off as pores in the membrane are opened or closed. This is the mechanism by which cells are sensitive to changes in their environment, the basis of their excitability. Thus specialized junctions between cells, as in the nervous system, heart, smooth and skeletal muscle are highly permeable structures with conductance for ions far greater than in non-junctional membranes. Each heart beat is preceded by a regulated switching off of the cell membrane voltages and the synchronized voltage changes can be detected on the surface of the body with an electrocardiogram.

Some drugs used in the treatment of cardiac rhythm disturbances, selectively act on the junctional cell membranes, particularly of the heart, to alter the flux of ion currents across cell membranes.

In 1914, Wenckebach, a Dutch physician was told by a sailor that when he took quinine for his malarial fever, his palpitation of the heart disappeared. Wenckebach confirmed the effect of quinine, and later its more effective optical isomer quinidine on atrial fibrillation and other cardiac arrhythmias. By a direct action on the conducting cardiac tissue quinidine decreases the velocity of conduction in atria, AV node and ventricles and reduces their excitability. It prolongs the functional refractory period of myocardial cells by slowing depolarization, without affecting the half-time for repolarization which determines the absolute refractory period. The cellular mechanisms for these electrophysiological effects are not well understood. It probably chelates calcium ions, hence the negative inotropic action. It also inhibits ATPase activity and decreases the permeability of cell membrane to sodium ions.

Xylocaine (lidocaine) is another drug which alters the pores through which sodium ions flow into the heart conduction system cells just before each contraction and so can control the speed with which the wave of excitability passes across the heart. Procaine prevents conduction in nerve axons by blocking channels for the entry of sodium ions. By contrast, cardiac glycosides interfere with outward movement of sodium ions from cells and at the same time reduce the entry of potassium, when this is linked to the extrusion of sodium ions. This action of cardiac glycosides is seen not only in junctional membranes of nerve and muscle, but also in red blood cells, the gastric mucosa and renal tubules. The effect may be metabolic since the glycosides influence the activity of ATPase, an enzyme which is normally activated by Na^+ , K^+ and Ca^{++} . Thus the actions of cardiac glycosides have been related to such biochemical concepts as the metabolically driven Na^+ pump and the role of calcium ions in the coupling of excitation with contraction in cardiac muscle. Digoxin produces an increased uptake of cell Ca^{++} and this probably facilitates the association between action and myosin and the contractile process, through Ca^{++} ATPase.

Membrane Transport and Drugs

All cell membranes restrict the movement of other molecules into and out of the cells and there are special arrangements to restrict the penetration of substances between the blood and the brain, or between the placenta and the fetus. To compensate for this, cell membranes are supplied with special chemical pumps or transport processes to move particularly valuable substances either way across the membranes. Regulated penetration is particularly important in the kidneys. The renal tubules have highly developed systems of transport processes located in their membranes and they actively pick out and return to the blood the molecules that the body needs such as glucose and amino acids, and leave behind the useless end products of metabolism such as urea and uric acid.

Many drugs influence transport in the cells with special functions such as the nephrons. Organic mercurial compounds and drugs containing the sulphonyl group (SO_2NH_2), notably acetazolamide, inhibit the reabsorption of filtered sodium, whereas aldosterone and corticosterone increase sodium reabsorption. The glycoside phloridzin blocks the reabsorption of glucose in the renal tubules as well as its absorption from the intestines. Vasopressin does not affect the transport of solutes but increases, by a highly selective action, the permeability of the renal tubular epithelium to water.

The effects of drugs on the traffic of ions and other solutes in the different regions of the renal tubules have far reaching consequences for acid-base regulation in the body and profoundly influences the action of other drugs. For example, drugs that promote the loss of sodium may also cause loss of potassium and a fall in the body store of potassium, thereby lowering the threshold for the toxic effects of cardiac glycosides.

Penicillin is an organic acid and is eliminated at high speed mainly because it is secreted out of the body into the urine by the tubular cells of the kidney. When it is desired to maintain very high blood levels of penicillin as in subacute bacterial endocarditis, a drug like probenecid (Benemid) is used, which is also an organic acid and competes for the same secretory process as used by penicillin so that the elimination of penicillin is impeded by competition and useful high blood levels are attained.

Drug Receptors and Receptor Blockade

There are probably thousands of chemical regulators in the body. The chemical structure of some of them is known (such as acetylcholine, noradrenaline, histamine) and where they are distributed to all cells in the body by the blood rather than released strictly localized to the site of action, they are classed as hormones. How does any one cell know what is going on if it is being bombarded by a large number of different regulators? The answer is provided by specific receptors. Each chemical regulator has built into its conformation and chemical properties some specific piece of biological information. For that information to be received by a cell the information has to be decoded in the same kind of way that a radio receiver decodes radio waves that it is tuned to receive and no others. A receptor has some similarity to the active site of an enzyme, that is, a macromolecular site which shows chemical complementarity in its spatial arrangement and distribution of electronic charges, to the corresponding hormone. However, whereas at an enzyme, the substrate is chemically altered and the enzyme remains unchanged, at a receptor, the hormone is not altered but the interaction changes the receptor. Changes in the conformation and charge distribution at a receptor then triggers off some predetermined change in cellular activity.

Receptors, like enzymes, are also common sites for drugs to act. After all, both of these sites are designed to be the basis for selective chemical effects in physiology, and if drugs happen to contain enough of the recognizable chemical information, they will be able to deceive the body's own selective machinery. Just as enzyme inhibitors (like allopurinol) are often closely related chemically to the normal substrate, so receptor antagonists are often closely related chemically to the natural hormone. Knowledge about the physiological function of a specified hormone/receptor system can be used to guess what the properties of a new interfering substance (antagonist) might be. There are many examples of this kind of speculation, but here is an example which led to the development of *propranolol*.

The noradrenaline receptors are the special chemical sites on the heart muscle cells which first recognize and combine with noradrenaline and then trigger the changes in cellular enzymes which make the heart beat faster and stronger. Propranolol binds to the β receptors, and not only by itself fails to trigger the receptor but also blocks noradrenaline from doing so.

The beta-blockers were discovered after it was found that the earlier antagonists, the alpha-blockers were unable to prevent the heart responding to adrenaline. New histamine blockers were discovered after it was found that the old antihistamines were unable to prevent the glands in the stomach lining which secrete hydrochloric acid, from responding to histamine stimulation. Histamine receptors of two types have now been identified. The antihistamines (frequently used for allergy) block the H₁ receptors. Cimetidine (tagamet) blocks the H₂ receptors.

Histamine is also present in the brain and along with several other chemicals may have a neurotransmitter function about which we know at present very little. With the help of histamine receptor blockers like cimetidine, there is a chance of knowing more about the role of histamine in brain function.

As we understand more and more how drugs make use of the body's own control machinery — receptors, hormones, transport systems, binding sites and so on — to produce selective action, we become interested in more and more varieties of configurations of molecules (derived from plant or animal origin) which might lead to the discovery of newer receptors and scope for newer drugs. Opiate receptors and amphetamine receptors in the brain are recent examples.

Interaction between a drug and its elective site of action is determined by its *goodness of fit* for the active site plus the likelihood that random molecular motion will bring a molecule into contact with that site. The likelihood of such a molecular encounter is mainly determined by the concentration of the molecules. Where a molecular species has high affinity for a site, a low concentration of molecules will achieve effective interaction.

But as concentration is increased, effective interaction may begin to take place at lower affinity sites, and new actions, perhaps unwanted and even damaging ones, can occur. This will be true whether the molecule is a natural one (say a hormone) or a foreign one (a drug). For example, a polypeptide hormone secreted by the posterior pituitary regulates the body water content by controlling its reabsorption by the distal renal tubular cells. If however, large unphysiological doses are given intravenously, a new action, vasoconstriction, appears. The latter action was discovered first, hence the hormone was called *vasopressin*. The action on renal tubules was discovered much later and is now called the *antidiuretic hormone*. All kinds of hormones and chemical regulators in the human body such as insulin, histamine and vitamin D can be lethal when used as drugs and given in overdose.

The Adenylate Cyclase System

Cyclic 3-5 adenosine mono phosphate (c AMP) acts as an intracellular "second messenger" for a diverse array of peptide hormones and biogenic amines, drugs and toxins. Many hormones (ACTH, MSH, Calcitonin, parathyroid hormone, FSH, LH, HCG, TSH, TRH, vasopressin, glucagon, beta-adrenergic catecholamines, prostacyclin and prostaglandin E_j) initiate their action by binding to specific receptors on the external surface of the plasma membrane. The hormone-receptor complex activates the membrane-bound enzyme adenylate cyclase which synthesizes cyclic AMP from intracellular ATP. Within the cell, c AMP relays the hormonal message by combining with its own receptor, cAMP-dependent protein kinase. Activated by cAMP, protein kinase transfers the terminal phosphate of ATP to specific protein substrates (usually enzymes). Phosphorylation of these enzymes enhances (or in some cases inhibits) their catalytic activities. Altered activities of these enzymes produce characteristic effects of the hormone on its target cell. An example is glucagon-mediated activation of hepatic phosphorylase and subsequent release of millions of glucose molecules from glycogen from each single liver cell.

Each of the protein molecules involved in the intricate "pull-push" mechanisms which increase or decrease or turn off the synthesis, intracellular accumulation and action of the second messenger, represents a potential site for regulation of hormonal responsiveness, for therapeutic and toxic actions of drugs and for pathological alterations in disease.

Cyclic AMP provides a simple, economical and highly specific way of communicating diverse and complex messages.

Several pharmacological antagonists act by blocking the binding of neurotransmitters and hormones to their specific receptors e.g., propranolol at beta-adrenergic receptors and cimetidine at H₂ - histamine receptors. The therapeutic action of these agents depends upon elevations or decrease in c AMP

content of target cells and tissues in patients. In addition, the methylxanthines, (caffeine & theophylline) block cyclic nucleotide phosphodiesterases and may produce some of their therapeutic effects (e.g., bronchodilation in asthma) by elevating cellular cAMP.

At present cAMP provides an important tool in understanding normal and pathological regulation and in developing new drugs. Adenylate cyclase assays are now routinely used to screen new compounds for their ability to stimulate or block adrenergic, histaminergic and many peptide receptors. Hormone receptors are not the only critical and specific control points in regulation mediated by cyclic AMP. Possibly other proteins (like nucleotide-binding N protein) will serve as targets of useful therapeutic agents in the future.

Discovery of New Drugs

Discovery of new drugs has been mainly a matter of chance (serendipity), and accident. Of course, it needed observant persons who could notice the unpredicted or the unexpected, draw the right conclusions from the chance or accidental happenings. In the 20th Century drug research has become a planned and deliberate effort, although chance and good luck still play their part. The modern synthetic chemist can reproduce in the test tube substances known in nature; he can also make modifications of the existing structure, or make completely new substances that have never existed before. The design of such chemicals is actuated by the knowledge already acquired about basic physiology and biochemistry of the living cell.

The "screening" programme for testing new drugs begins with animal experiments. The greatest difficulty for the laboratory pharmacologist lies in designing his animal experiments to yield the maximum information from a relatively few animals and to be relevant to human physiology and pathology. Random screening approach uses a whole battery of different animal tests. In this several doses of the compound to be tested are given to groups of mice and their behaviour is monitored by trained observers, or automatic apparatus. Heart and respiratory rates, temperature, body activity etc., are recorded and compared with undosed control groups. All changes or lack of change are registered on special form or fed into a computer which provides a "profile of activity". This profile is examined and compared with the profiles of standard drugs. Observers must always be kept ignorant of what the animals have received, to avoid their bias. Sedatives, hypnotics, tranquillizers, psychic stimulants, muscle relaxants, analgesic, convulsant, neuromuscular-blocking, atropine like, ganglion blocking, sympathomimetic, antipyretic, vasodilator acetylcholine-like drugs can be detected by this approach.

Any such screening test is a compromise based on the need for simplicity and speed and the sensitivity in detection of useful drugs. No one knows whether more valuable drugs have been missed than have been found.

Any compound which shows some promise in the "primary random screen" is then subjected to more detailed pharmacological and biochemical study devised in the light of the initial results. Either whole animals or isolated tissues may be used. Several species of animals will be used, generally mice, rats, cats and dogs and sometimes guinea pigs and rabbits.

Many experimental disease models are used for screening of drugs, such as high blood pressure, peptic ulcer, arthritis, convulsions. These diseases may be induced in those animals or there may be available spontaneous disease models in animals, like the New Zealand Black mice with an autoimmune disease similar to the human disease SLE (systemic lupus erythematosus).

A great deal of imaginative skill and experience is used by the medicinal chemist when he moves from a parent compound to make chemical variants. A cycle of chemical modification, screening test, evaluation and then a new chemical modification will usually lead to new drugs which are more active, less toxic, or easier to use than the original one.

As well as testing the effects of graded single doses, chronic pharmacologic studies are sometimes needed for drugs can not only alter some bodily functions acutely, but also alter some others more slowly. Many drugs are now given to human beings for many years such as the anti-hypertensive drugs, tranquillizers & oral contraceptives.

Animal studies give valuable information about pharmacokinetics (absorption, distribution, elimination). Whole body auto radiography using H-3 (tritium) labelled drugs has provided a valuable method of studying drug distribution, and hence prediction of its effects.

Pharmacological studies are integrated with toxicological studies to get a complete picture of the unwanted as well as the wanted drug effects. Some information on toxicity will generally be obtained during the initial pharmacologic testing, which is extended by the special toxicologic investigations. Acute toxicity testing is done to establish the ratio between the maximum tolerated dose and minimum curative dose to give some indication of the safety in relation to efficacy. The usual method of calculating toxicity is the ratio LD50/ED50 i.e., the dose that is lethal to 50 percent of the animals (LD50) divided by the dose that has the desired effect in 50 percent of the animals (ED50).

It is more important to know how the compound acts as a poison. This may need biochemical studies and microscopic studies with repeated or long-term administration of the drug. Sub-acute (short term up to one week) and chronic (long term, even life-long) toxicity studies will differ widely according

to whether a drug may be needed to be given once or a few times (for instance, a general anaesthetic) or continuously for years (for instance in epilepsy).

Generally, a drug is given daily and the appearance, activity, food intake, growth and reproductive ability in groups of animals on different doses are observed. Biochemical studies (urine, blood etc.) are commonly done and microscopic examination of most tissues, especially the liver, kidneys and bone marrow are done in animals that die as well as in sample animals killed at intervals during the test.

There are special problems of testing for adverse effects on the fetus and for carcinogenesis or genetic changes. As knowledge of basic mechanism advances it may become routine to use tissue cultures to predict what effects a drug will have in man but till that happens, animals will have to be used. A dominant problem is that of predicting from experiments with chemicals on animals what effects these chemicals will have in man. Failures of prediction will occur from time to time (e.g., Thalidomide disaster) although, with growth of adequate systems for monitoring possible adverse reactions it should be on a much smaller scale.

Proper Perspective about Safety of Drugs

For the alarmists who have exaggerated the risks of modern drugs, the following figures on the general safety of drugs in relation to accidents and to smoking in Britain (population 57 million) in one recent year will have a sobering effect:

Deaths due to drug adverse effects	43
Deaths due to accidents to children	1700
Deaths due to motor vehicle accidents	7084
Deaths due to accidents in the home	6000
Deaths due to lung cancer, largely due to smoking	28252

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Rational clinical introduction of a potential new drug requires study in four successive stages:

1. The pharmacodynamics (effect of the drug on the body) and the pharmacokinetics (absorption, distribution, metabolism and excretion) in healthy human volunteers or patients often in a special clinical pharmacology laboratory.
2. Wider use on patients to establish potential therapeutic utility, dosage schedule and some notion of common adverse effects.
3. Formal assessment of its therapeutic merits, compared with those of other remedies, when these exist.
4. Monitoring for adverse reactions as well as therapeutic benefits after general release.
5. Since testing new drugs on volunteers as well as patients raise ethical questions, it is now mandatory in all countries to subject all such projects to formal ethical review by an independent committee comprising medical, nursing, legal and lay members. Furthermore "informed consent" has to be obtained from the patients or healthy volunteers who agree to participate in the clinical trials.

The emergence of *Clinical Pharmacology* in the last quarter century as a special sub-specialty was a response to a pressing need for clinical scientists qualified to test the effects of new drugs and to design suitable trials in human beings. Critical clinical pharmacology of Ayurvedic drugs has been carried out in India by several investigators. I will give a brief review of the utility of such efforts and also indicate what directions such efforts in future would take. Table II gives a list of popular Ayurvedic drugs whose scientific validation may be taken up immediately.

20th Century Look at Ayurvedic Pharmacopoeia

In 1908, Dr. K. M. Nadkarni published "The Indian Material Medica". In 1918 Dr. Kirtikar and Basu published in two volumes, "The Indian Medicinal Plants". In 1923 Sir Ramnath Chopra began work on a large number of plant extracts in experimental animals. The animals used for screening have been dogs, rabbits and rats. In 1955, Chopra & Chopra published a review of Indian Medicinal plants.

Biological evaluation of plant material presents some uncontrolled and complex problems. Phytoconstituents are known to vary depending upon climate,

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soil, humidity, harvesting, harvesting time etc. Distinct chemical races of plants are known to exist, which vary in their biological activity. The selection of an appropriate solvent method of extraction is of crucial importance. Many solvents are deleterious to essential plant constituents, or may fail to extract the desired active ingredient. The method of extraction is equally important. Volatile materials will be lost in the solvent extraction or in solvent boiling at low temperatures. The presence of antagonistic substances can result in a failure to detect either of the two or more active constituents. Many plants accumulate large quantities of toxic inorganic constituents such as selenium, nitrates, copper, magnesium etc. All of these may produce biological action by themselves, or interfere with actions of organic constituents present in the plant material. This may lead to a premature abandonment of interest in the plant material.

The most important single event that aroused interest of modern physicians in the Ayurvedic Pharmacopoeia was the published report in the British Heart Journal by Dr. Rustum Jal Vakil in 1949 on the usefulness of Serpina (whole extract of *Sarpagatidha* or *Rauwolfia* Serpentine) in the treatment of hypertension. Its pharmacological properties were earlier investigated by Paranjape in 1942, and then by Sen and Bose. As we know now, reserpine, the active alkaloid depletes the stores of catecholamines and 5-hydroxytryptamine in the various tissues such as the heart, blood vessels, intestines and adrenal modulla. The catecholamines and 5-HT in the brain are also markedly reduced, thereby producing tranquillization, mental depression and Parkinsonism-like syndrome.

Reserpine gave an impetus to a vigorous search for newer drugs of the same class. The novel and very interesting actions of reserpine heralded a new era in the field of psychopharmacology, and the advent of tranquillizers. That the possibilities of discovering new gems from Ayurvedic pharmacopoeia are by no means exhausted is shown by yet another recent discovery—Forskolin. The Indian plant *Coleus forskohlii* (Willd.) Briq is mentioned in Nadkarni's Material Medica. Scientists from Hoechst Pharmaceuticals recently showed Forskolin to be a unique diterpene, which activates adenylate cyclase and cyclic AMP, thereby producing inotropic action on myocardium, increasing the amplitude of contraction of the heart and increasing coronary blood flow. HL 725, a synthetic compound derived from Forskolin is shown to selectively lower peripheral vascular resistance in essential hypertension. HL 725 is shown to inhibit phosphodiesterase in platelets and cardiac muscle, thereby increasing cyclic AMP activity. These examples illustrate the adoption of stereo chemistry in response to the clinicians' demands for biologically active compounds.

Professor U. K. Seth has reviewed the literature of 135 indigenous diuretics and clinical & experimental evaluation of 52 plant diuretics. It is

obvious that none of them comes anywhere near the effectiveness of modern diuretics. The diuretic activity of watery extracts of *Punamava* and Gokhru were attributed to their high potassium content. For this reason these herbal remedies, so also coconut water (74 mEq potassium per litre) would provide a useful adjunct to overcome the undesirable loss of potassium common to many modern diuretics.

In the treatment of rheumatoid arthritis *Guggulu* (*Commiphora mukul*), *Eranda* (*Ricinus communis*), *Nirgundi* (*Vitex negundo*), *ourakh* (*Dalbergia lanceolaria*) *Rasna* (*Pluchea lanceolata*), *Gandha prasarini* (*Paederia foetida*), *Bala* (*Sida humilis*) were shown to be significantly effective by Chaturvedi and Singh as anti-inflammatory agents in formaldehyde-induced arthritis in rats. In view of the undesirable side-effects of most modern non-steroidal anti-inflammatory drugs, there is an obvious need for effective remedies or adjuncts for rheumatoid arthritis.

An ICMR-sponsored clinical trial on Ayurvedic treatment of rheumatoid arthritis is going on for the last five years. I am awaiting; the publication of their results with great interest, and I must confess, with a lot of skepticism, and reservation.

The subject of wound healing, described as *Vrana-Ropana* in *Sushruta Samhita*, continues to evoke current interest. Ropana drugs are described as the promoters of healing. Deshpande, Pathak and Gode from the Post-Graduate Institute of Indian Medicine at Varanasi, have studied the effect of several Ropana drugs on various parameters; biomechanical wound contraction, tensile strength; biochemical estimation of mucopolysaccharides and collagen; histological and histochemical, and radioisotopic tracer uptakes. *Helianthus annuus* or Suryamukhi ointment showed significant reduction in total healing period. *Jasmina auriculatum*, as medicated ghee (Jati Ghrita) showed excellent results in different types of ulcers, burns, abscesses and surgical wounds. *Vernonia cineria* (Sahadevi) showed uniformly better pattern of wound healing.

Dr. Ashok Vaidya and Vaidya Antarkar have shown in a controlled clinical trial in viral hepatitis that *Arogya Vardhini* (50 percent of which is *Picrorrhiza kurroa*) given in a dose of 750 mg three times daily compared to placebo produces significant fall in serum bilirubin, SGOT and SGPT, apart from reducing symptoms of anorexia, nausea and malaise.

New ways of looking at Ayurvedic drugs

In recent years many Ayurvedic drugs, both herbal and mineral, have been tried in diabetes mellitus, under experimental and clinical conditions. To mention a few: *Gymnema sylvestra*, *Momordica charantia*, *Tinospora cordifolia*

among the herbs and Tribhanga Shila, Shilajit and Jasad Bhasma (Zinc), and Nawajas (mixture of many minerals like zinc, iron, calcium, mica, tin, copper, sulphur, Shilajit etc.) have shown significant results. It is remarkable that unlike insulin or oral hypoglycaemic sulphonylurea compounds, the hypoglycaemic effects of these Ayurvedic drugs are seen in only a small percentage of the diabetic patients. Rather than be disappointed that a particular Ayurvedic drug has been effective in only 20 to 30 percent of patients, I suggest that we should use these drugs as *pharmacological probes* to unravel the different mechanisms in the diabetic syndrome. If drug A is effective in patient P and not in patient Q, it may well be that two patients represent two different mechanisms of hyperglycaemia. In recent years the IDDM (insulin dependent diabetes mellitus) is seen to have entirely different pathophysiology and clinical course than the NIDDM (non-insulin dependent diabetes mellitus). There is every reason to believe that NIDDM is a mixed bag and various Ayurvedic drugs could serve as pharmacologic probes to further characterise the subgroups of the mixed bag.

Levamisole, the levo-isomer of tetramizole (introduced into veterinary practice in 1966 as a nematocidal drug) has evoked great interest among immunologists. Both in experimental animals and man, levamisole have been shown to be an immunostimulant. It appears to act by restoring cell-mediated immune mechanisms in peripheral leucocytes; precursor T lymphocytes are also stimulated, to differentiate mature T cells (OKT3), helper T cells (OKT4) and suppressor T cells (OKTs). Many Ayurvedic drugs can be evaluated from this angle, since several Ayurvedic drugs have been claimed to be effective in infections and auto-immune disorders.

Bacteria and viruses must attach themselves to specific receptors on target organs. We can think of Ayurvedic drugs in terms of receptor blocking properties as distinct from bactericidal properties.

Another new area is photochemotherapy, which involves combination of non-ionising electromagnetic radiation like ultraviolet rays and systemically administered photochemically reactive drugs. It has been shown that in the presence of certain naturally occurring tricyclic furocoumarin compounds (psoralens), irradiation with UVR-A (320-400 nanometer) can result in covalent bonding of psoralens to pyrimidine bases in DNA. This photoconjugation may lead to interstrand cross-linking of psoralen between two base-paired strands of DNA, inhibition of DNA synthesis and cell death. Two hours after oral dose of methoxsalen, UV-A radiation is given for psoriasis.

In vitiligo, methoxsalen plus UV-A treatment can be used in restoring normal skin colour to pigment less areas. Over 70 percent of repigmentation in vitiliginous areas can be achieved. Over 100 to 200 treatments are needed and this long duration of treatment can be frustrating.

INTRODUCTION OF NEW DRUGS

Antarkar and Dr. N. H. Wadia used *Atmagupta (Mucuna pruriens)* in a dose of 15—30 gm per day in 23 cases of Parkinsonism, and found significant improvement on the North Western University Disability Scale and other functional parameters. *Mucuna pruriens* contains L-Dopa and the cost of treatment is only Rs. 15 per month, with minimal side effects. The main problem is the bulk of the drug to be taken daily. Dose for dose comparison of the activity of *Mucuna pruriens* with L-DOPA suggested that there might be *other non-DOPA active ingredients*. Recent animal experiments with a Dopa-free fraction of *Mucuna pruriens* have confirmed this additional non-DOPA activity. These illustrative examples enthuse us to continue the endless search of biologically active compounds for use in therapy. In the wise words of Charaka, "Nothing exists in the realm of thought or experience that cannot be used as a medicine".

TABLE I

50 Categories of Drugs described in Charaka Samhita according to their actions.

1. Life Promoters	18. Galacto-depurants	35. Diuretic
2. Roborants	19. Spermatopoietic	36. Bechics
3. Revulsives	20. Spermato-depurants	37. Anti-dyspnoea
4. Laxatives	21. Adjuvants to oleation	38. Anti-inflammatory
5. Synthesizers	22. Adjuvants to sudation	39. Anti-febrile
6. Digestive stimulants	23. Adjuvants to emesis	40. Acopics
7. Promotive of strength	24. Adjuvants to purgation	41. Refrigerants
8. Promotive of complexion	25. Adjuvants to corrective enema	42. Calefacients
9. Promotive of voice	26. Adjuvants to unctuous enema	43. Anti-urticarial
10. Cordials	27. Adjuvants to errhines	44. Anodyne
11. Appetizers	28. Anti-emetic	45. Analgesic
12. Anti-haemorrhoids	29. Adiposus agents	46. Haemostatic
13. Curative of dermatosis	30. Anti-hiccup	47. Sedatives
14. Anti-pruritic	31. Intestinal astringents	48. Resuscitative
15. Anti-helminthic	32. Fecal pigment restorers	49. Procreants
16. Antidotes to poison	33. Ischuretics	50. Rejuvenators.
17. Galactagogue	34. Urine pigment restorers	

Table – II

Four New approaches for the validation of Ayurvedic herbal drugs, whose scientific validation may be taken up immediately

A. Alimentary System

1. Arogyavardhini
2. Arshaghnnavati
3. Bilvadichurna
4. Drakshasava
5. Ichabhedi
6. Gandharvahrataki
7. Hingvashtaka
8. Jatiphaladichurna
9. Kumari Asava
10. Mayurpichhamashi
11. Nagkeshar
12. Sanjeevanivati
13. Samudradichurna
14. Shankhavati
15. Shankhabhasma
16. Shunthichurna
17. Suta Shekhar
18. Suranavatak
19. Triphala

B. Arthritis

1. Dashamularishta
2. Narayan Taila
3. Yogaraj guggulu

C. Fever

1. Pravala bhasma
2. Pravala pishti
3. Suta shekhar.

D. Dermatology

1. Gandhak Rasayana
2. Gulabi Malhar
3. Haridrakhandayoga
4. Manjishtha
5. Ral malahar
6. Tankana mishrana malahara

E. Respiratory System

1. Anu taila
2. Gojihvadikwath
3. Laghumalini
4. Shvasakuthar
5. Yashtimadhuchurna

F. Urinary System

1. Arogyavardhini
2. Chandrapravati
3. Gokshuradiguggulu
4. Punarnava

G. Gynaec & Obst.

1. Boladivati
2. Dashamularishta
3. Nagkeshar

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TOXICOLOGY - ANCIENT AND MODERN

Introduction

One complete section of the octapartite *Charaka Samhita* is devoted to “*Vishatantra*” or toxicology. Ayurveda recognized poisons of animal and vegetable origin. *Charaka Samhita* lists 21 vegetable poisons and many animal poisons such as serpents, scorpions, insects, spiders, rats, fishes, dogs and so on. Scientists were to learn much later that bacteria, the simplest of free-living organisms, produce some of the most lethal poisons known to man. For instance, *botulinum* toxin and *tetanus* toxin are several million times more toxic than the plant poison strychnine. The human species has had to contend with bacteria and fungi, snakes and scorpions, jellyfish and starfish, sting rays and spiders, and an enormous variety of poisonous plants. The list of poisons furnished ready-made by nature has been extended mightily in recent years by human ingenuity and the chemical industry. Thinkers and environmental and ecological experts are very much concerned with the immediate and long term effects of such chemical poisons like pesticides.

A poison is difficult to define with legalistic rigour. Even pure water is toxic when it is retained by the body in excess, and can kill the patient (water intoxication). Even small quantities of water can cause death when inhaled into the lungs. The accepted pharmacological definition of poison is “any substance that, in relatively very small quantities, can cause illness or death in the living organism by *chemical action*.” No reasonable definition of poison can exclude the thousands of substances which in small doses produce physiological changes which, being used customarily for the treatment of disease, are identified as *drugs*. William Withering, who defined the clinical use of fox glove leaves (*digitalis*) in heart failure and “dropsy”, wrote in 1787: “Poisons in small doses are the best medicines; and useful medicines in too large doses are poisonous”. That is to say that *drugs are useful poisons*, with *selective toxicity*. In fact pharmacology and toxicology go hand in hand.

Poisons represent a major public health hazard particularly to children. Millions of people all over the world suffer from non-fatal poisoning, a quarter of them is children. There are thousands of fatalities by poisoning for suicidal (and less commonly, homicidal) purpose. The effects of “socially accepted poisons” like ethyl alcohol and tobacco are discussed in a different section of this book.

Mechanism of Action of Poisons

“Poisons can be employed as agents of life’s destruction or as a means of relief of disease, but for the physiologist poison is an instrument for analysing and understanding the most delicate phenomena of the living

machine, and by studying attentively the mechanism of death in diverse types of poisoning he can learn indirectly much about the physiological processes of life". These words of Claude Bernard written a hundred years ago, still summarise concisely the scientific significance of poisons. Curare, the specific agent that he was discussing, remains one of the best examples of the tripartite nature of this loose category of substances. Curare first came to the attention of scientists as an arrow-poison used by South American Indians to kill game and enemies. Bernard himself first applied it as a physiological scalpel in his pioneering studies of nerve and muscle function. More recently tubocurarine is used as a muscle relaxant during surgical anaesthesia. As Bernard anticipated, poisons have taught us a good deal about the chemistry of living matter. Scientists constantly strive to elucidate the chemical mechanisms by which poisons derange or destroy cells; so far the attempts to reduce toxicity to molecular mechanisms have succeeded in only a few cases.

Drugs and poisons may act at two levels of cellular organization; firstly, on mechanisms that are entirely intracellular, primitive and self-regulating such as those required for *respiration*, *division* and *growth*, and represented in unicellular organisms; and secondly, on controls that are superimposed on the cell from without, as by neurochemical transmitters and general and local hormones or autacoids. In the multicellular organisms these potent molecules not only control specialized activities within the community of cells but also exercise a continuing influence on the metabolic function of all cells.

The distinction is useful, since many drugs that act on the basic metabolic functions of the cell are those that inhibit respiration (utilisation of oxygen by cells) and growth and so destroy life. Hence those drugs are all potential poisons in large doses. Such drugs include chemotherapeutic agents which act selectively on organisms parasitic in man and animals, and also pesticides and insecticides and disinfectants.

In contrast are drugs that interfere with the synthesis, storage, release and destruction of neurochemical transmitters, or general or local hormones or which are the pharmacological antagonists of these molecules. In all these instances it can be assumed that the drug acts mainly on enzyme systems that control specialised functions of the cell, and not on the systems that are responsible for survival.

Corrosive Poisons

The corrosive poisons, strong acids and alkalis have the most obvious effects on living matter. By massive destruction of cells, they can produce death from shock, haemorrhage (from the gastro-esophageal lining in ingested poison) or incapacitation of some vital organ. Thus the corrosive gas *phosgene* used in chemical warfare during World War I, reacts with water in

the lungs to produce hydrochloric acid, which destroys lung tissue and by its irritant action fills the lungs with fluids. Death ultimately results from asphyxiation.

With most corrosive poisons, however, the mode of action is not so clearly discernible. Concentrated sulphuric acid, for instance, does so many things to the body that its specifically lethal activities are hard to isolate. Moreover, its catastrophic effects on tissue leave little for the physiologist to examine.

Some corrosive poisons may produce death simply by shifting the delicate acid-alkaline balance of the body to the point where vital chemical reactions can no longer occur.

Metabolic Poisons

More subtle in their effects are the metabolic poisons that include most of the powerful drugs in the pharmacopoeia, as well as many other chemicals which have no place in medicine. These compounds do not destroy tissue like the corrosive poisons. Many of them produce no visible tissue change whatsoever. Instead, they accomplish their lethal effect by disrupting one or another of the intricate chemical reactions upon which life depends.

Carbon-monoxide is a major constituent of automobile exhaust-gas and a common agent of suicide in USA. Almost any flame or combustion device emits carbon-monoxide. Its lethal effects are largely attributable to its strong affinity for haemoglobin, the protein in the red blood cells that transports oxygen from the lungs to the tissues. Carbon monoxide combines with haemoglobin 200 to 300 times more readily than does oxygen. Hence a carbon-monoxide concentration of only 0.5 percent in the air will convert half the haemoglobin in the blood into carboxyhaemoglobin, a compound that cannot transport oxygen to the tissues. Moreover, the presence of carboxy haemoglobin alters the properties of normal haemoglobin, so that even the remaining fraction functions with reduced efficiency. The victim undergoes a sort of internal asphyxiation.

The treatment of acute carbon-monoxide poisoning is based on the fact that the association between carbon-monoxide and haemoglobin is reversible. If the victim is removed from the contaminated atmosphere and given pure oxygen to breathe, the carboxyhaemoglobin gradually gives up its carbon-monoxide to yield active haemoglobins. For the same reasons hyperbaric oxygen is helpful in seriously poisoned patients. Transfusion of packed red cells is also of value. Unfortunately a few persons who recover from carbon-monoxide poisoning suffer damage to the vision or to the nervous system that may be permanent.

The cyanide ion is an exceedingly potent and rapid-acting poison. The extreme toxicity of cyanide is due to its ready reaction with the trivalent ion of

cytochrome oxidase, an enzyme somewhat similar to haemoglobin, which plays an almost ubiquitous role in cellular respiration. The cyanide ion, introduced into the body in the form of hydrocyanic acid, or its salts, is believed to inactivate cytochrome oxidase somewhat as carbon-monoxide inactivates haemoglobin. Formation of the cytochrome-oxidase-cyanide complex blocks electron transport, thus inhibiting oxygen utilization. This results in cellular dysfunction and death.

Inhalation of hydrogen cyanide may cause death within a minute. Oral dose acts more slowly requiring several minutes for the appearance of symptoms and up to several hours for death. The first effect is an increase in ventilation because of the blockade of oxidative metabolism in the chemoreceptor cells.

The objective of treatment is the production of methaemoglobin by the administration of nitrite. The trivalent iron of methaemoglobin competes with cytochrome oxidase for the cyanide ion. The cytochrome oxidase-cyanide complex dissociates and enzymatic function and cell respiration are restored. Further detoxification then is achieved by the administration of thiosulphate. Rhodanese, an *enzyme* with obscure function found in many mammalian tissues catalyzes the reaction of thiosulphate with cyanide liberated by the dissociation of cyanmethaemoglobin. Thiocyanate, which is relatively non-toxic is formed and readily excreted in the urine. Since speed is of the essence, nitrite should be immediately administered by inhalation of amyl nitrite perles, one every two minutes unless blood pressure is below 80 mm Hg. This is followed as soon as possible, by I.V. injection of 10 ml of 3% sodium nitrite over a 3-minute period. Then 50 ml of 25% sodium thiosulphate should be given I.V. over a 10-minute period.

Toxic Metabolites of Drugs

Paracetamol or acetaminophen has become a popular alternative to salicylates as an analgesic and antipyretic. It is a frequent cause of suicidal poisoning in Britain. While the toxic and lethal dose may vary from patient to patient, hepatic damage may be expected if an adult has taken more than 8 g as a single dose. Hepatic toxicity becomes evident 1 to 2 days after ingestion. There is good evidence that damage to tissue, especially liver is caused by *metabolites* of acetaminophen and not the drug itself. At therapeutic doses acetaminophen is eliminated mainly conjugated to sulphate or glucuronic acid. A small amount of acetaminophen is activated by the cytochrome P450 system and conjugated with the sulphhydryl group of glutathione to yield a non-toxic mercapturic acid. After an overdose, the pathway of conjugation to the sulphate and glucuronic acid becomes saturated, an increasing fraction of the drug is activated by the P450 system, glutathione stores are depleted and the reactive intermediaries then become free to bind covalently to liver macromolecules and cause necrosis. Treatment of acetaminophen poisoning

should begin with induction of emesis or gastric lavage followed by the ingestion of activated charcoal. Since endogenous glutathione appears to have a protective effect, several other sulphhydryl compounds have been studied for protection against hepatotoxicity. N-acetylcysteine 140 mg/kg, given orally within 10 hours of ingestion of the drug as a loading dose, and a maintenance dose of 70 mg/kg every 4 hours for 3 days, effectively reduces hepatotoxicity.

Chlorinated Insecticides

These compounds are ingredients of insecticide sprays, dusts or solutions. The great majority of these compounds are chlorinated diphenyls (e.g. DDT, TDE, DFDT, DMC, Neotran) or chlorinated polycyclic compounds (e.g. aldrin, chlordane, dieldrin, endrin, heptachlor). Lindane is a hexachlorobenzene. The chlorinated insecticides are soluble in lipids and organic solvents but not in water. They are poorly absorbed unless dissolved in a vehicle such as kerosene, petroleum distillates or other organic solvents. Under these circumstances they readily enter the body through the skin, airways or gut.

The initial symptoms of acute poisoning are nausea, vomiting, headache, dizziness, apprehension, excitement and muscular tremors and weakness, followed by generalized hyperexcitability of the central nervous system leading to delirium, tonic and clonic convulsions followed by progressive depression with paralysis, coma and death. In addition endrin is strongly hepatotoxic. Cholestyramine accelerates the excretion of chlorinated hydrocarbon chlordecone by preventing reabsorption following biliary excretion, and it may well have similar effects on the excretion of pesticides such as DDT & dieldrin which remain in the body for prolonged periods.

Cholinesterase Inhibitor Insecticides

In agriculture, control of soft-bodied insects is achieved by organic phosphates (e.g. Parathion, Malathion) or by carbamates (e.g. carbaryl, Mactacil).

The toxicity of these agents results from inactivation of acetylcholinesterase which allows accumulation of excessive amounts of acetylcholine at a number of sites: Central nervous system, autonomic ganglia, parasympathetic nerve endings and motor nerve endings.

Toxic muscarine effects include nausea, vomiting, diarrhoea, involuntary defecation and urination, blurring of vision due to miosis, sweating, lacrimation and salivation. Nicotinic effects include muscle twitching fasciculations, weakness and flaccid paralysis. Respiratory depression and coma occur due to central nervous system effects. Cardiac arrhythmias and pulmonary edema as well as EEG abnormalities also occur.

Atropine is the antidote for excessive acetylcholine action on the central nervous system and parasympathetic nerve endings. A dose of 2 mg is injected intramuscularly and repeated every 10 minutes until parasympathetic manifestations are controlled and signs of atropinisation appear. Atropine is virtually ineffective against autonomic ganglionic actions of acetylcholine and against the peripheral neuromuscular paralysis, whose recovery must await the gradual manufacture of fresh, unpoisoned cholinesterase.

As a fruit of fundamental research into the mechanism by which cholinesterase breaks down acetylcholine, a new antidote has been found. The enzyme cholinesterase has two "active sites" which interact with different parts of the acetylcholine molecule. By attaching itself to these two sites the acetylcholine molecule splits into free choline and an acetyl group (CH₃CO) that remains bound to the enzyme. The acetyl group then reacts with water, forming free acetic acid, and liberating the enzyme for further work.

The organic phosphates, probably by means of the electron-seeking phosphorus atoms which all of them contain, tenaciously pre-empt the site on the cholinesterase molecule that normally accepts the acetyl group. Irwin N. Wilson and David Nachmansohn of the Columbia University College of Physicians and Surgeons were able to devise a compound, pyridine aldoxime methiodide that can pry the organic phosphate molecule and *reverse* the phosphate-ester bond formed by the organic phosphate at the enzyme active site. *Pralidoxime* is useful in the treatment of organic phosphate cholinesterase inhibition, when given in a dose of 1gm I.V. over a 5-minute period, and repeated every 8 to 12 hours upto 4 times. Energetic therapy with artificial ventilation, atropine and pralidoxime allows survival after doses of organic phosphate esters vastly exceeding the usual fatal dose.

The nerve gases including di-isopropyl-fluorophosphate, tetraethyl-pyrophosphate, irreversibly bind to cholinesterase. Though interest in the nerve gases originally stemmed from their possibilities in chemical warfare, the compounds have yielded an abundant non-military harvest. For example, DFP has helped to unravel the fine structure of several enzymes which, like cholinesterase, bind it tightly at their active sites. Molecules of trypsin and chymotrypsin (the protein digesting enzymes secreted by the exocrine pancreas) can be labelled with DFP containing radioactive phosphorus atoms and then be degraded into small fragments; the labelled fragments identify their active segments of the enzyme molecule.

Botulinum Toxin

The botulinum toxin, an occasional cause of human food poisoning, disrupts the acetylcholine cycle no less efficiently than do the

anticholinesterase poisons, but it works in the opposite side of the biochemical cycle. Instead of raising the concentration of acetylcholine, it lowers it to paralytic levels. Botulinum toxin binds to the nerve terminal membrane and blocks the calcium stimulated release of acetylcholine from the vesicles in the terminals. Botulinum toxin has the distinction of being the most poisonous substance yet discovered. A lethal dose for a mouse is as little as 10 - 13ng/kg.

Similar in action to botulinum toxin and almost as deadly is the toxin secreted by the poisonous dinoflagellates. These microscopic marine organisms can kill fish by the millions when they multiply explosively in "red tides". The concentration of their toxin in the digestive tracts of mollusks accounts for many cases of shell-fish poisoning in man.

Mercury Poisoning

In the early 1950's fishermen and their families around Minamata Bay in Japan were stricken with a mysterious neurological illness. The disease produced progressive weakness of the muscles, loss of vision due to visual cortex lesions, impairment of cerebral functions especially cerebellar ataxia, eventual paralysis and in some cases coma and death. It was soon observed that Minamata seabirds and household cats, which like the fisherfolk subsist mainly on fish, showed signs of the same disease. This led to the discovery of high concentrations of mercury compounds in fish and shell-fish taken from the bay, and the source of mercury was traced to the effluent from a factory.

Since then there have been several other alarming incidents in other parts of the world: Iraq, Pakistan, Guatemala, Sweden, North America and Canada. Mankind has become acutely fearful of mercury in the environment. The alarm is understandable; mercury or quicksilver has always been regarded as being magical, in part because of its unique property as the only metal that is a liquid at ordinary temperature. The un-compounded element in liquid form is not a poison; a person could swallow upto a pound or more of quicksilver with no significant adverse effects. Certain compounds of mercury have been used safely for thousands of years. There is evidence that cinnabar or mercuric sulphide (HgS) was mined in China, Asia Minor, the Cyclades and Peru at least two or three millennia ago. Hippocrates is believed to have prescribed mercury sulphide as a medication.

By the Middle Ages, when alchemists had synthesized chlorides, oxides, and various other inorganic compounds and mixtures of mercury, its use in medications began to spread. Calomel (mercurous chloride, HgCl) came into wide use as a cathartic, and in the 16th Century mercury compounds were introduced as a treatment for syphilis.

In agriculture, corrosive sublimate (HgCl_2) is used to disinfect seeds and to control many diseases of the tubers, corns and bulbs (including potatoes), and also to protect a number of vegetable crops. Corrosive sublimate is toxic, causing corrosion of the gastrointestinal tract leading to bloody diarrhoea, injury to the kidneys, ultimately leading to death from renal failure.

What causes concern to environmentalists at present is the alkyl compounds—methyl and ethyl mercurials. The alkyl mercury compounds can cause congenital mental retardation, cerebral palsy and chromosomal abnormalities. The chemical basis for these effects is mercury's strong affinity for sulphur, particularly for the sulphhydryl (S-H) groups in proteins (for which arsenic and lead have a similar affinity). Bound to proteins in a cell membrane, the mercury may interfere with a number of enzymes systems essential to cellular metabolism and alter the distribution of ions, change electrical potentials and thus interfere with the movements of fluid across the membrane. There are also indications that binding of mercury to protein disturbs the normal operation of structures, such as mitochondria and lysosomes within the cell.

Research on mercury poisoning in the past has focused primarily on occupational hazards involving prolonged exposure, principally by way of inhalation, for example, among mercury miners and workers in felt hat factories employing mercury nitrate for processing. These exposures are not necessarily incapacitating; they produce tremors, gum inflammation and general irritability. The main threats to which we shall have to give attention now are solid and liquid wastes that may ultimately enter bodies of water, thus threatening fish and eaters of fish, and agricultural uses of mercury that may dangerously contaminate food. We do not yet have enough information to estimate the magnitude of these threats or to establish realistic standards of control. The best way to deal with the problem is to apply the techniques of epidemiology, preventive medicine, public health and industrial hygiene. To implement a control programme, realistic education of the public and legislative action with adequate enforcement will be needed.

Lead Poisoning

Lead has been mined and worked by men for millenniums, because its ductility, high resistance to erosion and other properties make it a very useful metal. The inappropriate use of lead has, however, resulted in outbreaks of lead poisoning in humans from time to time since antiquity. "Plumbism" (from the Latin word for lead) or "Saturnism" (from the alchemical term) was a disease first described by the Greek poet-physician Nicander more than 2000 years ago. Lead poisoning results from inhalation of fumes as from burning storage batteries, solder, paint spraying or processes that require the remelting of metallic lead. Ingestion of lead-containing material such as paint (especially

by children who like its sweetish taste), or water which has stood in lead pipes, illicit whisky contaminated by lead solder in the pipes of stills, have all been responsible for cases of poisoning. Lead is a cumulative poison excreted slowly. Most of the absorbed lead is deposited in the bones; only small amounts are contained in the blood, urine and feces.

Manifestations of lead poisoning are colic, encephalopathy, peripheral neuritis and anaemia. The basis for ill-effects is lead's affinity for S-H groups; due to this interaction S-H groups are not available to certain enzymes that require them. The clearest manifestation of the inhibitory effect of lead on the activity of sulphhydryl-dependent enzymes is the disturbance it causes in the biosynthesis of *haem*, the iron-containing constituent that combines with protein (globin) to form haemoglobin, the oxygen carrying pigment of the red blood cells. Haem is also an essential constituent of the other respiratory pigments, the cytochromes, which play key roles in energy metabolism. The normal pathway for haem synthesis begins with activated succinate (produced by the Krebs's cycle, a major stage in the conversion of food energy to biological energy) and proceeds through a series of steps. Two of these steps are inhibited by lead; two others may also be inhibited, but at higher lead concentrations. Lead is implicated specifically in the metabolism of delta aminolevulinic acid (DALA), catalyzed by the enzyme *ALA dehydrase*.

The functional effect of the metabolic disturbance in the blood is *anaemia*. The metabolism of haem returns to normal and the anaemia improves when the patient is removed from the exposure to lead.

In the kidney, visible changes in the structure of mitochondria are seen under electron microscope; consequently the renal tubular cells consume more oxygen than normal cells. The damaged tubular cells fail to reabsorb amino-acids, glucose and phosphorus, which are lost in the urine.

In the brain, edema and direct injury to the nerve cells cause lead encephalopathy. In the peripheral nerves, the mitochondria of the Schwann cells are affected, resulting in demyelination and impaired conduction of impulse primarily in the motor nerves of the extremities.

Three highly effective chemicals are now available for the treatment of systemic poisoning with heavy metals by forming non-toxic stable compounds with polyvalent metallic ions, which can be safely excreted in the urine.

The first to be developed was BAL (British anti-lewisite, 2, 3, dimer-captopropanol) which was originally intended as an antidote against the arsenical war gas, lewisite. Its tendency to combine with certain metallic ions such as arsenic, mercury, cobalt, nickel, antimony and gold is so great that it can remove them from combination with the enzyme whose function they impair in the body.

The second antidote to metal poisons is the chelating agent Versene [Ethylenediamine tetra-acetate (EDTA)] which forms cyclic, stable, soluble, non-toxic compounds with most metals. Because Versene reacts with calcium in the same way as with other metals, it must be given as a calcium salt (calcium disodium Versenate) to avoid hypocalcaemia. The material has been used with notable success in lead poisoning (in which BAL by itself is not useful).

Penicillamine (Cuprimine, B, B dimethyl-cystine) is an excellent chelating agent for copper, mercury and lead, promotes their excretion in the urine. It may be given orally while the other two antidotes require systemic injection. N-acetyl-di-penicillamine is even more effective than penicillamine in protecting against the effects of mercury.

Cytotoxic Poisons

Amanita phalloides (death cap), *Amanita virosa* (destroying angel), some other *Amanita* species, and *Galerina Venenata* contain heat-stable cyclopeptide cytotoxins which are rapidly bound to tissues. The principal toxin is amanitin which binds to and inhibits specifically the mammalian RNA polymerase responsible for messenger RNA synthesis. Severe cell damage and fatty degeneration may occur in liver, kidneys, striated muscles and brain. Ingestion of these dangerous mushrooms is followed by a latent period of 6 to 20 hours. Manifestations of cytotoxicity then may appear suddenly and consist of severe nausea violent abdominal pain, bloody vomiting and diarrhoea, and cardiovascular collapse. The victim may die from acute hepatic neurosis within 4 days.

Poisoning by cytotoxic mushrooms is treated mainly symptomatically
Venoms, Bites and Stings.

Humans have the propensity to come into contact with a great variety of venomous animals. In general, two types of injuries result; those due to the direct effect of venom on the victim, as exemplified in snake bite; and those due to indirect effects of the poison, of which hypersensitivity reaction to bee sting is an example. A third type of injury is described by Charaka — "fear poison".

"When a person bitten by anything in pitch darkness, gets alarmed and suspects a poisonous bite, he develops symptoms of pseudo poison, in the form of fever, vomiting, fainting and burning as well as prostration, stupefaction and diarrhoea. This is regarded as 'fear poison'".

Snake Venoms

The venoms of most species which have been analysed have been found to be mixtures of several toxic proteins and enzymes with diversified and complicated pharmacologic effects. For example, the Indian Cobra

(*Naja Naja*, "*Naga*") contains a neurotoxin, a haemolysin, a cardiotoxin, a cholinesterase, at least three phosphatases, a nucleotidase and a potent inhibitor of cytochrome oxidase. Several venoms including those of the pit vipers contain hyaluronidase and numerous proteolytic enzymes.

The venom of a given species is usually predominantly neurotoxic or necrotising and is frequently associated with haemolysis, blood clotting abnormalities, alterations in vascular resistance and changes in cardiac dynamics. The venom of elapids including the coral snake, is neurotoxic, with death resulting from respiratory paralysis probably caused by damage to the brain and a curariform interference with transmission at the neuromuscular junction. The venom of crotalid snakes produces local tissue injury, haemorrhage and haemolysis; pooling of blood in microcirculation and loss of plasma due to increased capillary permeability cause a marked fall in circulating blood volume and circulatory collapse followed by death. Systemic absorption of venom occurs through lymphatics, hence therapeutic measures designed to reduce lymphatic function are helpful in controlling symptoms.

Following the bite of a pit viper, severe burning pain develops within a few minutes at the site of the wound. Local swelling rapidly develops and spreads in all directions, accompanied by the appearance of ecchymoses and bullae over the involved area. Serosanguineous fluid oozes from the puncture wounds. Later gangrene of the skin and subcutaneous tissue may develop. Systemic effects include fever, nausea, vomiting, circulatory collapse, pupillary constriction, delirium and convulsions. Death may occur within 6 to 48 hours.

The bite of the coral snake causes little pain and local swelling. There are usually multiple fang marks. Within 10 to 15 minutes numbness and weakness begin in the region of the bite, followed by ataxia, ptosis and pupillary dilatation, palatal and pharyngeal paralysis and slurring of speech. The patient becomes comatose and dies within 8 to 72 hours due to respiratory paralysis.

Cobra bites are painful, often accompanied by severe haemolysis, local necrosis and sloughing in addition to neurotoxic effects.

Treatment of Snake Bite

Charaka Samhita gives the following advice: "In case of a poisonous bite the physician should apply a ligature above the region of the bite and squeeze the part well, before poison has spread in the body, or should try to cut out that part except in the region of the vital organs; or, the physician, filling his mouth *with* barley-flour or earth must suck up the poison from the bitten area with his mouth".

"The blood is the vehicle of poison as the wind is of fire, so blood must be forced out or congealed by cauterization".

This ancient advice is equally valid today. *Incision and suction are extremely important and should be carried out diligently in every poisonous snake bite.*

Antivenin is the only specific treatment of snake venom poisoning and its use in severe bites is vital. Intravenously administered antivenin leads to the most rapid and effective response. It is a great pity that in our villages many unsubstantiated and useless therapies are practiced out of ignorance, thereby delaying antivenin therapy.

Scorpion venom may be fatal to young children or old people, but rarely, healthy adults succumb due to myocarditis. Death usually occurs within 12 hours but sometimes as late as 48 hours after the sting.

Specific antivenin, reconstituted from lyophilized cat serum is available in USA but has never been available in India.

Hymenoptera venoms (bees, wasps, hornets, yellow jackets and fire ants) contain histamine, various kinins and other vasoactive substances, phospholipases and hyaluronidase. They are haemolytic and neurotoxic in addition to being effective hypersensitizing agents. In hypersensitive individuals, a single sting may produce serious anaphylaxis with urticaria, nausea, abdominal or uterine cramps, bronchospasm, massive edema of the face and glottis, dyspnoea, cyanosis, hypotension, coma and death.

Management of Acute Poisoning

Poisoning by chemical agents, accidental, suicidal and criminal, is a common and serious medical problem. In addition to fatal poisoning there is a much greater number of persons who are made seriously ill by poisoning but recover after appropriate therapy. Every effort should be made to avoid accidental poisoning by educating the public in simple preventive measures. All toxic substances should be kept out of the reach of small children. Household chemicals and medicines should be kept in the original containers and all such containers should be labelled. Before taking or administering any medicine one should check the label carefully.

Physicians should always remember the protean manifestations of poisoning and maintain a high index of suspicion, in any unexplained illness. Correct treatment of poisoning requires knowledge of both the general principles of management and the details of therapy for specific poisons.

Success often depends upon speed of treatment, and when indicated by the clinical situation, several approaches should be used simultaneously. The medical profession can help maintain high standards of therapy by creating and supporting *poison information* in cities and towns, to which any physician should have access day and night.

Many modern hospitals now have facilities for dialysis which effectively removes many poisons including barbiturates, barbiturates, chlorate, ethanol, glycols, methanol, salicylates, sulphonamides, theophylline and thiocyanate. *Peritoneal dialysis* can be performed easily in any hospital and may be continued for long periods. *Haemo-dialysis* is unquestionably a more effective procedure for removing large amounts of dialyzable poisons. For barbiturates dialysance rates of 50-100 ml/minute have been achieved, a rate of 2 to 10 times faster than during peritoneal dialysis or forced diuresis. Perfusion of blood through activated charcoal or exchange resin achieves even higher clearance rates than haemodialysis for many poisons. Extracorporeal dialysis and haemoperfusion are clearly the procedures of choice for the rapid removal of poisons from patients who have absorbed amounts which make survival unlikely even under the best supportive care.

The removal of some poisons is accelerated by chemical interaction with other substances followed by renal excretion.

Table I gives an outline of modern treatment of acute poisoning by chemicals. Supportive therapy is crucial even when an antidote is available, to maintain vital functions.

Incidentally, this Table also illustrates the scientific basis of modern therapy, which is intellectually very satisfying.

TABLE I
Treatment of Acute Chemical Poisoning

- I Prevention of further absorption of poison
 - A Poisoning by ingestion
 - 1. Emptying the stomach
 - a. induction of vomiting
 - b. gastric lavage
 - 2. Minimising gastrointestinal absorption
 - a. absorption by activated charcoal
 - b. catharsis.

- B. Poisoning by other routes
 - 1. Skin — wash with soap and water
 - 2. Bite or injection site — proximal tourniquet application of cold to site
 - 3. Inhalation — Remove to clean air—Protective mask

II Removal of absorbed poisons from body

- A. Detoxification — enzyme induction
- B. Biliary excretion — interruption of enterohepatic circulation
- C. Urinary excretion
 - 1. Forced diuresis
 - 2. Alteration of urinary pH
- D. Dialysis
 - 1. Peritoneal dialysis
 - 2. Haemodialysis
- E. Charcoal or resin haemoperfusion
- F. Exchange transfusion
- G. Chelation and chemical binding

III Supportive therapy

Meticulous nursing care and close observation
Anti-convulsant drugs — diazepam, phenytoin I.V.
Reducing cerebral edema — corticosteroids, mannitol
I.V. Maintenance of ventilation and circulation
Maintenance of fluid and electrolyte & acid base balance

IV Administration of systemic antidotes

- A. Chemical agents which help reduce the concentration of toxic substances, by
 - 1. combining with the poison EDTA with lead BAL with mercury
Penicillamine for copper, lead, mercury
SH-containing reagents with toxic metabolites of acetaminophen.

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2. increasing excretion of the poison
Chloride or mercurial diuretics in bromide poisoning
- B Pharmacological antagonists
compete with poison for its receptor site atropine with muscarine
naloxone with morphine
physostigmine with anticholinergics like atropine.
- C. Anti-venins

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UNDERSTANDING MENTAL ILLNESS

Introduction

Understanding of the mind is the central problem for man. Religious and political beliefs, scientific and cultural advances, the evaluation of life and man's part in life all depend upon concepts, products of the mind. Ancient Indian thinkers and Philosophers have laid great stress on '*Atmanam Viddhi*' or '*Know thyself*'.

One's own mind is subjective experience, a personal world which can be explored only by *introspection*. The minds of other persons can be *inferred* from their behaviour, their speech, writing and actions. The minds of animals can be inferred from their actions alone.

We can only talk about the attributes of the mind. A pre-requisite for the phenomenon of mind is consciousness which may be described as a state in which there is ability to be aware of sensation — that is, a state in which perception may take place. Components of the mind (or mental process) can be considered as perception, memory, emotion, propositional thought and response. Since the end-products of the mind are apparent only in so far as they can be expressed in speech, writing or other action which together constitute "*behaviour*" in a broad sense, modern scientific study of the mind has mainly concentrated on the study of behaviour. Past and present patterns of behaviour create an image of the subject as "*personality*".

The brain is the organ of the mind and till recently psychology attempted to treat the brain as a black box. Indeed, much of biology was learnt by the black box method. The difficulty with the black box approach is that unless the box is inherently very simple, a stage is soon reached where several rival theories all explain the observed results equally well. Attempts to decide among them often prove unsuccessful. In the last three decades, scientists have been able to poke inside the black box and gain valuable insights.

The complexity of the brain is yielding to scientific analysis and new pathways are being opened to the study of behaviour. The recent discovery of several neuropeptides and study of their possible functional roles is one of the most active areas of scientific research and is at the frontier of work in neurobiology. The recent development of PET (Positron emission tomography) and appropriate radioactive tracers labelled with positron emitting radionuclides has now made it possible to relate regional biochemistry within the human brain to measurements of behaviour in normal subjects and to elucidate abnormalities in patients with Alzheimer's disease, Huntington's disease, depression and multiple-infarct dementia (see also: Chemistry of behaviour, in chapter 7 — Chemistry of Life).

There is a growing realisation that much of the world's burden of illness is *behavior related*. Major institutions concerned with the science base for health have increasingly addressed the relation of behaviour to health. The World Health Organization is actively planning a new programme of research on health and behaviour in developing countries. This chapter therefore, attempts to review our current understanding of human behaviour in health and illness.

Understanding Human Behaviour

What a piece of work is man! How noble in reason! How infinite in faculty! In form, in moving, how express and admirable! In action how like an angel! In apprehension how like a God! The beauty of the world! The paragon of animals!

Shakespeare, *Hamlet* — Act II Scene II.

Man, "the paragon of animals", scales the heights and plumbs the depths in his behaviour. The study of human behaviour has always interested scientists from the time of Charaka and Sushruta. The science of psychology tries to understand human behaviour in all its forms. How are we to understand what other people do, think and feel? How are we to understand ourselves? There are no easy answers to these questions. The promise of psychology is that rational means will give us a sure guide to understanding human behaviour.

In *Charaka Samhita* we find the earliest attempts to classify human behaviour.

Behavioral Types in 'Charaka Samhita'

In *Charaka Samhita*, Sharira Sthana, chapter IV, there is a detailed account of the varieties of human mind: "the minds of three kinds — *Sattvic* (pure), *Rajasik* (passionate) and *tamasik* (ignorant)": the pure mind is considered to be without any taint as it represents the beneficial aspects of the intelligence. The passionate mind is tainted as it represents the violent aspect. The ignorant mind is also tainted on account of its representing the deluded aspect.

Each of these three types of mind reveals an infinite number of variations on account of the differentiating factors of degree, origin and body, and the mutual concomitance of body and mind; thus a particular type of body goes with a particular type of mind; and conversely a particular type of mind with a particular type of body. Some samples are given below:

"One who is pure, devoted to truth, self-controlled, of right discrimination, endowed with knowledge, understanding and power of exposition and reply,

possessed of memory, free from desire, anger, greed, conceit, infatuation, envy, dejection and intolerance, and equally well disposed to all creatures is the '*Brahma* type'.

"One who commands status, honour, luxuries and attendants, who is devoted to the constant pursuit of virtue, wealth and pleasure, who is clean and given to pleasures of recreation and whose modes of anger and favour are patent is the '*Kubera* type'. "One who is fond of dance, song, music and praise, and is well versed in poetry, literature, history and legend, who is constantly addicted to the pleasures of fragrant flowers, women and recreation and is free from envy is the '*Gandharva* type'." Thus the *sattvic* type is of seven varieties (*Brahma, Rushi, Indra, Yama, Vanina, Kubera and Gandharva*) all of these are the beneficent types, of which the most perfect mind is *Brahma*.

"One who is valiant, despotic, of an envious disposition, possessed of authority, given to poses, terrifying, pitiless and fond of selfadulation is the '*Asura*' type.

"One who is intolerant, of implacable hate, bides his time and then strikes, is cruel, gluttonous, inordinately fond of fleshy foods, of an excessively somnolent and indolent disposition and envious, is the '*Rakshasa*' type.

"One who is a great eater, luxurious, fond of keeping company of women in secret, unclean, a hater of cleanliness, a coward, a bully, given to abnormal recreations and foods is a '*Pishacha*'.

"One who is fond of food, whose character, conduct and pastimes are of a very painful description, who is very covetous, envious and without discrimination and who is disinclined to work is the '*Preta* type.'" Thus the *Rajasa* type comprises of six varieties: *Asura, Rakshasa, Pishacha, Sarpa, Preta, Shakuna*; they are all tinged with passion.

"One who is of a forbidding disposition, unintellectual, disgusting in his behaviour and food habits, abandoned to sex pleasures, and given to somnolent habits is the '*Animal* type.'"

"One who is pusillanimous, unintelligent, greedy for food, unstable, of persistent likes and dislikes, of itinerant habits and fond of water belongs to the '*Fish* type.'"

"One who is lazy, exclusively devoted to the business of eating and devoid of mental faculties belongs to the '*Vegetable* type.'"

"Thus the *tamasa* type comprises of three varieties—Animal, Fish and Vegetable. They represent the inert aspect of mind".

“Similar to the office of God in the world is the might of the individual soul in man. God’s greatness in the universe is seen as creator; in the human body the soul’s greatness is seen as the mind”.

Evolution of Modern Psychology

In the late 1800’s and early 1900’s as psychology evolved from philosophy, Schools and “isms” of psychology grew up to provide their own answers to the question, how should we study human behaviour? One school, *Structuralism*, perhaps influenced by the chemistry of its day, started a search for the elements into which mind could be analysed. For example, a subject was trained to “introspect” what he experienced when exposed to a certain stimulus such as a coloured light, a tone, an odour, and describe it as minutely as possible. The structuralists hoped that in this way the elements of experience would be discovered. Although the “elements” approach of structuralism has disappeared, the interest in mind has persisted in psychology.

Another school, *functionalism* tried to study the adaptive functions of behaviour and mental life, not merely the structure of the mind. *Behaviorism* as it was originally developed in the tens and twenties of this century by John B. Watson (1878-1958) rejected the introspective method completely and insisted that psychology be restricted to the study of behaviour, the things people and animals do. The study of behaviour has remained a dominant theme in psychology.

Another school, *Gestalt psychology* was developed in Germany in the early 1900’s. According to this school our experiences and behaviour are patterns or organizations analogous to a magnetic field, in which events in one part of the field are influenced by events in another part. For example a grey piece of paper is grey only *in relation* to its background or to something with which it is compared. On a black background it appears light; against a white background it appears dark. It is this stress on the relationships between elements that characterized Gestalt psychology. According to it, “the whole (experience) is more than the sum of its parts (elements)”.

While these schools were developing within psychology itself, psychoanalysis originated within psychiatric practice. Sigmund Freud (1865-1939) developed a method of treatment and a theory of personality, based on his experience with neurotic patients. The emphasis of this treatment is on free association—the patient freely associates, or thinks and says whatever comes to mind. The psychoanalyst uses these free associations to analyse and understand the sources of the patients’ problems. The theory of personality elaborated by Freud is quite elaborate, stressing the role of motives that are often repressed (not recognized by the individual and other people).

Modern behaviorists like B. F. Skinner stress that it is the *observable behaviour* that counts. Information about human and animal behaviour is gained by controlled experiments and observations rather than by more subjective or intuitive methods, which may only lead to fictional explanations of behaviour. Behaviorism attempts to demonstrate that human and animal behaviour can be predicted, controlled, and understood without recourse to explanations involving the "mind".

In recent years some psychologists have argued that the reductionist approach (breaking down of the whole into its component parts for the purpose of analysis) cannot give us an understanding of the individual as a whole. This viewpoint, *humanistic psychology* developed in the early 1960's as a reaction against the totally reductionist, observation-based analysis of human behaviour. Charlotte Buhler points out that "existential" considerations form the underlying philosophical basis of humanistic psychology. She believes that a totally objective approach to studying human behaviour overlooks the internal, integrative constituents of a person's total self—motives, wishes, internal conflicts, feelings, realizations and so on. Humanistic psychology tries to plumb a person's total self by conceptualising processes within the individual. Needless to say, the merits of this approach as an alternative to empirical reductionist approaches is questioned by the behaviorists.

Species-specific Behaviour Patterns

The impact of the Darwinian theory of evolution on psychologists' thinking has been that *behaviour, as well as structure, evolves*. Many adaptive changes help the individual and the species fit better into some niche, or special habitat, within an environment. A small change in behaviour, like a small change in structure, may make an animal species more suited for life in some niche. The adaptive changes in behaviour will be selected so that they become part of the species' heritage in the same way that certain adaptive structures do. The important point to be appreciated is that species-specific behaviours *evolve* just as do structures. In the last 40 years the study of animal behaviour has been spurred on by the development of *ethology*, a subfield of zoology that studies animal behaviour from a biological point of view. The pioneer ethologists Konrad Lorenz, Niko Tinbergen and K. Von Frisch (who jointly won a Nobel Prize in 1973) have brought to us an appreciation on the great importance of species-specific behaviour in the adaptation of animals to their environment. Although species-specific behaviour is genetically based, environmental factors play a role in its expression. Responses controlled entirely by genetic factors might be called instinctive, but since environmental influences continually modify the expression of genetically based responses it is difficult to find true instincts, hence behaviorists prefer the term "species-specific" to "instinct". As evolution has proceeded, the nervous systems of animals have

become more and more complex. The behaviour of higher animals has come to be controlled more and more by the unique experiences and environments they encounter. *Learning* and *reasoning* have become more and more important especially for human species. However, recent books by Konrad Lorenz, Desmond Morris and Robert Ardrey have made us wonder again about our animal nature. There is some biological basis for aggressive behaviour but this biological potentiality does not inevitably direct man to kill or destroy. The important question is, to what extent can educational measures direct man's behaviour into productive rather than destructive endeavours.

Emotional expression as a form of species specific behaviour has been much studied since the time of Darwin. Expressions tell other members of the species about an individual's emotional state, and they are sometimes considered to be incipient movements of attack or flight—the so-called intention movements.

Man's evolutionary heritage expresses itself behaviorally in a more general way. This heritage has resulted in the development of a nervous system that sets limits on, and provides potentialities for, our behaviour. Because of elaborate development of certain parts of the cerebral cortex, we are the species of animal best able to represent the world in symbols. We do this in speech and in visual imagery for the most part. Related to our ability to symbolize events is the ability to think about our world and ourselves in it. Each of us is aware that he is different from other people, and all of us try to fit our experience into some meaningful framework. We construct philosophies in our effort to explain ourselves and our place in the world.

Many other potentialities for behaviour are made possible by functional capacities built into the human brain through evolution. It has been shown experimentally that electrical stimulation of the limbic system leads to aggressive outbursts. Tumours in this region can also lead to aggressive behaviour. On the other hand aggressive behaviour is inhibited by electrical stimulation of other portions of the limbic system. Hunger, thirst, sexual behaviour also have specific controlling in the brain.

Chromosomes and Behaviour

Most of the behavioral traits that interest psychologists are determined by many genes, and it is not possible to pinpoint the particular gene responsible. But it is possible to show that certain chromosomes are necessary for the development of complex behaviours in both animals and humans. For instance, Down's syndrome (Trisomy of No. 21 Chromosome) is associated with severe mental retardation. Antisocial behaviour related to 47 XYY chromosomal pattern has attracted great interest. There seems to be a greater proportion of 47 XYY men in institutions for

the criminally insane, than in normal population and in ordinary prison population. Human intelligence is determined by multiple genes. The strongest evidence for a genetic basis of human intelligence comes from two types of study: (1) comparison of monozygotic or identical twins reared together or apart, and (2) correlation between foster-parents and their foster-children. The average correlation between pairs of identical twins reared apart is quite high, although it is lower than for identical twins reared together. The influence of environment is brought out in the second type of study.

If we have so much trouble assessing the role of genetics and environment in twin studies, it is small wonder that we have far greater difficulty with racial studies. In a controversial article published in the *Harvard Education Review* in 1969, Arthur R. Jensen a professor of educational psychology at Berkeley U.S.A. reported that blacks as a group score significantly lower (about 15 points) on IQ tests than whites. Jensen attributed 80 percent of an Individual's intellectual potential to genetic inheritance and only 20 percent to environmental factors. These conclusions have been hotly disputed by others. Most of Jensen's critics, including the geneticist Joshua Lederberg, Nobel Prize winner, hold that culture, not race determines a man's intellectual potential.

The genetics of Personality & Temperament

Personality is a difficult concept to define but it is made up of various distinctive and enduring traits that are characteristic of a particular person. We differ from each other behaviourally in many ways: in the expression of emotions, in motivations, interests, attitudes; in tendencies towards behaviour disorders; in the ways we protect ourselves against stress, guilt, fear and anxiety. Temperament is that aspect of personality which has to do with emotionality—a person's ease of emotional arousal, his characteristic forms of emotional expressions and his typical mood states.

Environmental factors, especially the learning experiences of people, play a very large role in shaping personality. Evidence for the inheritance of human personality traits is rather weak. There is much stronger evidence for the inheritance of certain abnormal personality traits. Heredity undoubtedly plays a role in chronic alcoholism, manic-depressive psychosis, schizophrenia. This evidence comes from the analysis of concordance rates for monozygotic and dizygotic twins. If schizoid behaviour disorders are considered along with schizophrenic disorders, the case for a genetic basis of this type of behaviour disorder becomes even more convincing.

Studies which change the environment, or nurture, by impoverishing or enriching it, attempt to unravel the intertwined factors of nature and nurture. The impoverishment studies have shown that for some behaviours there is a *critical*

period during which certain environmental features must be present if the behaviour is to develop.

Social Development

Getting along with others is one of the most important things people do in our complex social world. The origins of each person's social behaviour go back to the earliest days of infancy. The first social responses are to be found in the attachment of babies to their mothers in the first few days and weeks of life. Attachment has great adaptive value because it keeps the infant close to the mother, where he or she can be fed and sheltered from harm. But as babies grow, they cannot remain tied to mother; they detach themselves to explore the environment. So the first theme in the development of human social behaviour is the attachment—detachment story.

As children grow older they meet many other people and getting along with others becomes the compelling, and continuing, theme of social development. Development of both positive and negative aspects of getting along with others - altruism and aggression - are of great importance. Another crucial aspect of social growth is moral development ideas of what is right and wrong. As moral ideas develop, they come to be important in determining our responses to others.

Harriet L. Rheingold, a developmental psychologist has shown that sharing behaviour is observed in 18-month old children and perhaps even younger children. She speculates that this sharing behaviour may originate as a result of the many things that are shared with the infant during its early dependency on others. In addition, sharing behaviour probably develops as a result of both subtle and not-so-subtle rewards received for it. Unfortunately many of life's experiences work to thwart this development. Rheingold believes that society's task is to learn "how to build upon that generous nature" which infants develop but which can be lost.

As children grow older, parents and other children come to shape their behaviour more and more. Social behaviour is very much determined by particular experiences that children have. Parents who provide models of pro-social behaviour (helpfulness, co-operation and altruistic behaviour), who reward pro-social behaviour, and who give their children practice in it can expect to have helpful, co-operative and altruistic children. Unfortunately, the reverse of this statement is also true.

In getting along with others, children must learn to curb their aggressive tendencies and to express them at appropriate times in socially approved ways. Things that parents do will either increase or decrease aggressive behaviour in their children. Aggression is often, though not always, caused by frustration. As

with pro-social behaviour, learning and modelling have a great influence on aggressive behaviour. Experiments have shown that if aggressive behaviour is rewarded, it will occur frequently. Furthermore, aggressive behaviour learned in one situation will generalise or spread to other situations. Ultimately, much of a child's social behaviour as also that of the adult, is determined by ethical and moral ideas about what is right and what is wrong. Moral development, like cognitive development, seems to move through levels and stages. At the first level the child has little true moral feeling, and behaviour is dominated by selfishness and deference to superior authority. At the second level ethical ideas are dominated by conventions and a law-and-order orientation. At the third, abstract principles of law or human dignity govern ethical decisions. If the future lies with the world's children, the world's urgent problem is how to provide environments that do not limit children's moral development.

Principles of Learning

Learning is the key process in human behaviour. Learning can be defined as any relatively permanent change in behaviour which occurs as a result of practice or experience. It pervades everything we do and think. *Socialization* is the name given to the learning processes through which the infant is trained in the attitudes, beliefs and behaviours appropriate to his culture. Training reinforces the behaviours desired, and extinguishes the others. Learning takes place in many different kinds of situations. We will discuss four learning situations: (1) classical conditioning (2) operant conditioning (3) cognitive learning (4) punishment and negative reinforcement. In the first two, positive reinforcement (reward) is typically used to promote learning. In the third, learning takes place without reinforcement. The fourth is somewhat like the first two except that negative reinforcement (unpleasant stimulation) is used to promote learning.

Ivan Pavlov (1849-1936), the famous Russian physiologist introduced the concept of conditioning and established many of its basic principles. Pavlov discovered very early that if he conditioned an animal to salivate at the sound of a bell, it would also salivate, though not quite so much, at the sound of a buzzer or the beat of a metronome. The animal tended to *generalize* the conditioned response to stimuli that were different from, but somewhat similar to, the one to which it was specifically conditioned.

Many human responses and characteristics seem to be acquired through the process of *conditioning and generalization*. The greater the similarity between stimuli the greater the generalization between them. People develop fears and phobias by acquiring them through accidental conditioning to some stimulus and then generalize them to situations that otherwise would not be frightening. It is the emotional responses which become conditioned to certain stimuli that are important in human life.

Reinforcement is the key term to understand operant conditioning. "Well done!" from the boss, is an example of reinforcement. The word 'operant' signifies that when a response operates on the environment in the appropriate fashion, a reinforcer or strengthener of the tendency to make that response is forthcoming. Many attitudes and beliefs, customs, learned goals and certain aspects of the use of language can result from shaping behaviour by means of reinforcement, through the mechanisms of operant conditioning. B. F. Skinner in a book entitled "Science and Human Behaviour" has pointed out the importance of operant conditioning in the socialization process.

Besides being everpresent in human situations, operant conditioning is sometimes deliberately used to shape desired behaviours. Programmed learning and certain types of therapy for behaviour disorders are examples. Behaviour therapy is an attempt to treat behaviour disorders by reinforcing socially adaptive behaviour and extinguishing maladaptive behaviour.

There is some evidence that visceral responses such as heart rate, intestinal contractions and blood vessel dilatation can be operantly conditioned. This has promising implications in the treatment of many problems like high blood pressure.

Social Motives

The social motives are the complex motive states or needs, that are the well-springs of most human actions. Three of the most studied social motives are the *need for achievement, need for affiliation and need for power and status*. Motives are inferred from behaviour. Measurement of social motives can be done by various techniques such as projective techniques, questionnaires or inventories, observations of actual behaviours in certain types of situations designed to bring out the expression of social motives, and analysis of the literary and artistic output of an entire society in order to get an idea of the main social motives of its people at a particular time in history.

The best known projective tests are the Rorschach Inkblot Test and the Thematic Appreciation Test (TAT) which consists of pictures of scenes and people.

Knowledge of the social motives dominant in a society may help us understand its history and predict its future. This application of psychology to history and contemporary political trends is relatively new but it may turn out to be a major contribution.

The course of motivations does not always run smoothly. Things happen to prevent us from reaching the goals towards which we are driven. This leads to frustration, depression, anxiety, guilt or anger. Generally speaking, the causes of frustration are to be found in environmental forces that block motive fulfilment,

personal inadequacies that make it impossible to reach goals, and conflict between motives.

Frustrations

Of the three general sources of frustrations described above, motive conflict is the most important in determining a person's anxieties, or "hang-ups". Three major kinds of conflict have been identified, called approach-approach, avoidance-avoidance, and approach-avoidance.

Approach—approach conflict occurs between two positive goals that are equally attractive at the same time. The proverbial donkey starved to death because it stood halfway between two piles of hay and could not decide which to choose. Such a conflict is usually resolved by satisfying one goal first, then the other, for instance, eating and then going to bed if a person is both hungry and sleepy— or by choosing one goal and giving up the other. Compared to other conflict situations, approach-approach conflicts are easy to resolve and generate little emotional behaviour.

Avoidance—avoidance conflict is a fairly common experience, like being caught between the devil and the deep blue sea. We can all think of things we do not want to do but must do, or face even less desirable alternatives. Vacillation and attempt to leave the conflict situation are two kinds of behaviours emerging in such a situation. People in avoidance-avoidance conflicts may try a different means of running away. They often rely on imagination to free them from the fear and anxiety generated by the conflict. They may spend much of their time in day-dreaming—conjuring up an imaginary world or regressing into a childhood fantasy. Many intense emotions are generated in avoidance-avoidance conflicts—fear, resentment, anger at being trapped in a situation where the goals are negative.

Approach—avoidance conflict is often the most difficult to resolve. In this kind of conflict a person is repelled and attracted by the same goal object. A young bride for instance, may have been brought up in an atmosphere where sex was treated as ugly and sinful. At the same time, her normal sex drive as well as other social values involved in marriage, give the marital situation a positive valence. Caught between conflicting sexual motives, social motives and attitudes learned in childhood, she experiences anxiety. The obstacles to the satisfaction of motives may be *internal* (like values acquired in childhood), hence much more difficult to handle than external obstacles.

Coping with the emotional reactions caused by such an internal conflict can create major problems of adjustment. In the human motives there is a constant struggle between "*Shreyas*" (what is the right thing to do) and "*Preyas*" (what one would love to do).

Common Conflicts

Owing to the number of needs that people have and the many ways of satisfying them, all sorts of frustrations and conflicts are possible. Conflict is likely to occur whenever pleasure and pain, or reward and punishment, are associated with the same thing. In different cultures and at different times completely different patterns of conflict may be seen. Achievement need versus fear of failure, independence versus affiliation needs, sexual desire versus fear of sex, hostility versus need for social approval are common conflicts in many cultures. There are almost as many sources of conflict as there are motives, situations and people.

Development of Attitudes

From birth to puberty a child's attitudes are shaped primarily by his or her parents. Parental influences wane as children grow older, and other social influences become increasingly important with the beginning of adolescence. During the period from 12 to 30, most of a person's attitudes take final form and thereafter change little. During the critical period three main factors are at work: peer influences, information from news media, and other sources, and education. Of all the three factors, education stands out consistently. The more educated people are, the more liberal their attitude.

Is there indeed a generation gap? Many studies show that there are indeed differences in attitudes between two generations. Social scientists think that differences of opinion between today's youth and their parents are ideological rather than generational.

Although their general attitudes may be well formed, adults are continually acquiring new attitudes, or changing their attitudes towards specific people and objects. Through advertising, political campaigns and many other means, a great barrage of attitude-shaping messages is directed at us day in and day out. There are three principal aspects of any situation in which attitude change is attempted, the source of the message, the message itself and the characteristics of the recipient.

Three characteristics of the source of message strongly affect our response—credibility, attractiveness and power.

As regards the message, advertisers and propagandists often rely on *suggestion* or the uncritical acceptance of a statement, without requiring facts. The most common form of suggestion is prestige suggestion, in which the message appeals to people's regard for authority or prestige. *Appeal to fear* is another method to persuade people. The use of *loaded words* is another technique.

UNDERSTANDING MENTAL ILLNESS

Certain characteristics of the person receiving a message influence its effectiveness: his influence ability, his needs and goals, selective interpretation, avoidance of threatening information, and prior “immunization” by mild arguments.

Prejudice refers to an unjustified attitude, usually unfavourable. Discrimination often results from prejudice. It is the behaviour of treating a person or a group in an unfavourable way. The factors that help to minimise prejudice are acquaintance potential, equal status, friendly association, co-operative rewards, and similar personality characteristics.

Defense mechanisms and Coping behaviour Freud described a number of ways in which people typically behave to avoid or lessen anxiety. These he called *defense mechanisms*. Many psychologists now do not accept Freud’s theories, but they do accept these mechanisms as descriptions of the way people behave in coping with their problems.

Forgetting (*repression*) is a refusal to think about something because we find the thought unpleasant. If we don’t think about it, we don’t rehearse it—which is what we need to do to preserve something in long-term memory— and so we forget it.

Reversing motives (*reaction formation*) like being too modest, too solicitous, or too affectionate to disguise the opposite feeling. A quotation from Shakespeare captures the idea of reaction formation: “The lady doth protest too much, methinks”.

Blaming others (*projection*) is a common coping mechanism. Carried to the extreme, projection is the mark of the behaviour disorder paranoia. The paranoid has projected his own hostile feeling about others into a whole system of thinking in which he feels that others are out to get him.

Making excuses (*rationalization*) is another kind of coping behaviour in which an acceptable motive is substituted for an unacceptable one. We give a different reason from the real one for what we are doing. ‘Sour grapes’ is another version of rationalism— something which we cannot get becomes something we did not want anyway.

Kicking the dog (*displacement*)—in this coping behaviour, the motive remains unaltered but the person distorts the goal of the motive by substituting a different goal object for the correct one. Most often the motive of displacement is aggression, which for some reason the person cannot vent on the “true” object.

Fantasy or day-dreaming is a coping pattern in which a person resolves conflicts by simply fleeing them — or trying to. Fantasy is very common, especially among adolescents. Upto a point it is a harmless way of getting some satisfaction by temporarily escaping from reality (like a boy who is not popular with girls but wants to be, conjures up a fantasy in which he is a Don Juan). But it rarely leads to constructive action.

Identification with someone else is another way of coping with frustration. Becoming friends with an important person, for example, can make us feel important. Youths often identify with popular film stars, wearing the same kinds of clothes, trying to talk in the same manner and so on. In this way, they secure some of the satisfaction their model enjoys which they themselves would not have.

Acting childish (*regression*) is often seen in children 4 or 5 years old because at this age they begin to face an increasingly complex set of frustrations. In regression the child frequently reverts to baby talk and to all sorts of 2-year-old behaviour. Adults too sometimes revert to childish behaviour when they are unable to find an “adult” way of approaching a problem.

Compensation: here a person finds a substitute activity to satisfy a social motive. Failure or loss of self-esteem in one activity is made up by efforts in other areas. The unattractive girl may become a book worm and eventually a distinguished scholar thereby commanding the respect and prestige that she was unable to win with good looks. Life is full of compensations through which people achieve satisfactions that they might not obtain otherwise.

Almost everyone resorts to defense mechanism at one time or another, and when they are used sparingly for minor conflicts, they are nothing to worry about if they do not damage other people. If they allow us to feel more comfortable at times, as they often do, then they have served a useful purpose in restoring our mental equilibrium. But if a person comes to depend on them, these defensive attempts to cope with problems are harmful. They never solve real problems; they only allay anxiety about them. Even more seriously, defensive behaviour often does not dispel anxiety. If certain situations make us anxious, we will meet them time and again and sooner or later come up against one for which we have no defense.

Behaviour Disorders

A behaviour disorder is some pattern of abnormal behaviour. “Abnormal” however is difficult to define. The fact is that there is no behaviour which is abnormal in itself. Behaviour exists on a continuum. When a person shows complete lack of behaviour that is seen in most people, it is abnormal.

Ten years back, D. L. Rosenhan, a professor of psychology and law at Stanford University thought that diagnoses of behavioral abnormality are based on less substantial grounds than most people realize. He therefore conducted an experiment in which eight *sane* people (3 female and 5 male pseudo-patients) gained admission to a variety of hospitals. Beyond giving phony symptoms like "hearing voices", that said "empty, hollow and thud", and concealing the fact that they were psychological researchers, the pseudo-patients told the truth and acted normally. They answered all the questions about their past experiences honestly. And though their symptoms were preposterous, they were admitted to the psychiatric wards of every hospital they went to. Once in the hospital, each pseudo-patient stopped pretending to have any abnormal symptoms.

Their task now was to get out of the hospital by convincing the staff that he or she was sane. On the average it took pseudo-patients *19 days* to be discharged from a hospital. Each however, was discharged with a diagnosis of "Schizophrenia in remission". This means that in the hospital's view the patient was not normal, and had not been, upon admission. Such a diagnosis carries personal, legal and social stigmas, yet there was a uniform failure by institutional personnel to question their conclusions, much less to recognize that the pseudo-patients were normal and sane.

Oddly, other patients in the wards often did suspect that the pseudo patients were sane. One reason why the hospital personnel did not, is that patients are not carefully observed by the staff in psychiatric hospitals. In fact, psychiatrists were rarely seen in the wards. Failure to detect sanity may also be due to the fact that *physicians operate with a strong bias towards calling a healthy person sick*, rather than vice versa. Rosenhan concluded that any diagnostic process which lends itself to such errors needs review.

Psychoneurotic Disorders

People suffering from "neuroses" or "psychoneuroses" are anxious people. Often their anxiety is obvious. They may be constantly apprehensive and worried, or full of complaints about themselves or about the world. But sometimes the anxiety is not so obvious; the person may appear relatively free of it, yet show reactions that can be traced to anxiety and the learned avoidance of it. Indeed the principles of learning, discussed earlier, are important in understanding psychoneurotic disorders.

Conversion reactions are a learned behaviour which enables the patient to avoid or escape from the intolerable and insoluble anxiety-producing situations. The soldier with "combat fatigue" is an example. Some soldiers in an avoidance-avoidance conflict situation, where they risk death if they obey commands, and incur disgrace or imprisonment if they do not, develop symptoms that resolve the conflict by removing them from the whole

situation. For instance the soldier might become paralysed so that he is no longer fit for combat. But he is not consciously malingering—he really cannot move although nothing is wrong with the muscles and nerves.

The symptoms of conversion reactions do not have a biological cause; they are not caused by a lesion, a germ or other detectable physical agency. The ailment which is real enough, however, is a device for coping with conflict and anxiety. Similarly, when a patient improves markedly on a placebo, we do not accuse him of faking. He has experienced real physical discomfort and his expectations of the power of the drug have led to real improvement.

Dissociative reactions are in a mild form, a normal pattern of behaviour shown by many people. The college student who cusses and jokes in the common room, but becomes serious when talking to her lover's parents, seems to display two different personalities. In a relatively harmless form, dissociative reactions may involve no more than a corn-part mentalization of a person's thinking and way of living. In the more extreme forms, dissociation reactions are incapacitating.

Amnesia is one well-publicized type of extreme dissociative reaction. In Amnesia as a neurotic disorder the person may forget his own name, where he has come from, who his relatives are, and what he has been doing for weeks, months or years.

Multiple personality is another dramatic form of dissociative response, in which a person's system of memories and traits seems to dissociate into two or more complete personalities. Typical example is the fictional case of Dr. Jekyll and Mr. Hyde. The change is triggered by stress or emotional trauma and it stems from a deep-seated conflict of motives.

Phobic Reactions

Some people who are otherwise normal and healthy have phobias or fear of small places, high places, the dark, animals and so on. The phobia may be so powerful and irrational that it alters the whole course of the person's life. Phobias may have their origins in fears learned by association of painful or unpleasant events with particular situations. Although the fear is rational when initially learnt, it subsequently diffuses. This is an example of stimulus generalization. There is no qualitative difference between a rational and irrational fear; the distinction is based on how society perceives the fear.

Obsessive Compulsive Reactions

An *obsession* is defined as unwanted idea that constantly intrudes into a person's thoughts, while a *compulsion* is an act that constantly intrudes into a person's behaviour. Both may be regarded as operant behaviours. One compulsive person must wash his hands every few minutes; another must

count all the steps she climbs. Some people are compulsive in a more general way; they find ambiguity and uncertainty extremely uncomfortable, and they strive for orderliness in thought, dress and in work. Indeed any unusual emphasis on "doing things the right way" may be regarded as compulsive.

Depressive Reactions

A certain amount of depressive behaviour is considered normal in our society. When a spouse dies, or when a loved relationship breaks up, the person is left without a source of reward (attention, affection, sex) for a great range of behaviours, the individual ceases to emit many of these behaviours because they no longer lead to reinforcement. Until the depressed patient learns new responses to replace the old, that is, new responses which bring reinforcement, his level of activity will be naturally low and his mood sad.

Ayurveda and Insanity

Charaka Samhita attributes insanity to vitiation of the humours. It is interesting that current research is focused on neurotransmitters like dopamine, noradrenaline and serotonin in relation to schizophrenia, depression and pre-senile dementia (Alzheimer's disease). Charaka described the symptomatology as under:

"Confusion of intellect, extreme fickleness of mind, agitation of the eyes, incoherence of speech, mental vacuity, unsteadiness, these are the general symptoms of insanity'.

"Insanity which is characterized by such derangement of understanding, mind and memory, is of exogenous or endogenous origin". "Possession by the Gods, sages, Gandharvas, Pisachas, Yakshas, Rakshasas and the manes, and the failure in the proper discharge of observances and vows in this life or the previous one—these are the causes of insanity of the exogenous type".

"Provoked Vata, Pitta and Kapha are the causes of insanity of the endogenous type".

Apart from various therapeutic measures for the treatment of insanity, Charaka states:

"If the patient continues to behave violently, then he should be made gentle by soft but strong bandages and put into a dark room free from metallic and wooden articles (lest he should harm himself with these).

"Flagellation and giving shock to the patient's mind, intellect and body are advised in difficult cases. Thus he may be terrorised by means of snakes whose fangs have been removed or by trained lions and elephants, or by men dressed as bandits or foemen with weapons in their hands or men impersonating the king's officers may, having dragged him out securely bonded, intimidate him with threats of immediate execution by the order of the king".

"It has been well said that the threat to life is more potent than fear of bodily injury; accordingly that measure may succeed in helping the disordered mind of the insane patient to regain its composure when all the other measures have failed".

"The man of strong mind, who abstains from flesh and alcohol, observes a wholesome diet and is always dutiful and pure, will never fall a victim to insanity, whether exogenous or endogenous".

Treatment of Behavioral Disorders

Hippocrates, the "Father of Medicine", around 300 BC, concluded that mental disorders arise from the same natural causes as physical ailments. According to Hippocrates, melancholia (depression) is caused by an imbalance of the body's four humours in which "black bile" ascends to the brain.

From time to time, religious notions have strongly influenced the treatment of the mentally ill. In the 10th and 11th Century Europe, for instance, nearly all physicians were also clergymen, and the monastery served not only as a church but also as a university and mental hospital. Bizarre behaviours were sometimes viewed as signs of divine intervention, sometimes attributed to possession by demons. Exorcism was the logical treatment to rid the body of demons. Other remedies used included herbs, human and animal excrements, prayers and holy water, the breath and spits of priests, pilgrimages, relic handling, and lucky charms. Later on, cruel treatments were devised for abnormal behaviour. The last part of the Middle Ages was marked by extremely violent treatment of behaviour disorders, including torture and burning at stakes. Belief in witchcraft, astrology and alchemy grew during the 13th and 14th centuries. As late as 1692 nineteen witches were executed in Salem, Massachusetts, USA.

By the end of the 19th Century, religious interpretation of abnormal behaviour had gone out of favour. People returned to the earlier beliefs that the behaviour disorders are like physical ailments, and that no one can be "blamed" for mental illness. Severely disturbed people were put into mental hospitals. But most patients received no treatment, and care and facilities in the hospitals were poor. Only in the early 20th Century did conditions in mental hospitals begin to improve.

Psychotherapy was initiated by Freud who was himself a physician, and psychoanalysis through much of its history has been in the hands of physicians. Psychologists, in contrast to physicians, began to treat behavioral disorders only in the last three or four decades.

Over the years, a variety of medical therapies have been tried out with mental patients. Three principal methods in current use are ECT, psychosurgery and chemotherapy.

Electro-convulsive Therapy (ECT)

ECT was introduced in 1937 by Cerelleti and Bini. Since then it has been widely used in mental hospitals for the treatment of psychotic depressive states. In this procedure the patient lies on a table in a supine position and with the help of special electrodes, an alternate current of 110 volts is passed for less than a second between the temples, or, less frequently, between the vertex and the non-dominant hemisphere, till convulsions are produced. The patient awakens from the ECT with a headache and has no memory for the events that immediately preceded ECT. Generally 2-3 treatments are given in a week. A patient with depression requires on an average 4-8 treatments, while schizophrenia needs about 10-20 treatments.

Antidepressant drugs have brought down the number of ECT procedures over the years. Antidepressant drugs are slow in action and take about 1-2 weeks for optimum response. The outstanding reason for ECT rather than drugs in severe depression is the lessened danger of suicide which rarely occurs after initiation of ECT. To prevent dislocations or fractures that may occasionally occur in ECT, use of muscle relaxants and anaesthetic agents is made, with endotracheal tube and oxygen always at hand. Modified current (200 milliamperes) for a brief duration seems to show better conservation of memory and better results on intelligence tests. Unilateral ECT over the non dominant hemisphere shows similar results.

Psychosurgery

In 1933, Moniz, a Portuguese psychiatrist, originated the idea of performing brain surgery as a treatment for psychosis. He believed that the fixed ideas and repetitive behaviour seen in some psychotic patients are accompanied by "abnormal stabilization of cellular connections", especially in the pre-frontal lobes of the brain. To "unstabilize" the connections he recommended severing or removing some of the brain tissue involved. The operation introduced by him, prefrontal lobotomy, severed the nerve pathways in the brain that connect the most forward parts of the frontal lobe with the underlying regions of the brain. Prefrontal lobotomy is rarely performed now since

the advent of effective psycho-active drugs. Instead, psychosurgery on the centres for emotion has come into vogue.

On August 1, 1966, a 25-year old man Charles Whitman climbed to the top of a tower on the campus of the University of Texas at Austin and began firing at passers-by with a high-powered rifle, wounding 31 people and killing 13, before he was himself shot dead by the police. At autopsy on Whitman's body, a tumour in the temporal lobe was revealed. The temporal lobe is the area of the brain most often related to episodes of violent behaviour. Experimental stimulation of the particular part of the temporal lobe called medial amygdala causes loss of control and an outburst of rage. When another part of the amygdala is stimulated, a feeling of relaxation is produced. Based on these observations, Vernon Mark, a neurosurgeon and Frank Ervin, a psychiatrist introduced the idea of operatively destroying the medial amygdala. The operation reduces violent outbursts, but the patient may remain confused and delusional, and unable to work or care for himself. Evidently not enough is known about the ways in which the amygdala and other areas of the brain control aggressive behaviour. Many psychiatrists maintain that the value of psychosurgery has not been firmly established.

Chemotherapy

Different drugs affect different parts of the brain and thus affect the way the brain works. In recent years, 30 different small molecules functioning as Neurotransmitters have been identified and their distribution in different parts of the brain has also been studied. For instance the most widely used tranquillizers, the benzodiazepines (valium etc.) are shown to be active at the GABA (gamma amino-butyric acid) receptors which are mediators of the inhibitory neurons in the brain. Approximately 1/3 of neurons are inhibitory.

Phenothiazines act on the dopamine receptors. According to current hypothesis, an over-activity in the brain dopamine systems (particularly in the limbic system, a region involved in emotional behaviour) may underlie the symptoms of schizophrenia. Amphetamine triggers the release of dopamine at nerve terminals and produces in high doses disruption of thought processes, hallucinations and delusions of persecution, symptoms very similar to those found in some forms of schizophrenia. Hallucinogenic drugs show a strong structural resemblance to the monoamine transmitters. Mescaline possesses the benzene ring structure of dopamine and noradrenaline; LSD incorporates the indole ring structure of serotonin.

The wide variety of anti-schizophrenic drugs that have been developed, such as chlorpromazine and haloperidol, share the property of binding tightly to dopamine receptors thereby preventing the natural transmitter from activating them. This discovery has proved to be one of the

most promising leads in modern schizophrenia research. The latest evidence suggests that schizophrenia is associated with an over-production of dopamine or an over-responsiveness to the transmitter in certain regions of the brain.

Another important group of currently popular drugs are the *antidepressants*. One category of drugs is represented by iproniazid and other drugs that inhibit the enzyme monoamine oxidase, which degrades noradrenaline, dopamine and serotonin. As a result of the blockage of this enzyme the arousing effects of those monoamines are enhanced, accounting for the anti-depressant actions of the drugs. A second category of anti-depressant drugs, the tricyclics, also amplify the effects of noradrenaline and serotonin in the brain. Those drugs, of which the best known are imipramine and amitriptyline, block the reuptake of noradrenaline and serotonin from the synapse; the stimulant drug cocaine appears to work by the same mechanism. Such observations have suggested that depression may be associated with low levels of amine transmitters at brain synapses, whereas mania may be associated with excessively high levels of those transmitters.

The greatest benefit of these drugs is that they have largely eliminated the need for psychosurgery. They quieten down aggressive and over-reactive hospitalized patients without damaging the brain tissue irreversibly. Owing to the use of these drugs, many hospitals have now fewer restraints on mental patients (locked and barred rooms, straight jackets, isolation rooms). And hospital confinements are shorter because the patient's families are more willing to take them back home when they are calm and cooperative. The quiet and Cooperative patient can be trained in the method of relaxing, of lowering anxiety, and of mastering the conflicts of life. As people learn to modify their behaviour, their drug dosage can be gradually reduced and finally stopped.

Lithium and Mania

People suffering from mania or bipolar disorders (manic-depressive psychosis) often improve impressively when they are treated with salts of lithium.

Cade, a physician and psychiatrist in Australia in 1949, found in guineapig experiments that an injection of a solution of lithium carbonate made the animals extremely placid and lethargic and unresponsive. Cade speculated that the calming effect of lithium on guineapigs might be repeated in human beings. Oral administration of lithium salts to a 51-year old man who had been hospitalized with chronic mania for 5 years, showed such improvement that within two months he was able to leave the hospital and resume his job while remaining under lithium therapy.

Lithium is the third lightest element, following hydrogen and helium, in the periodic table of elements. It is fascinating that a simple salt, an ion, an extract of rock, is able to alter such an ephemeral and subtle property of mind as mood. People are more accustomed to the idea that states of feeling are affected by relatively complex organic substances such as opium, marijuana, cocaine and alcohol. The physico-chemical simplicity of lithium arouses the hope that it will shed light to clarify the neuronal basis of mood.

Psychotherapy

The term psychotherapy is conventionally limited to the form of treatment which depends upon direct and personal relationship between the patient and the physician. What the psychotherapist does, can be described by metaphor and analogy. He promotes the *ventilation* and *desensitization* of emotional disturbances; he *elucidates* latent or obvious muddles, *disentangles* conflicting tendencies, giving them new incentives and a different direction; and so guides the patient through the maze of his life's experience as recalled in memory, that he is better fitted for dealing with current experience, knows himself better, and has somewhat "*purged*" himself of past harms. All "*analytic*" methods review the patient's life as he recalls it under special conditions, e.g. of free association, hypnosis, biographical schemes etc. Of late, much effort has been, put into "group" psychotherapy rather than individual patients. The groups, usually of about 5 to 20 people, have a minimum of structure. In an atmosphere where facades are dropped and emotions are stressed, members work through their initial negative feelings, aggressive behaviour, and confrontations, and more positive feelings emerge; previously unloved, lonely people may begin to experience positive regard for others in the group.

The psycho therapies, as distinguished from behaviour modification, pay attention to the elements in the patient's problem: environmental barriers, personal frustrations, motivational conflicts, deeply rooted personality disorders, inadequate learning of necessary social skills or learning of inappropriate behaviours.

Psychoanalysis relies on the technique of free associations and dream analysis to help patients gain insight into their problems. Often a patient shows resistance in free association, then later develops transference to the analyst. The transference must be dissolved at the end of analysis.

The *existential therapist* tries to accept the patient as he is and to understand the ways the patient seeks for meaningfulness and value in life.

Client-centred therapy puts the patient in a permissive situation where he or she has freedom to explore and express attitudes, hopes and fears. The therapist does the minimum of interpretation.

~*Gestalt therapy* attempts to get the patient to be more aware of his true self to allow his natural impulse to emerge.

Play therapy, used mainly for children, permits a child to release feelings without fear of reprisal.

Behaviour modification begins with a functional analysis of a person's behaviour, attempting to see what antecedents lead to the disordered behaviour and what consequences the behaviour produces.

Then a particular form of therapy is chosen.

Various *operant conditioning techniques* may be used for behaviour modification. Among these are: the application of positive reinforcement for desired behaviour and the use of extinction or punishment for non-desired behaviour.

Token economics established in hospitals and outpatient clinics provide the patients with tokens as secondary reinforcements for doing desirable things. The tokens are later traded for something the patient wants.

The classical conditioning techniques of behaviour modification include aversion therapy to eliminate undesirable responses; *covert sensitization*, in which the patient imagines unpleasant things associated with his bad habits; and *systematic desensitization* in which the patient combats anxiety with deep muscular relaxation.

Modelling techniques of behaviour modification are based on observational learning. For example, a patient may lose a fear of snakes by watching someone else handling snakes.

Biofeedback techniques permit a patient to monitor his internal organs, such as heart or stomach and gain some control over their function.

Brain-washing

In the early 1950's a new word entered our vocabulary "brainwashing". As a result of the Korean War, American soldiers were exposed to "coercive persuasion" — an intensive indoctrination programme combined with sophisticated techniques for undermining the social structure of the captive group. Typically, the procedure consisted of first removing from the group anybody who showed signs of leadership. This robbed the "followers" of a source of emotional support they needed to maintain tolerance of stress. The remaining members were treated in different ways in order to foster guilt and suspicion among the captives and build mistrust among them. This procedure breaks down group cohesiveness and discourages personal interaction.

Under these conditions, as well as being underfed, physically tortured and isolated, some individuals were systematically brought to the point where they had to choose between maintaining their old attitudes and possibly not surviving internment. The prisoners became uncommunicative and non-committal about everything. Next, the indoctrinators began daily "instructions in an attempt to induce cooperation from the men and try to change their attitudes about various things. Those who resisted were punished and those who behaved "correctly" were rewarded. The whole process was aimed at establishing a need for change and then providing a direction for the change.

Schein and his colleagues report that almost all the prisoners showed some compliance. Fewer than 5 percent resisted the pressure with no discernible attitude change. For the most part, however, the prisoners' compliance consisted of *doing* what was expected of them. But later, when the prisoners were released, only a very few appeared to have undergone any significant change in ideology. Thus coercion does not appear to be the best way to produce long-lasting changes in attitude; education is the best way, since, by definition, education is concerned with behaviour shaping and behaviour modification. Positive reinforcement is a more effective way than punishment or negative reinforcement, to elicit desirable behaviour.

Behaviour shaping

The social bonds established between the new-born and the mother within the first few hours or days of life are critical in shaping the primary adaptive social attitudes and social behaviour. The sense of security derived from the rhythm of the mother's heart-beat when she holds the baby in arms and the loving and affectionate care given in prompt, consistent, and confident manner, ensure normal emotional growth. Lack of care at this stage may result in life-long retreat, anxiety or hostility. The parent is the child's first and most important teacher or model, whom the child will imitate. The relationships established with parents in infancy are extended to other familial and extrafamilial contacts; love and affection, security, approval, encouragement, recognition and pride all facilitate normal emotional growth and development.

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MAINTENANCE OF MENTAL HEALTH

Mental health is a problem that concerns everyone. So many people suffer from behavioral disorders that we cannot escape some personal contact with them. Neurotic people undoubtedly make up the largest single group. Roughly five percent of the adult population in our society consists of people who have been severely handicapped in social adjustments. Alcoholism and drug addiction, and anti-social behaviour, represent another kind of social maladjustment.

About half the hospital beds in the United States (as also United Kingdom) are occupied by mental patients, roughly constituting one million beds. As the number of old people in the population increases, the problem of senile psychosis is going to be aggravated. Senile psychotic behaviour is characterized by delusions, defects of memory and general dis-orientation. A person may imagine that he has been talking to someone who really was not there; he may forget what he has just said, at the same time insisting he remembers things which never happened. He may be disoriented in time and space. The brain damage resulting in senile psychosis may be the result of cerebral atherosclerosis, hardening of the blood vessels that supply the brain, resulting in diminished blood circulation. Additionally, there is a loss of neurons due to ageing. The severity of the disability depends on the degree of brain damage as well as the person's skills and patterns of adapting to stress. For some people, mild brain damage is just another stress for which they may be able to compensate, depending upon previously learned adaptive skills.

Prescription for Mental Health

Charaka has emphasised good conduct as a means to maintaining mental health and happiness.

"Those who are desirous of their welfare both in this and the next world should suppress the rash and evil impulses of the mind, speech and body."

"The wise man should control the impulses of greed, grief, fear, anger, vanity, impudence, jealousy, excessive attachment and malice".

"One should control the impulse for speech that is harsh, extravagant, insinuating, untrue and untimely".

"One should control the impulses for all such activities of the body as are injurious to others, such as adultery, theft, inflicting pain etc.

Avoidable Men

“Those who are sinful of conduct, speech and disposition, back-biters, quarrelsome, sarcastic and niggardly; those who are envious of others’ prosperity; those who are fickle minded, those who have a foot in the enemies camp, those who are without compunction, all such, the scum of humanity, should be shunned”.

Associable Men

“Those who are mature in understanding, learning, years, character, courage, memory and one-mindedness; those who frequent the company of such; those who are endowed with insight into the nature of things; those who are free of all ailments; those who are well-disposed towards all creatures; those who are tranquil of heart; those who are of commendable character; the teachers of the right path; and those who hear and see only that which is meritorious, are to be sought”.

“The wise man who seeks happiness both here and hereafter, should exercise the highest care in selecting what is wholesome in the matter of food, conduct and behaviour”.

Preservation of the Normalcy of the Mind

“The right, as well as excessive, deficient, and erroneous perceptions are the causes Respectively of the order and disorder of the mind and understanding.

“For preserving the normalcy of the mind and for protecting it from abnormality, efforts should be made by the following means: the wholesome contact of the sense organs and their objects, the proper performance of actions after intelligent and repeated scrutiny”.

“Fellowship with all creatures, winning over the angry, consoling the frightened, befriending the destitute; bearing with harsh words from others, overcoming impatience, showing a tranquil disposition, and removing the causes of passion and aversion”. “Speak no untruth; take not away other’s goods; covet not another’s wife nor another’s wealth; delight not in vengeance; sin not even against a sinner; expose not another’s shortcomings; try not into others’ secrets; keep not the company of those who are irreligious, disloyal to the king, arrogant, deprived, mean and wicked. Do not speak ill of good people and your elders. Transgress not the majority decision; break not a rule: do not develop a taste for drinking, gambling and the company of prostitutes”.

“Be neither timid nor overbold; be not ungenerous to your dependants; be not distrustful of your kinsmen; take not your pleasures alone; regard not the

MAINTENANCE OF MENTAL HEALTH

maintaining of character and social observances as a tax on you; do not trust everyone nor distrust everyone; be not always ruminative”.

“Do not let slip the right moment for action; do not undertake anything without deliberation; do not be a slave to your sense-appetites; do not pander to the fickle mind; Do not over-burden the senses and the understanding; do not over-procrastinate”.

“Do not give way to anger and joy; do not nurse your sorrows; be not arrogant in success and dejected in defeat; remind yourself constantly of the vanity of things; be decided as to causes and their effects and consequently devoted to benevolent enterprises; do not grow complacent with your achievements; do not lose heart; do not recall calumny”.

“Be devoted to *brahmacharya*, knowledge, charity, friendliness, kindness, joy, impartiality and peace”.

Self-discipline

Discipline has been defined as training in proper conduct and action. As a verb, discipline means to educate, to train, especially to bring under control. Discipline is a complex set of attitudes, behaviours, formal or informal instruction, rewards and punishment, which serve not to inhibit, restrict, subjugate or repress children but help them internalize appropriate cognitive processes, ideas and values; with these they will be able to ultimately exercise their own judgement and choose their own behaviour in ways best adapted to their situation. The wisdom of Ayurveda lies in incorporating a code of conduct in the Science of Life, as a means to ensuring mental health and happiness.

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MOLECULAR BIOLOGY — A NEW INTERFACE BETWEEN AYURVEDA AND MODERN MEDICINE

Introduction

In the chapter on “**Classification: Ancient and Modern**”, in the section: The full circle, I had stated the following. “In the reductionist approach of experimental medicine, we went on from the whole person to the level of individual organs and tissues, to look for specific causes. When we reach the level of cells and sub-cellular organelles, the doctrine of specific causes becomes blurred, because various types of insults may produce the same result in terms of biochemical lesions. In future classification of disease we might emphasise what underlying disturbance of control mechanisms we are required to correct, rather than “treating a disease”.

As we enter the new millenium, we are indeed in a position to *understand at the molecular level* all the chemical processes associated with living cells. Biochemists have sought to isolate the numerous molecules found in cells, determine their structures and analyse how they function. To give one example, the efforts of many biochemists to understand the molecular basis of contractility - a process primarily but not exclusively associated with muscle cells - have entailed purification of many molecules, both simple & complex, followed by detailed structure function studies. Through these efforts, some of the features of the molecular basis of muscle contraction have been revealed. Applications of modern molecular and cellular biology of cardiac muscle and vascular smooth muscle already permeate both cardio vascular diagnosis and therapeutics, examples of which will be encountered in subsequent sections.

Since the publication of the 1st edition of this book in 1986, several important biomolecules have been well studied, which have important role in health and disease, such as Nitric oxide, cytokines. These will-be reviewed in this chapter & the role of oxidative stress & antioxidants!

Characterization of biomolecules

The confluence of several powerful methods - chemical analysis, electron microscopy, x-ray crystallography, electron spin resonance spectroscopy and nuclear magnetic resonance spectroscopy - have enabled determination of the precise 3 dimensional structure of the DNA double helix, the DNA sequences that determine the structure of mRNA and the structure of protein molecules. Some protein molecules are *structural proteins* (such as action and myosin responsible for muscle contraction, haemoglobin and myoglobin; collagen and elastin etc. and transport proteins). Other protein molecules are *enzymes* which

catalyze biochemical conversions of one molecule into another and synthesis of complex lipids, carbohydrates and other macromolecules. Still other proteins are *regulatory proteins* which dictate *how much* of each structural protein or enzyme is to be made by *which cell* and *when & for how long*. Mutations in genes exert their effects by altering the structure (and therefore function) of enzymes, structural proteins or regulatory proteins. Both normal & abnormal cell proliferation is under control of polypeptide growth factors and differentiation factors that serve as intercellular messengers - they act through endocrine, paracrine or autocrine mechanisms. Multiple parallel and criss-crossing intracellular signaling pathways are active in health and disease. Ultimately these activation or inhibition pathways result in the transfer of a transcription factor from cytoplasm to nucleus that binds the promoter of a specific gene. Although the cell is continuously bombarded with hundreds of stimulating or inhibiting molecules during the phases of embryogenesis to differentiation and maturation, the cell obviously chooses ones that keep us healthy or make us sick. A sick cell under the inflammatory stress tends to avoid proliferation. However, smooth muscle cells proliferate in atherosclerosis or after angioplasty, even under those conflicting stimuli from multiple growth factors, Cytokines and their inhibitors present in plasma proteins.

Nitric oxide

Nitric oxide (NO) is a simple heterodiatomic molecule with broad and diverse effects in human biology that have been recognised only recently. In 1980, Furchgott and Zawadzki reported that a product of the endothelial cell causes vasorelaxation, and this Endothelium Derived Relaxing Factor (EDRF) was eventually shown to be NO.

NO is synthesized by a family of enzymes known as nitric oxide synthases (NOSs).

Three distinct isoforms have been identified : Neuronal - n NOS (Nos 1 gene product) inducible NOS - iNOS (Nos 2 gene product) present in monocyte / macrophages, smooth muscle cells, microvascular endothelial cells, fibroblasts, cardiomyocytes, hepatocytes and megakaryocytes; and endothelial-eNOS (Nos 3 gene product). L-arginine, a non-essential aminoacid is the substrate for the production of NO. As a free radical, NO readily undergoes addition, substitution, redox and chain-terminating reactions, which serve as the molecular basis for its biological effects.

NO is implicated in a wide variety of physiological effects. The reaction of NO with the haem group of guanyl cyclase leads to activation of cyclic GMP (cGMP) which causes vasorelaxation in blood vessels and smooth muscle cells of other organ systems; relaxation of gastrointestinal smooth muscle leads to reduced motility, relaxation of the spincter of Oddi and relaxation of lower

esophageal sphincter. Inhaled NO causes relaxation of bronchial smooth muscle, and endogenously produced NO may contribute to the maintenance of basal bronchial and basal pulmonary arterial tone as well.

Endothelium-derived NO maintains vascular integrity, prevents leucocyte adhesion and platelet adhesion and aggregation in the vasculature and inhibits vascular smooth muscle cell (SMC) migration and proliferation. Endothelial NO is an important determinant of cerebral blood flow, n NOS in neural and glial cells contributes to the regulation of cerebrovascular tone and to memory and learning through its involvement in long term potentiation in the central nervous system. NO is a likely transmitter of non-adrenergic and non-cholinergic (NANC) neurons and may thereby participate in the regulation of myocardial contractility, heart rate, gastrointestinal motility, bronchial tone and penile erection.

It is an interesting thought that NO fully conforms to the Ayurvedic concept of "*Vata*" or "*Vayu*", since indeed it is a gas (*vayu*) which constitutes non-adrenergic, non-cholinergic (NANC) neuronal pathway. Nitric oxide and Carbon monoxide (CO) are two gases which have a unique two-way traffic between the pre-synaptic and post-synaptic neurons, unlike other neurotransmitters which have a one way traffic. The production of NO by iNOS in macrophages, lymphocytes and neutrophil leucocytes is an important determinant of immune and inflammatory responses. The robust elaboration of NO contributes to the killing of bacteria, fungi, viruses and parasites & tumour cells. NO produced by iNOS is a weapon of non-specific immunity especially in the lung and liver. Similarly it is involved in apoptotic responses in a variety of cell types.

Pathological effects of Nitric Oxide

Both a deficiency and an excess of NO are believed to be involved in several pathophysiological states. NO is a critical determinant of basal vascular tone. Deficiency of NO or increased inactivation of NO lead to hypertension. Infusion of N-monomethyl Larginine a competitive inhibitor of NOS in healthy subjects can produce hypertension. In chronic renal failure the plasma concentration of dimethyl arginine, a naturally occurring derivative of L-arginine is increased and competitively inhibits NOS activity possibly contributes to the hypertension of chronic renal failure.

Common disorders that promote atherosclerosis, such as hypertension, diabetes, hyperlipidemia and smoking are all associated with abnormal endothelial function, one manifestation of which is a comparative deficiency of bioactive NO. This may be either a true deficiency (diminished formation from L-arginine) or excessive inactivation by reactive oxygen derived free radicals, as happens in heavy smokers and diabetics. In the latter, advanced glycosylation end products (AGEs) inactivate NO.

Normal daily diet contains 8 gm. L-arginine. It is possible to supplement this with additional 8 gm/day as a therapeutic measure. An alternative is to use nitroglycerine, isosorbide mononitrate and dinitrate as nitric oxide donors on a long term daily basis.

NO inhibits smooth muscle cell proliferation (which causes restenosis following balloon angioplasty or stent). Gene therapy with NOS-3 is a promising approach to prevent restenosis.

NO is important in penile erection which is mediated by cholinergic parasympathetic pathways and NANC pathway which releases NO. Endothelial cells also release NO, which induced vascular smooth muscle cell relaxation allowing enhanced blood flow and leading to erection. Sildenafil (viagra) enhances erectile function after sexual stimulation by inhibiting the enzyme phosphodiesterase type-5 (PED-5), the predominant PDE isoform found in the penis, thereby maintaining high levels of cGMP. Sildenafil has become available since 1998 and has markedly improved the management of erectile dysfunction including psychogenic, diabetic, vasculogenic, post-radical prostatectomy & spinal cord injury. Sildenafil is contra indicated in men receiving nitrate therapy for cardiovascular disease (including oral, sublingual, trans-nasal or topical routes) since these agents can together cause hypotension and may result in profound shock. Sildenafil has also been reported to improve female sexual function, (see also pages 426, 427).

Extracellular Matrix & Adhesion Molecules

An early response to tissue injury is inflammation. Tissue injury releases cytokines that induce the expression of adhesion factors in the vascular endothelium and induce the migration of leukocytes to the injury site. Adhesion factors are surface molecules that mediate cell-cell and cell-extracellular matrix interactions. The more important adhesion molecules for endothelial-leukocyte attachment are members of the immunoglobulin superfamily: the selectins (E, L, and P), ICAM-1, VCAM-1, and beta 2 and beta 1-integrins (LFA-1 and LA-4). These molecules mediate the extravasation of leukocytes inducing infiltration of the extracellular compartment and inflammation.

In addition to mediating inflammation, leukocyte adhesion plays a pivotal role in other host defense mechanisms, triggering T lymphocytes and natural killer cells to become cytotoxic, B cells to develop into antibody secreting plasma cells, and myeloid cells to exhibit chemotactic responses and to become phagocytic. The role of cell adhesion molecules is important in a variety of pathological conditions, including graft rejection, septic shock, atherosclerosis, reperfusion injury, late-phase hypersensitivity reactions and immunologically mediated lung and kidney disease. Also research on adhesion molecules has direct clinical applications in diagnostics and therapy.

Cytokines, growth factors & Hormones

Cytokines, growth factors and hormones mediate intercellular communication. The modulation of nuclear and cellular functions by cytokines, growth factors, and peptide / protein hormones is initiated through the activation of cell surface receptors that are linked to intra-cellular second messenger pathways.

Many growth factors bind to receptors that are linked through G-proteins to membrane bound phospholipase C(PLC). Activation of PLC cleaves phosphatidylinositol 4,5-bisphosphate (PIP₂) to form diacylglycerol (DAG) and D-myo-inositol-1,4,5-trisphosphate(IP₃). IP₃ regulates intracellular Ca²⁺ by stimulating its release from the endoplasmic reticulum (ER). Ca²⁺ can bind calmodulin and this complex in the presence of cyclic-AMP (cAMP) activates protein kinase C (PKC). Other hormone receptors are linked through G-proteins to adenylate cyclase. Activation of this enzyme increased the cellular content of cAMP and in the presence of the calmodulin-Ca²⁺ complex will activate PKA (protein Kinase A).

Some growth factors and cytokine receptors are protein tyrosine kinases (PTK) that are directly activated by receptor occupation. Activation of PKA, PKC or PTK catalyzes the phosphorylation of other proteins (primarily enzymes) within the cell. Enzymes activated (or inhibited) by phosphorylation may mediate functional processes within the cell while others may enter protein kinase cascades that regulate nuclear events. Steroid hormones, thyroid hormone, vitamin D₃, and retinoids are small lipophilic molecules that easily penetrate the cell and nuclear membranes and bind to intracellular receptors that are transcription factors. These ligand-receptor complexes bind to DNA and regulate gene expression.

Lipids in Cell Signaling

Many of the lipids involved as second messengers in cell signaling arise from arachidonic acid pathways. Arachidonic acid (5, 8, 11, 14-eicosatetraenoic acid) is a 20-carbon unsaturated fatty acid that is a normal constituent of membrane phospholipids. It is released from these phospholipids by the action of phospholipase A.

Alternatively, cleavage of the glycerophosphate bond of membrane phospholipids by phospholipase C, results in the formation of diglycerides from which arachidonic acid can be released by the action of diglyceride lipase.

The action of cyclooxygenases on arachidonic acid leads to the formation of prostaglandin G₂, from which the biologically active prostaglandin (PGD₂, PGE₂, PGF₂, PGH₂, prostacyclin (PGI₂), and the

thromboxanes (TxA₂ and TxB₂) are synthesized. Lipoxygenase (lipoxidase) acts on arachidonic acid to produce 5-hydroperoxyeicosatetraenoic acid (5-HPETE) that is converted to leukotriene A₄ (LTA₄). LTA₄ is the precursor of LTB₄, that induced inflammation by its chemotactic and degranulating actions on polymorphonuclear leucocytes, and of LTC₄, LTD₄, and LTE₄, the amino acid-containing leukotrienes that induce vasoconstriction and bronchoconstriction and are involved in asthma and anaphylaxis.

Free radicals: Oxidative stress

The most glaring example of understanding disease at the molecular level is the damage done by free radicals. Free radical induced damage is now implicated in over one hundred human diseases hence it is important to understand how free radicals are generated, what natural mechanisms in our body protect us from their ill-effects, and what measures can be adopted to strengthen the protection eg. Anti-oxidants.

Free radicals are atoms with an unpaired electron because of which they are highly reactive. The following free radicals are produced constantly in the cells of our body with very short half-lives (microseconds or milliseconds).

Water	$H + OH^{\bullet}$	Hydroxyl radicals
$O_2 + e^-$	$O_2O^{\bullet -}$	Super oxide
L-Argenine	NO^{\bullet}	Nitric oxide
$O_2O + NO^{\bullet}$	ONOO	Peroxy nitrite
$O_2 + \text{iron/ copper}$	OH^{\bullet}	Hydroxyl radicals

Those free radicals derived from water are called reactive oxygen species (ROS) and these derived from Nitric oxide are reactive nitrogen species (RNS). Free radicals have several important physiological functions including anti-microbial killing activity, regulation of cell proliferation and growth through apoptosis (programmed cell death) and regulation of vascular tone (through Nitric oxide). Free radicals are produced in the mitochondria of cell during biological oxidation (see page 154) and if not quenched rapidly, they damage the lipid membrane by a process called *lipid peroxidation*. Free radicals can also damage the mitochondrial DNA causing mutations.

The body has protective enzymic & non-enzymic mechanisms to quench the free radicals as soon as they are formed. These are superoxide dismutase, catalase and glutathione peroxidase, glutathione (GSH) and anti-oxidants vit-E (tocopherol and tochtrienols), vitamin C, carotinoids (vitamin A) and flavonoids. Imbalance between production of ROS and NOS & anti-oxidant defense results in oxidative stress.

Human plasma has many anti-oxidants - albumin, bilirubin, ceruloplasmin, transferrin, Haptoglobin and hemopexin, which protect the vascular endothelium from oxidative stress.

Lipid peroxidation can be measured by diene conjugates and thiobarbituric acid reactive substances (TBARS) assays of human tissues and body fluids. Diabetic patients have high oxidative stress so do smokers.

Antioxidants

An antioxidant is a substance that when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate. Simple methods are available for assessing the capacity of physiologically feasible scavenging of important biological oxidants (superoxide, hydrogen peroxide, hydroxyl radicals, hypochlorous acid, haem-associated ferryl species), both lipid-soluble and water-soluble.

In atherosclerosis, lipid peroxidation due to oxidative damage makes an important contribution to plaque development and the chain-breaking antioxidant *probuco* is useful to prevent this process.

Levels of anti-oxidant action

Anti-oxidants can act at different levels. These are broadly classified into 5 levels.

Level 1	Prevention of radical formation: mainly by enhancing the levels of SOD and catalase, or by sequestering transient metals like iron.
Level 2	Scavenging of primary radicals (OH^\bullet , O_2^\bullet , $^1\text{O}_2$) or by breaking of chain initiation.
Level 3	Scavenging of secondary radical (ROO, LOO) or breaking of chain propagation (Conventionally studied as inhibition of lipid peroxidation).
Level 4	Repair and reconstruction of lipid membrane aided by glutathione peroxidase or by increase in level of glutathione.
Level 5	Repair of DNA & other cellular constituents.

Ayurvedic Herbs as anti-oxidants

Ayurvedic herbal drug provide a rich source of antioxidants at different levels.

Level 1	Enhancing level of SOD and catalase.	
	Amalaki	(<i>Emblica officinalis</i>)
	Anantmool	(<i>Hemidesmus indicus</i>)
	Tulsi	(<i>Ocimum sanctum</i>)
	Katuka	(<i>Picrorrhiza kurroa</i>)
	Guduchi	(<i>Tinospora cordifolia</i>)
	Ashwagandha	(<i>Withania somnifera</i>)
	Ardrak	(<i>Zingiber officinales</i>)
Level 2	Kumari	(<i>Aloe vera</i>)
	Haridra	(<i>Curcuma longa</i>)
	Tulsi	(<i>Ocimum sanctum</i>)
Level 3	Garlic	(<i>Allium sativum</i>)
	Onion	(<i>Allium cepa</i>)
	Kumari	(<i>Aloe vera</i>)
	Shatavari	(<i>Asparagus racemosus</i>)
	Neem	(<i>Azadirachta indica</i>)
	Haridra	(<i>Curcuma longa</i>)
	Amalaki	(<i>Emblica officinale</i>)
	Yashtimadhu	(<i>Glycerrhiza glabra</i>) (<i>hemidesmus indica</i>)
	Mango	(<i>Mangifora indica</i>)
	Tulsi	(<i>Ocimum sanctum</i>)
	Katuka	(<i>Picrorrhiza kKurroa</i>)
Level 4	Garlic	(<i>Allium sativum</i>)
	Kumari	(<i>Aloe vera</i>)
	Green tea	(<i>Camelia sinensis</i>)
	Haridra	(<i>Curcuma longa</i>)
	Amalaki	(<i>Emblica officinalis</i>)
	Tulsi	(<i>Ocimum sanctum</i>)
	Guduchi	(<i>Tinspora cordifolia</i>)
	Ashwagandha	(<i>Withania somnifera</i>)
	Adrak	(<i>Zingiber officinale</i>)
Level 5	Tulsi	(<i>Ocimum Sanctum</i>)

It appears from the above list that Tulsi, Amlaki, Kumari, Haridra, Ardrak, Guduchi, Katuka Shatavari and Ashwagandha are versatile anti-oxidants and are part of the Ayurvedic Rasayan drugs. It is amazing how experiential wisdom has chosen the most appropriate antioxidants for routine use to maintain people in positive health by Rasayan drugs. Furthermore many anti-oxidants are part of the normal Indian vegetarian diet (haldi, garlic, onions, adrak (ginger), amlaki and beverages (green tea). In the Indian culture Tulsi has a symbolic role as "protector". Green vegetables and fruits (400 gm/day) give us adequate amounts of antioxidants in the form of Vit C, Vit E, Carotinoids, flavonoids. These can be grown in the backyards of the poorest of poor Indians villagers. The amount of water used for bathing by the family can sustain a kitchen garden of green vegetables and fruits like papaya & banana.

Precursors of glutathione such as substances containing SH groups are also anti-oxidants (such as captopril, an ACE inhibitor). N. acetylcysteine, a sulfur-containing amino acid has been tried as an antioxidant in HIV positive subject to prevent the death of CD4 + T cells which die of apoptosis, mediated by free radicals.

Probucol is a cholesterol-lowering and anti-oxidant drug shown to be useful in inhibiting the progression of atherosclerosis. It acts by removing oxidised LDL. Oxidative stress (as measured by 5-fold increase in TBARS) induced signaling in the vascular endothelium results in increased expression of cell adhesion molecules - ICAM-1, E-selectin and VCAM-1, and NF- κ B activation (Transcription factor). The addition of anti-oxidants like *probucol* prevents all these consequences of oxidative stress.

Dr. Nityanand has shown that *Guggulsterone*, the active principle of *Guggul* (*Commiphora mukul*) has similar properties like probucol in *reducing oxidised* LDL by 40%. This property is more crucial than the cholesterol lowering property of hypolipidemic drugs. Unfortunately this beneficial effect of Guggul has been overlooked by clinicians.

Synthetic peptide RGD (arginine - glycine - aspartic acid) prevents von-Willebrand factor mediated adhesion of cells to the endothelium.

Protein kinase C inhibitors also block expression of endothelial CAMs via NF κ B and activating protein 1 (*AP-1*), two redox-sensitive transcription factors playing a key role in inflammation. Tocopherol *inhibits* NF κ B and PKC activity. Alpha tocopherol (vit E) blocks DAG-PKC *pathway* by activating DAG kinase a key enzyme in metabolising DAG.

The nervous system has maximum oxidative stress and cumulative stress over decades contributes to the development of neurodegenerative disorders such as Parkinson's Disease and Alzheimer's disease. Antioxidant enzymes

such as SOD and chelators of transition metal ions may be more protective than chain-breaking antioxidants. In Alzheimer's disease, the amyloid neurotoxicity is mediated by reactive oxygen species.

Cytokines and chemokines

As the name suggest, cytokines are active substances produced by cell - small proteins 10 - 20 KDa in size. Over 70 separate proteins and glycoproteins have been identified in human with biological effects. Each Cytokine is encoded by a separate gene Cytokines are critical for both normal innate and adaptive immune response, and their expression may be perturbed in most immune, inflammatory and infectious states. Cytokines have several important functions:

1. Immunoregulatory Cytokines : IL-2, IL-4, IL-10, INF and TGF.
2. Pro-inflammatory Cytokines produced by activated monocytes and macrophages IL-1, IL-6, TNF and Chemokine family of inflammatory Cytokines including IL-8, macrophage chemotactic proteins MCP-1, MCP-2, MCP-3, MIPI & RANTE
3. Regulatory to growth & differentiation of immature leucocytes eg. IL-3, IL-7, GM-CSF. Cytokines influence gene activation by activating several Cytokine receptors, classified into 5 families.

Haemato poietic receptor family: include IL-2 through IL-9, G.CSF, GM. CSF and erythropoietin.

Tyrosine kinase family: include thrombopoietin PDGF, CSF.I, FLT-3 ligand, C-kit.

Chemokine receptors: 7 transmembrane G protein linked receptors that signal cell activation & migration IL-6 family involved in inflammatory states. Neutrophils, monocytes and lymphocytes are the main sources of inflammatory cytokines.

Cytokines can be stimulated by any kind of tissue injury - microbial infection, trauma, myocardial pulmonary or cerebral infarction, antigen-antibody complexes. IL-1, IL-6, TNF cause fever and weight loss in sepsis, AIDS, chronic inflammation congestive heart failure and cancer.

Interferons induce the expression of many genes - inhibit protein synthesis and exert a number of different effects on diverse cellular processes. Anti-tumour effects of IFN 2a and 2b have been exploited therapeutically similarly IL-2 has been used therapeutically by its ability to promote the growth and activity of T cells and natural killer (NK) cells which attack and destroy cancer cells.

Ayurvedic immunomodulatory drugs

Dr. S. S. Agrawal and V. K. Singh have extensively reviewed Ayurvedic medicinal plants for their immunomodulatory properties immunostimulants, immunosuppressants and immunoadjuvants. Upadhyaya has brought out two monographs viz. immunomodulation and immunopharmacology based on proceedings of national symposia on the subject. A list of plants identified to have these properties is given below. Prominent among them are Haldi, Neem, Shatawari, katuka and Guduchi.

Clinically proven immunomodulatory Ayurvedic drugs:

1. Ashwagandha (*withania somnifera*)
2. Aparajita (*Clitoria ternatea*)
3. Beheda (*Terminalia beticica*)
4. Daruharidra (*Berberis aristata*)
5. Guduchi (*Tinospora cordifolia*)
6. Haridra (turmeric) (*curcuma longa*)
7. Ishwarimula (*Aristolochia indica*)
8. Jatamansi (*Nardostachys jatamansi*)
9. Kalamegh (*Andrographis paniculata*)
10. Katuka (*Picrorrhiza kurroa*)
11. Kumari (Aloe Vera)
12. Lashuna (garlic) (*Alium sativum*)
13. Neem (*Azadirachta indica*)
14. Shatawari (*Asparagus racemosus*)
15. Shirish (*Albizzia lebbek*)

Molecular recognition

Ayurveda considers disease as disequilibrium at the molecular level, and restoration of that equilibrium as the objective of medicine. The tridosh (Kapha, Vata, Pitta) concept is essentially a concept of molecular biology.

Today, our understanding of health and disease has been profoundly extended by advances in molecular cell biology & recombinant DNA technology. We now appreciate that homeostasis is maintained among the 70 trillion cells in the human body through constant communication with each other through a diverse variety of *signaling molecules* (proteins, peptides, aminoacids, amines, nucleotides, steroids, retinoids, eicosanoids, and small molecules of diffusible and dissolved gases like carbon dioxide, carbon monoxide and nitric oxide).

All cells have receptors - on the cell membrane, in the cytosol or on the nuclear membrane - which recognize the signaling molecules. Binding of the

signaling molecule to the receptor triggers signal transduction to produce a specific response. This is achieved via information transfer by several specific groups of secondary and tertiary messengers. Each type of receptor elicits distinct responses in the target cell by activating genes. Molecular recognition is a fundamental feature of all biological processes encompassing ligand-receptor, enzyme-substrate and antigen-antibody reactions. A receptor is a protein to which a ligand or a drug binds to activate or suppress a signal. Thanks to recombinant DNA technology, most of the important signaling molecules, enzymes and their receptors have been cloned and are now available for research using radioactive ligands. It is now possible to image the distribution and function of the receptors in the living human body including the brain. The technology of whole body auto radiography and micro-imaging in small animals, and PET (positron emission tomography) and SPET (single photon emission tomography) in humans provides direct quantitative information about the distribution and function of receptors and the action of drugs at the receptors sites.

Table 1 lists the various receptors (for which radiolabelled ligands are available for study) along with their signal transduction mechanisms. Table II lists the various cell-membrane bound & cytosolic enzymes connected with signal transduction.

The mechanism of information transfer can be thought of as “bumping, fitting and sticking together” of macromolecules at *recognition sites*. An enormous amount of information transfer is possible because proteins such as enzymes contain between 125 to 5500 aminoacid sequences arranged in specific configurations that correspond to *specific recognition processes*.

There is little expenditure of energy in the recognition process because stereo specifically complementary macromolecules are held together by hydrogen bonding.

A series of intermediary molecular interactions pass the message to the inside of the cell. The ligand-receptor complexes catalyze the next chemical reaction along the pathway that eventually lead to the cellular response; which can be one of the following :

- A. Synthesis and secretion of substances via activation of gene to produce new mRNA (transcription) to make new protein (translation) at the ribosome.
- B. Synthesis of new DNA (replication) to make new cells.
- C. Repair damaged DNA by a variety of DNA repair enzymes.
- D. Apoptosis - programmed cell death, in the absence of signals for survival

DNA repair enzymes

Much recent knowledge has been acquired about DNA replication and repair mechanisms in the events of DNA damage. Environmental, Physical and Chemical agents can cause 4 types of DNA damage : single base alteration; two base alteration; chain break and cross-linkage. The cell has 4 mechanisms of DNA repairs - viz. mis-match repairs; base excision repair; nucleotide excision repair and double strand break repair. Their repair mechanisms exploit the redundancy of information inherent in the double helical DNA structure. The defective region in one strand can be returned to its original form by relying on the complimentary information stored in the unaffected strand.

Nature has provided a guardian gene-P53 as a transcriptional regulator of genes involved in the cell cycle. It acts as a G1 check point. If DNA damage has occurred, the activity of P53 gene transcription ensure two things:

1. The cell will not go into replication cycle, so as to allow time for repair of damage DNA.
2. If the DNA damage is not repaired, P53 activates a programme of apoptosis - cell death thereby eliminating any further possibility of replication.

Hence P53 is described as the guardian of the genome and as a “molecular policeman”. It is interesting to note that P53 mutation (making it non-functioning) is observed in most human cancers. The old concept of cancer resulting from a “single hit” is now given up as cancer is a *multi-hit* process in which several cancer preventing genes (eg. P53, Rb, APC, DCC) are knocked out and many cancer-stimulating genes (eg. bC12, kRas) are activated. Platelets, IL-2 TNF etc. CD20 mAb have been successfully used for treatment of non-hodgkins lymphoma.

Mechanism based screening

Molecular pharmacology provides a new interface between Ayurveda and modern medicine. Based on experiential wisdom, Charaka, Sushruta & Vagbhat described 700 herbal drugs with their properties and clinical effects. Based on clinical effects they described 50 categories of drugs such as appetisers, digestive stimulants, laxatives, anti-diarrhea, anti-emetic, anti-haemorrhoid, anti-inflammatory, anti-pruritic, anti-asthmatic, anti-epileptic, anti-helminthic, haemopoietic, haemostatic, analgesic, sedative, promoters of life, promoters of strength, complexion, voice, semen and sperm, breast milk secretion, fracture & wound healing, destroyers of kidney stones etc. (see page 387). Based on our current knowledge of molecular pharmacology we can attempt the characterization of Ayurvedic drugs at the molecular level. One example illustrates this approach. Reserpine acts by blocking pre-synaptic neuronal

vesicular reuptake and storage of monoamines - norepinephrine, dopamine & serotonin.

Today there is a world-wide search for biologically active molecules of plant origin. Many renowned multinational drug houses have launched very active programmes of mechanism based natural product-discovery research. In one such programme undertaken by Smith Kline Beecham, more than 61000 primary screening assays in 21 different mechanism based assay systems yielded less than 0.03% true leads. It is my belief that subjecting Ayurvedic herbal drugs to mechanism based screening will be far more rewarding because their choice has already been backed by experiential wisdom. The 40 single herbs described by Vagbhat should be studied with mechanism based screening for their anti-oxidant, antiinflammatory and immunomodulatory actions as well their ability to decrease advanced glycosylation end products (AGEs).

Considering the multifarious properties ascribed to each one of the popularly used Ayurvedic drug such as Ashwagandha, Guduchi, Katuka, Shatavari etc. it is most likely that their targets are shared by many cell systems and shared cell membrane components - eg. phospholipase A2, phospholipase C, adenylyl cyclase, cyclic nucleotide phosphodiesterases, eicosanoids, autonomic neuroreceptors, adenosine receptors, ion channels & cell adhesion molecules. Stress-activated Protein kinase (SAPK2) is an enzyme highly activated by bacterial lipopolysaccharides and cytokines. Blockage of this enzyme prevents downstream activation of pro-inflammatory cytokines. Many Ayurvedic Rasayan drugs could possibly act by blocking this enzyme - a testable hypothesis using mechanism based screening.

There is seemingly an infinite list of old and new molecules which interact with an ever-expanding array of cellular targets. As Charaka has said : "There is in the world no substance that may not be used as medicine in this or that manner, for this or that purpose". Chemistry is going to be the language of health and disease because the body is a vast network of interacting molecules. If the definition of disease is molecular, diagnosis becomes molecular and therapy also becomes molecular. Dysregulation of the intercellular and intracellular communication process by which molecular reactions are regulated, results in disease. For example an imbalance between the action of cell division stimulating molecules and cell division suppressing molecules leads to the uncontrolled and indefinite proliferation of cancer cells.

In today's era molecular medicine, disease is dissonance - due to excessive interaction, absent interaction or erroneous interaction between signaling molecules and their receptors. This concept is beautifully described by Ayurved in three words - *Atiyoga* - excessive interaction *Ayoga* - absent interaction *Mithyayoga* - erroneous interaction.

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CHEMOPREVENTION OF CANCER

Chemoprevention of cancer is a relatively new concept. It involves the use of specific natural or synthetic chemical agents to reverse, suppress or prevent carcinogenesis before the development of invasive malignancy.

Cancer develops through an accumulation of genetic changes that are potential points of intervention to prevent cancer. Like most human diseases, cancer arises through an interaction between genetics and environmental exposures. Initiating agents can be tobacco smoking, ultraviolet rays of sunlight, viruses, chemical pollutants etc. Promoting agents include hormones (androgens for prostate cancer, estrogens for breast & ovarian cancer). Antioxidants, anti proliferatives and anti-mutagenics can be used for this purpose. Many Ayurvedic herbal drugs with antioxidant and immuno-stimulant properties are ideal candidates for chemoprevention of cancer. This hypothesis should be tested by a planned randomised placebo-controlled clinical trial on a large population.

Vata, pitta, kapha and signal transduction

A look at the table on receptors and signal transduction will show that although the signaling molecules are diverse, the signal transduction mechanisms are limited viz.

1. Increase or decrease in cAMP or cGMP
2. Increase or decrease in IP3/DAG
3. Increase or decrease in Ca²⁺ and other ion channels.

Conceptually one can see a close similarity of this with the Ayurvedic concept of Vata-Vrudhi or Vata-shaman, Pitta-vrudhi or Pitta-shaman and Kapha Vrudhi or Kapha-shaman either individually or in combination (Vata-Pitta, Pitta-Kapha) etc.

Although there can be no one-to-one parallel between the 2 vocabularies the modern Vaidya may think of assimilating all the 20th Century knowledge of molecular biology to expand his old concepts which are also derived from molecular biology. This is what the spirit of Charaka, Sushruta and Vagbhat would expect of him.

Chemoprevention of infection

T L Lentz et al., reported in Science January 1982 that muscarinic acetyl choline receptors serve as receptors for rabies virus. In my letter to the Editor Science (8th October 1982 p. 110), T mentioned that Sushruta Samhita

recommended Dhatura as a prophylaxis for rabies to be given by mouth immediately after a dog bite in a dose sufficient to produce dilatation of pupils & delirium, which pass in a day or two when the next oral dose is given - several such doses should be repeated. The treatment should be started as early as possible once clinical symptoms manifest, the disease is fatal. The active principle of Dhatura blocks mACh R similar to atropine hence Dhatura for rabies represents the first documented example of "Chemoprophylaxis by receptor blockade".

This approach should be explored for Ayurvedic drugs for their ability to provide receptor blockade. Amantadine is the modern example for prevention of influenza by this approach. Asmanaan, derived from Kumari (Aloe Vera) is shown to block the entry of HIV in T cells by CXCR4 receptor blockade.

I suggest that *C. elegans* is a useful laboratory nematode model for in vivo testing of microbial virulence, pathogenesis and innate host immune defence mechanisms. Many human pathogens affect *C. elegans* - *Legionella pneumophila*, *Staphylococcus aureus*, *Streptococcus pneumoniae* & *Pyogenicus*, enterococci, *Salmonella typhimurium*, *Pseudomonas*, *Listeria monocytogenes*, *Cryptococcus neoformans* etc. and hence this is a useful model to study possible receptor blockade capability of Ayurvedic herbal drugs. (Ref 19).

Chemoprevention: future approach in Medicine

Based on the vast information provided by genomics, transcriptomics, proteomics, metabolomics and epigenetics, it has become possible to determine each individual's Prakriti on which Ayurveda lays great stress, and provide personalized medicine on which Ayurveda and Homeopathy lay great stress. Promotion of positive health and chemoprevention of infection (Tuberculosis, viral infections including HIV), malignancy, neurodegenerative disorders (Alzheimer's, Parkinson's Disease), metabolic syndrome (diabetes, hypertension, atherosclerosis) should be the major focus of future Ayurvedic drug research. By scientific validation of Ayurvedic herbal drugs, apart from health benefits, a large share of global drug market will flow to India. Current global herbal market of US \$ 70 billion is growing annually at 10-15%, Global nutraceutical market is US \$ 142 billion. India's share in this is very low. What we need is vision and imaginative thinking and swift action as outlined in my four ongoing DBT / DST supported Research Projects to validate 50 Ayurvedic herbal drugs and to capture India's share in this huge market (Ref. 20).

Far more valuable than money, for India and the world is the unique Ayurvedic emphasis on ethical conduct as a pre-requisite for health and longevity. "The wise man should control the impulses of fear, grief, anger, hatred, malice, jealousy, lust, greed and excessive attachment. These impulses are injurious to the body and to the mind."

I end up with the universal Ayurvedic prescription: "Anyone who takes proper diet and exercise regularly, who deliberates all his actions, who controls his sexual pleasures, who is just, generous, truthful and forgiving, and who can get along with his kin, is assured a long healthy and happy life".

Haritaki: *Terminalia chebula* (TCh), *Pippali*: Piper longum (PL), *Shatavari*: *Asparagus racemosus* (AR).

A dose of 100 mg/kg. was selected to be given orally as total aqueous extracts for one to two weeks. They showed that the aqueous extracts of Guduchi stimulated the phagocytic and bactericidal activity of neutrophils and macrophages. Pre-treatment with all six Rasayanas was effective in protecting the animals to a varying degree from infection. (Ref. 6).

At that time not much was known about the key role of NF κ B (Nuclear factor KB) as regulator of host inflammatory and immune response and cellular growth properties. (Fig. 2 and Fig 3).

It is noteworthy that the excellent review by SS Agarwal and VK Singh on Indian Medicinal Plants as Immunomodulators (1999) (Ref. 7) makes no mention of the NF κ B pathway. NF κ B increases the expression of specific cellular genes encoding at least 27 different cytokines and chemokines, receptors involved in immune recognition such as members of the MHC proteins involved in antigen presentation, and receptors required for neutrophil adhesion and migration. Cytokines stimulated by NF- κ B such as IL-1 β and TNF α also directly activate the NF κ B pathways thus establishing a positive autoregulatory loop that can amplify the inflammatory response and increase the duration of chronic inflammation (Ref. 8).

NF κ B also stimulates the expression of enzymes whose products contribute to the pathogenesis of the inflammatory process (eg. iNOS which generates NO and COX-2 which generates prostanoids).

NF κ B controls immune response by modulation of B lymphocyte survival, mitogen dependent cell proliferation and isotype switching which lead to the differentiation of B lymphocytes, IL-2 production which increases proliferation and differentiation of T lymphocytes.

I κ B protein normally binds to NF κ B thereby blocking its nuclear translocation. LPS, phorbol esters, viral infections, ultraviolet radiation and free radicals all lead to degradation of I κ B and thereby' release and nuclear translocation of NF κ B. There is a site and event specificity of NF κ B proteins. Tissue distribution differs for various I κ Bs. I κ B α is associated with transient NF κ B activation while I κ B β is associated with sustained NF κ B activation. Most interestingly NF κ B activation is also the key pathway for carcinogenesis.

(Ref. 9), as indicated by increased NF- κ B levels in the nuclei of several types of cancer- leukemia, lymphoma, solid tumours- breast ovary, prostate & colon cancer. There may be mutations inactivating I κ B protein that activate NF- κ B pathway. Inhibition of NF- κ B pathway may enhance the efficacy of cancer chemotherapy.

The pioneering work of Dahanukar and Thatte has shown that Ayurvedic Rasayans have the capacity of regulating chronic or dysregulated NF- κ B pathway.

"Ahar"-Nutrition and Nutrigenomics

Ayurveda lays great emphasis on "Ahar". nutrition. It describes "Satwik Ahar" which enabled Rishis and Munis to live for hundred years. In today's parlance Satwik. Ahar 400 g fruits and vegetables (Kanda, moola and phala) is a low caloric diet (1300 K. cal) which produces the least oxidative stress. It provides Essential micronutrients and minerals; high fibre and potassium, low fat and sodium, and osmotin (vegetable analogue of mammalian adiponectin).

Ayurveda lays great emphasis on breast milk which has ideal W6-W3 ratio and essential fatty acids EPA/DHA.

Cow's ghee (12 gm) provides 1.2 g EPA/DHA the essential daily requirement. It would be interesting to study, the various Ayurvedic "Ghruta" based medications for their EPA/DHA content comparing "fresh" ghee with "old" ghee recommended by Ayurveda.

Nutrition and immune response

Calder (2000) has given an excellent review of inflammation in health and disease. (Ref. 10). He has emphasized the important role of dietary omega-3 polyunsaturated fatty acids eicosapentaenoic acid (PUFA-EPA) and docosahexaenoic acid (DHA) in the suppression of pro-inflammatory cytokines, and the need and scope for dietary modification of inflammation. Increased EPA/ DHA in cell membrane phospholipids reduced production of prostanoid (PGI₂, TXA₂, PGD₂, PGE₂, PGF_{2a}) while increasing the production of prostacyclin and TXA₃, which inhibit platelet aggregation and inflammation. (Fig. 4).

Adequate amounts of EPA/ DHA in the cell membrane ensure the LOX-mediated production of lipoxins, resolvins (potent anti-inflammatory and immunoregulatory metabolites) and protectins (including neuroprotectins). At nanomolar and picomolar concentrations, they remove inflammatory cells and restore tissue integrity during resolution of inflammation.

CHEMOPREVENTION OF CANCER

Zinc, selenium, vitamins A, B6, B12, C, E, and folic acid are important nutrients whose deficiency affects host immune response and thus susceptibility to infection. The important role of vitamin D has only recently been appreciated. Macrophages have receptors for vitamin D, and vitamin D deficiency and vitamin D receptor polymorphism increase susceptibility to tuberculosis. (Ref. 11) There is a two-way interaction between nutrients and human genes. (Ref. 12) How genetic variations influence response to nutrients, and how nutrients influence gene expression, transcription and metabolism are the subject of Nutrigenomics. The effect of maternal malnutrition on fetal insulin-IRS-PI3K AKT pathway is well known to be a basis for insulin resistance and metabolic syndrome.

Chemoprevention of infection Cancer Chemoprevention by dietary phytochemicals

Carcinogenesis is a multi-step process the initiation of which can be blocked or suppressed by dietary phytochemicals. They can also halt or retard the progression of pre-cancerous cells into malignant cells. Central components of the intracellular signaling network that maintains homeostasis are MAPK, NF- κ B, API, NRF1 as well as β 3 catenin, a component of cell to cell adhesion machinery. Extensive work has been done to elucidate the molecular mechanisms of chemoprevention by Haldi, red chilli pepper, ginger, green tea, honey, garlic, cabbage, broccoli, carrots, tomatoes, grapes, grape seeds and pine bark. These are summarised in Table 3. (Surh YJ Ref. 13)

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RADIOLABELING OF HERBAL DRUGS

On 25th May 2009 in my Homi Bhabha Birthday Centennial lecture at BARC in Mumbai, I pleaded the urgent need for application of radiotracer technology for the validation of Ayurvedic Herbal drugs. Every new molecule introduced in modern therapeutics is first labelled with C-14 to study its absorption, bio distribution & excretion in small animals. The only tritium labelling effort of a Chinese herbal drug Gensing was published in French in 1992. Haffkine Institute's new project with financial support from DST and DBT has been launched in collaboration with BRIT (Board of Research In Isotope Technology¹). Tritium-labeling of Arum Sal an important Ayurvedic drug has been successfully accomplished as well as tritium-labeling of its active principle baicalein and it has been confirmed that labelling the whole extract also labels the active principle. Its bio-distribution in small animals is being studied by whole body auto radiography especially the brain and heart, since Baicalein inhibits fibrillation of a synuclein and disaggregates existing fibrils in neurons hence may prevent Parkinson's Disease. (Ref 14) Baicalein inhibits the binding of a number of chemokines to human leucocytes (CXC, CC (MIP-1 α , MCP-1) reducing their migration capacity⁷. This has great relevance to prevention of atherosclerosis which begins as endothelial inflammation. (Ref. 15)

Labeling Tulsi leaves with C-14 has also been achieved. Feeding C-14 urea as a manure in plants will be used as a novel approach for radiolabeling of various parts of the plant bark, leaves, flowers etc. and the C-14 radio-labeled plant parts will be fed to small animals and whole body⁷ autoradiography⁷ will be performed to study the bio-distribution of the herbal drugs. To begin with, forty single drugs described by Vagbhata will be taken for study. Details about auto radiography will be found in ref. 2.

Bioavailability of Ayurvedic herbal drug

Bioavailability of Ayurvedic herbal drugs is a totally neglected subject. Devasagayam's group at BARC used the inverted loop of rat intestine to study the intestinal absorption of Terminalia arjuna extracts as well as the active principle Baicalein. Almost 15% of the baicalein (4 mg/' ml) was recovered from the serosal surface as monitored by HPLC. Both aqueous and methanolic extracts of T. Arjuna were absorbed. (Ref. 16) Haffkine Institute is establishing this facility where 40 single herbs described by Vagbhat will be studied for absorption : (duodenum, jejunum, ileum, colon). This "blind spot" in herbal drug research is frustrating for clinicians who wish to translate the laboratory in vitro data to clinical application. The poor bioavailability⁷ of oral curcumin and resveratrol are important illustrative examples.

Medhya Rasayanas

Ayurveda has described 10 herbal drugs as Medhya Rasayanas - Amalaki, Ashwagandha, Bramhi, Bhrughraj, Jatamansi, Jyotishmati, Mandukpami, Shankhapushpi, Vacha, Yashtimadhu.

A transgenic mouse model of Alzheimer's disease has now become commercially available. At birth these animals are absolutely normal. Within three months they develop all the changes - amyloid plaque deposition amyloid angiopathy, Tau protein, loss of acetyl choline neurons, hypometabolism and hypoperfusion in parieto-occipital regions etc, and the animals die within the next 6 months.

All these changes can be non-invasively shown by small animal PET/CT and optical imaging without sacrificing the animals. This facility is now available at ACTREC, new Mumbai where a collaborative research project of Haffkine Institute is approved for studying the effect of the 10 medhya rasayanas - single and in combinations in 40 mice: first 3 months to assess the preventive potential and next 6 months to assess curative potential. At present there is no effective treatment for Alzheimer's disease yet \$ 15 billion are spent annually on its treatment. If this study provides validation of Medhya Rasayanas for prevention of Alzheimer's disease, a world market of \$ 15 billion will be available to India. Details of small animal PET and optical imaging will be found in Ref. 2.

High through-put screening for mechanism of action:

In my Haffkine Oration 2009, "Beyond Reverse Pharmacology-mechanism-based screening of Ayurvedic Herbal Drugs", (Ref. 17) I have proposed radioligand displacement assay (Table 1) for mechanism based screening of Ayurvedic drugs.

As an illustrative example Sukh Dev (1992) in collaboration with a group in USA studied Triphala. (Ref. 15). Using 1-125 c-holecystokin (CCK) as ligand and mouse pancreatic membrane as receptor they showed affinity of three Ayurvedic herbal extracts - *Termenalia Chebua* (96% ligand displacement) *Termenalia bellerica* (91%) and *emblica officinalis* (76%) showing that "Triphala" constituents act on CCK receptors. CCK has receptors in GI tract and nervous system, both peripheral and central, and plays a major role in gut function, digestive processes, in feeding behaviour and cognitive function. It is surprising that in the last two decades no further efforts were made in this direction. Haffkine Institute has launched a DBT - supported project of mechanisms-based screening of the 40 single drugs described by Vagbhata.

RADIOLABELING OF HERBAL DRUGS

Charaka States: "A single drug may have many appellations owing to its diverse actions just as a man is able to perform various actions". Many popular Ayurvedic drugs such as Ashwagandha, Bramhi, Guduchi, Katuka, Shatavari etc. have multifarious properties ascribed to them. Obviously, their molecular targets are shared by many cells! systems and cell membrane components such as phospholipase A2, phospholipase C, adenylyl Cyclase and cAMP, adenosine Mechanistic based screening of herbal extracts against known receptors (receptor panning).

1. List of receptors and transporters for which specific radiolabeled ligands are available for drug screening

Non Peptide	Peptide
Acetyl choline receptors	Angiotensin - AT1AT2
Muscarinic - M1, M2, M3, M4, M5	Bombesin - 8B1 B82, 883
Nicotinic four types	Bradykinin - 81, 82
Adenosine - A1, A2,A, A2B, A3	Calcitonin-gene related peptide receptor
Adrenoceptors - α 1A, α 1B, α 1, α 2A, α 2B, α 2X, α 2, β 1, β 2, β 3	CGRP1, 2, amylin, adrenomedullin
Biogenic amine transporters	Chemokine CXCR 1, 2, 3, 4 CCR4, 5, 6, 7, 8, 9, 10, 11 XCRI, CX3CRI,
NET, DAT, SERT	DARC ECRF3, US28, KSHV
Cannabinoid - CB1, CB2	Cholecystokinin/gastrin
Dopamine - D1, D2, D3, D4, D5	CCKA, CCKB
GABA receptors - A, B, C	Corticotropin releasing factor
GABA transporters - GAT-1, 2, 3, BGT, VGAT	CRF1, CRF2 α , 2 β , 2 γ , CRF-BP
Excitatory amino acid transporters	Cytokine Hematoprotein family
EAAT1, T2, T3, T4, T5	Il-2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 12, 15, 16,
Glutamate	17, 19, 21, 22
G protein family: eight types	Tumor necrosis family 9 ILIR/TIR
Ion channel family: three types	IL1R1, IliRII, IL-18 TNF receptor family
Glycinic receptor - GlyT1, GlyT2	TNFRSF 1, 2, 3, 4, 5, 6, 7, 8, 9, 10A, B, C,D,11
Histamine - H1, H2, H3, H4	Endothelin -ETA ETB
Imidazoline binding sites	Galanin - R1 R2 R3
1, 2, 3	Melanocortin - MCR1, 2, 3, 4, 5, 6
Leukotriene - BLT1, BLT2, CysLT, CysLT2	Neuropeptidase
Lysophospholipid - P1, P2, P3, P4, P5	Neuropeptide - Y1Y2Y4Y5Y6

RADIOLABELING OF HERBAL DRUGS

Melanin concentrating hormone	Neurotensin - NT1 NT2
MCH1, MCH2	Neurotrophin - TrK A, B, C, p75
Melatonin - MT1, MT2, MT3 Platelet activating factor receptor	Opioid receptors - δ (OP1) κ (OP2) μ (OP3), OP4 Orexin receptors - OX1OX2
Prostanoid - EP1, EP2, EP3, EP4	Proteinase-activated - PAR1, 2, 3
P2 P2X subtype (ion channel family)7	Somatostatin - SST 1, 2, 3, 4,5
P2Y subtype (G protein family) 7	Tachykinin - NK1, NK2, NK3
Serotonin	VIP - VPACu, 2, PAC1
5HT1A 5HT1B, 5HT1D SHT1f 5HT2, 5HT1D 5HT2c	Vasopressin and oxytocin
5HT3 5HT4 5HT5 5HT 5HT6 5HT7	receptor - V1a, V1b, V2, OT
Ion channels:	VEGF - 1, 2, 3
Calcium channels	
Chloride channels	
Potassium channels	
Sodium channels	
Sigma receptor	
Vanillo1d receptors	

2. Introduction

Traditionally, certain herbs have been known to have medicinal properties. More than 5000 herbs has been reported in India Aurvedic medicine against different diseases for therapeutic use. Unfortunately molecular mechanism of action of herbs in context to disease has not been well investigated. This is the major gap in the current knowledge of mechanism of action (MOA) of medicinal herbs.

Under this project, we will screen herbal extracts against known receptors. This will help us to develop the scientific mechanism and delineating receptor specific downstream potential metabolic pathways involved in therapeutic herbal extracts. This will help us in further replication of medicines with similar properties and functions. Using technology, Ayurvedic herbs can prove to be a huge boon for the field of medicines if enough research is done (Lele 2010).

Charaka states: "A single drug may have many applications owing to its diverse actions just as a man is able to perform various actions". Many popular Ayurvedic drugs such as Ashwagandha, Bramhi, Guduchi, Katuka, Shatavari, etc. have multifarious properties ascribed to them. Obviously, their molecular targets are shared by many cell systems and cell membrane components such as phospholipase A2, phospholipase C, adenylyl cyclase and cAMP adenosine receptors, eicosanoids, ion channels and neuroreceptors

dopamine, serotonin, norepinephrine (NE), gamma-aminobutyric acid (GABA), etc. Stress-activated protein kinase (SAPK2) is an enzyme highly activated by bacterial lipopolysaccharides and cytokines. Many Ayurvedic Rasayan drugs act by blocking this enzyme and prevent downstream activation of NF-kB. Interestingly, NF-kB pathway activation is common to both inflammation and cancer.

Reference work

As an illustrative example, Sukh Dev (1992), in collaboration with a group in USA, studied Triphala using I-125 cholecystokinin (CCK) as ligand and mouse pancreatic membrane as receptor. They showed affinity of three Ayurvedic herbal extracts - *Terminalia chebula* (96% ligand displacement), *Terminalia bellerica* (91%) and *Phyllanthus emblica* (76%), showing that "Triphala" constituents act on CCK receptors. It is surprising that in the last two decades, no further efforts were made in this direction.

Dahanukar and Thatte made pioneering contribution by showing immunomodulatory action of *Amlaki*, *Ashwagandha*, *Guduchi*, *Haritaki*, *Pipalli* and *Shatavari*, all of which are now shown to suppress NF-kB activation, and regulate chronic dysregulated NF-kB pathway. Curcumin and ginger have been studied extensively to elucidate their action at the molecular level.

2. Novelty:

- Screening of herbal extracts against the panel of known cellular receptors will help to understand which receptor/s has strong binding kinetics (rate of association and rate of dissociation).
- It will help to predict and understand the potential metabolic pathways expressed in context to particular herb extract.
- Active therapeutic ingredients against receptor in herbal extracts can be identified by LC-MS/MS technique.

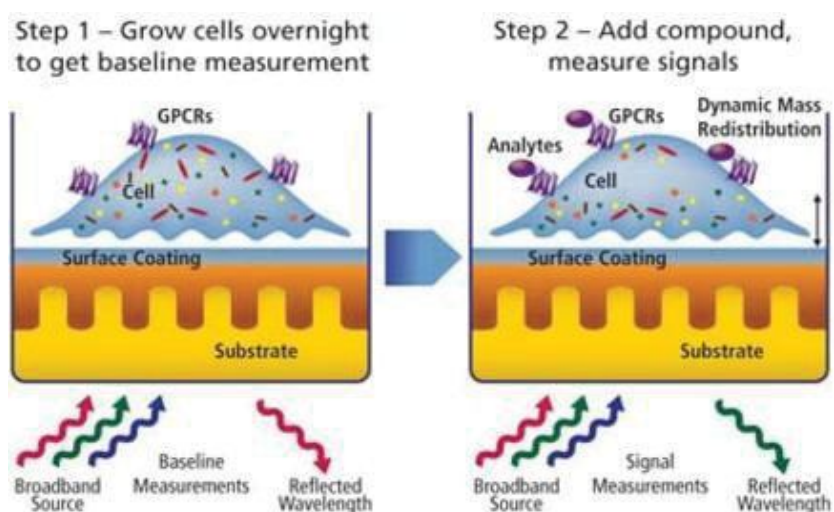
3. Applicability:

- Possibility of new molecules will be identified against receptors which can be further utilized for drug development.
- Based on knowledge of molecular mechanism, combination of herbal extracts can be considered against the certain diseases.
- Mechanism of actions for particular herbal extract through specific receptor/s and molecule inducing activity through specific receptor will be patented.

4. Description of the project:

Methodology

Receptor specific division arrested frozen cell lines will be procured from the company (Helix Bioservice Pvt. Ltd). These cells will be incubated in 96 well plate and herbal extract will be screen in triplicates against these receptors using ENSPIRE Label free multimode plate reader platform (Perkin Elmer). The EnSpire label-free platform includes optional patented Alpha technology, ultra-sensitive luminescence, fluorescence intensity and absorbance detection. Assay will be label free assay. Herbal extracts will be procured in 3 forms (Phenolic, Water and Oil) and there will be 3 dilutions per extract to study dose-dependent response.



Epic® technology (Perkin Elmer) measures changes in light refraction resulting from dynamic mass redistribution (DMR) within the cell. This occurs in response to receptor activation or deactivation in a zone within the cell's monolayer. The change is indicated by a change in wavelength. Binding parameters (K_D , K_A , k_d and k_a) will be recorded and compared using positive control.

Feasibility This study will be conducted in Haffkin Research Institute, Parel, Mumbai. **Outcome** Molecular mechanism of herbs will be identified (Ref. above mention 3 and 4)

6. Future plans:

Based on results of initial receptor panning, strong affinity receptors will be short-listed per herb and it will be validated further. Active product ingredient from

herbal extracts will be isolated by sub-fractionation on HPLC. Collected fractions will be tested against receptor/s identified from phase 1 to see whether it showing the same activity. Metabolite will be characterised in detail using LC coupled NMR technology from fractionated sample. Further purified metabolite will be revalidated against identified receptor/s using ligand-receptor interaction assay. In this way, we can narrow down our approach to drug discovery which has immense potential of Intellectual Property generation. This whole research will give solid platform for Modern Ayurveda Medicine.

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THOUGHTS ON MEDICAL ETHICS (The Traditional Indian Outlook)

1. Preamble

Medicine is undoubtedly an ancient calling. It has developed with the human race throughout its career on this planet. Its origins may perhaps be found in the shamanistic cults of all countries; the medicine-man filled an important role in tribal society, his business was not only to relieve the member of the tribe of his distress but to secure the well-being of the tribe as a whole. He was a healer, family counsellor and the tribal priest, all at the same time. Such is the background of the medical profession.

That this was the proper context for the practitioner of the art of healing has been suggested by Sir William Osler when he said that "the physician must be friend, philosopher, well-wisher and guide of the patient and the family under his care". The physician is a member of the society before he becomes the member of his profession; and his obligations include willingness to 'consecrate his life to the service of humanity', and to refrain from 'using his medical knowledge and skill contrary to the laws of humanity'. (The World Medical Assembly at Geneva, 1948). He is expected further to 'practice with conscience and dignity' and to 'maintain the honour and noble tradition of his profession'.

Medicine in comparatively recent times has sought to formulate its own code of conduct spelling out the physician's duties to the patient and his obligations to the society. The Hippocratic oath (around 450 B.C.) was probably the earliest attempt in the Western World to institute a normative code of conduct for the practising physicians. Its acceptance, albeit in broad principles and not in actual practice, was around the fourth century A.D. The medical world thought it fit to formulate the code of conduct afresh in 1948 (The WMA, Geneva Declaration), and this was amended several times (Helsinki 1964, Tokyo 1975, Venice 1983 and so on).

However, the Hippocratic oath had a quaint, almost spiritual, flavour of its own, despite the impracticability of many of its provisions, and thus continues to be relevant by and large, at any rate as an ideal to be known and cherished. For instance, the injunctions to "maintain absolutely confidentiality of all personal information, and to refrain from using the doctor-patient relationship of sexual advantage", to "apply dietetic measures for the benefit for the sick according to my ability and judgement", and to keep them (the patients) from harm and injustice" are valid for all time. Similarly, the provisions of the oath: "In purity and holiness, I will guard my life and my art"; "I will neither give a deadly drug to anybody if asked for it, nor will I make a suggestion to this effect"; "If I fulfil this oath and

do not violate it, may it be granted to me to enjoy life and art, being honoured with fame among all men for all time to come; If I transgress it and swear falsely, may the opposite of all this be my lot" are of enduring importance.

Ethics is a normative discipline, designed to secure orderliness in the lives of people and effectively in collective action. It seeks to restrain the usual sources of degradation, viz greed, cruelty, selfishness, impetuosity and perversions of all types. The individual as a member of a society and his rights, duties, commitments, obligations, judgments and actions come within the purview of ethics. There are naturally ethical implications which are specific to the medical profession; moral principles which constitute the essential part of the healing art. This was deemed necessary because the knowledge and skill of the doctor may possibly be abused owing to conflicting loyalties and distorted sense of values.

There were constitutional provisions, statutory restrictions, safeguards relevant to the medical professional, included in the laws of the land. And there were also medical guilds and councils which enunciated the professional code of conduct to maintain the dignity of the professional and to promote the usefulness of the profession. Professional misconduct was indicted by the latter, while it was brought under disciplinary proceedings by the former. However, the concept of medical ethics is different from both these compulsions. Ethical behaviour is a matter of conscience and personal judgment. It pertains to the character of the doctor, and to his appreciation of the dignity of the profession. Legal restrictions and restraints imposed by the medical councils are strictly not valid here.

2. The Present Context

Like all human endeavour, medical practice also has undergone enormous changes over the years. Science and technology have brought about revolutionary improvements in diagnosis and treatment. Science is basically concerned with understanding the phenomena of nature, while technology is interested in exploiting the resources of nature for satisfying man's needs (like those for food, shelter and protection). Normally, science and technology are expected to co-operate in the welfare of mankind, but it often happens that the co-ordination is absent or meagre. Medical research and drug-manufacture, for instance, do not always go hand in hand. Drug industry all too often loses the perspective of healing the sick; hospitals and nursing homes with high technology tend to become business houses.

The doctor today is a scientist, technologist and healer at the same time. His training is a long-drawn one, and comprehends a large number of specialized disciplines. It prepares him to become a general practitioner, specialist or consultant, specifying his area of contact with the patients and

their ailments. Medical science aims to provide an education which would facilitate the aspiring doctor to know the patient as a person, and to best judge the kind of service the patient really needs, and also to provide this service himself. However, medical technology which is at cross purposes forces him to an increasing employment of tailor-made drugs like sulphonamides, antibiotics, oral contraceptives, tranquillizers, and anti-cancer agents, which are all effective and for the same reason dangerous.

This attaches a greater responsibility on the doctor, which responsibility he is not trained to undertake. His wisdom, knowledge, discretion, judgment and integrity are involved in his practice. Especially is he bogged down by the technological pressures and constraints which are enormous and many-sided. It is here that ethics becomes a more important issue than ever. Man is born to be healthy; the laws of nature tend to make him healthy. But diseases do occur, and they are to be removed. But health as seen by the present-day science is not a mere absence of disease; it is a natural feeling of well-being, contentment, peace within and harmony. It is a total co-ordination of the physical, mental, social and spiritual aspects.

The growth of specialists and consultants, which removes the doctor from the general run of patients and increases intra-discipline interaction, is another dimension in the medical field today which has created problems. This has been caused by technology more than by science. There is now an entirely new approach to the 'business' of handling disease, owing to the explosive growth of medical technology; it splits medicine into an ever-enlarging number of specialities, amidst which interaction appears to be rather minimal.

Added to this is the ever-increasing number of people who aspire to take to this profession. They come from different backgrounds, have varying equipments, and cherish widely different values of life. They shape into a variegated group of assorted doctors, whose education and training do not emphasize, if they include at all, the obligations, responsibilities and commitments natural to the medical profession.

How hollow would the words sound when we read the declaration of the tenth World Medical Assembly in Havana during 1956: "The primary obligation of the physician is his professional duty; in performing his professional duty, the physician's supreme guide is his conscience". Does the medical education imparted today touch the mysterious 'conscience' in any palpable way?

The talk of medical ethics should revolve round this 'conscience', which is increasingly becoming the 'grin of the Cheshire cat'.

Unfortunately for the medical technology, there are now several hurdles which the 'conscience' of the medical practitioner should cross or circumvent, to maintain the so called professional dignity: what his judgment would be in cases like euthanasia, iatrogenic diseases, medico legal responsibilities, pregnancy tests, artificial insemination, organ transplantation, in vitro-sterilization, embryo-transfer technology, genetic engineering, use of cadaver or dying patients for their organ, and even blood transfusion (which is objected by many religious groups including the Jehova's Witnesses). These are issues which are vitally ethical in character and import.

The problems of the medical practitioner are compounded by the expectations of the patients from the doctors, from the ancillary staff and from the hospitals; the growing need for outdoor examination, admission to the ward, rehabilitation and so on: The modern patient demands an insight into his illness, and talks of medical negligence and dereliction of duty. He expects good hospital care with special arrangements for specific illnesses and for emergency treatment. High technology is like the Aladin's Lamp, which raises an ugly monster the moment it is rubbed.

These are some of the problems which pertain to the medical profession now and which involve ethical consideration in addition to the medical. We have moved far away from the Hippocratic context. The ethics germane to the medical profession cannot be simple or uniform. Nor is the ethics simply a matter between the doctor and the patient; the society (with all its economic and political dimensions) is involved in a much bigger way. The doctor's integrity is related now to the drugs, drug manufacturers, medical representatives, law, the patient's family, organized Medicare services (like nursing homes, high-tech hospitals, blood-banks and kidney centres) and the doctor's own standards of living.

What Dr. H. Mahler of WHO said about the ethics of prolonging life applies to several other issues in the field: "The terminally ill need peace, comfort and dignity, but advanced technology often deprives them of these things, in the misdirected effort to prolong the obfuscation of the borderline between life and death". He called our attention to the "sophisticated medical and surgical technology being easily abused". This is a reflection which underlines the need for a fresh reappraisal of medical ethics, independent of the technological advance in the field of medicine.

3. The Enduring Values

In the welter of all this confounding issues, certain basic considerations still become relevant. These were also touched by Hippocrates (assuming that he really existed and that he was the one who gave the Oath bearing his name) more than two thousand years ago, as well as by the ancient

Indian medical writers like Charaka, Sushruta and Vagbhata. The Indian texts prescribe elaborately how a physician must train himself to be an effective healer, and how he must conduct himself in society and with the patient.

It is high time we realized that ethics is an important part of the healing art. Medical ethics must focus attention on the proper and also effective therapeutic relation between the doctor and the patient founded on several factors like mutual consent, rapport, co-operation and reciprocity of responsibility.

Ethical values need to be emphasized because they are likely to be easily sidelined and quickly ignored in the present state of the Medicare systems where technology, industry, business and vested interests have a large say.

The traditional Indian approach to the problem is indeed a simple one. But it deals with the core of the problem. That the approach does not envisage the technological advance of more recent times or the population explosion, does not take away from the merit of the approach, which concerns itself with the essential values of the healing art. Disease is largely regarded as due to our errors of judgment (prajnaparadha) and it is sought to be remedied by self-discipline (like personal hygiene, dietary restrictions, periodical fasts, exercise and rules of conduct, dinacharya and ritucharya), home remedies (for preventive as well as curative purposes) and herbal medicines.

Health is not merely the absence of disease. It is a positive concept. In the words of Charaka, the earliest Indian medical writer who lived centuries before the Christian era, sickness prevents a person from pursuing his values of life, the purusharthas' : satisfying the normal desires and having the usual pleasures of life (Kama), acquiring wealth and securing financial comfort (artha), leading a life of virtue and social usefulness (dharma). The group of three values (known as trivarga) characterizes normal human life. The person who is sick is unable to lead a normal life, pursuing this triad, and to this extent he threatens the society in which he lives and of which he is a part.

There is a statement in *Skanda-Purana* to the effect that inasmuch the values of life are fulfilled only by a healthy person, the physician who restores the health of the person will indeed gift him with the values of life:

धर्मार्थकाममोक्षणामारोग्यं साधनं यतः ।
तस्मादारोग्यदानेन तद्वत् स्याच्चतुष्टयम् ॥

The physician as a professional aims at bringing back the errant individual into the mainstream of social life. Herein lies his sense of obligation to society. The professional with his sense of duty and responsibility naturally evolves

an ethics which comprehends his privileges and commitments. The context of this ethics is the suffering individual (viz. the patient, atura) as well as the social group in which the physicians and the patient coexist. The patient includes the family to which he belongs, and the social group includes the economic and social factors which contribute to the well-being of the group. Four are the gifts praised in society: providing defence for the weak and helpless, feeding the hungry, teaching those who want to learn, and treating the sick; and the best among them is the providing of health to the sick.

भीतेभ्यश्चाभयं देयं व्याधितेभ्यस्तथौषधम् ।
 देया विद्यार्थिने विद्या देयमन्नं क्षुधातुरे ॥
 न हि जीवितदानाद्धि दानमन्यद्विशिष्यते ।

The Smṛti texts, which define the dimensions and prescribe the norms of the social organization in the country, are found to regard the physician in an exceptional light: the usual disabilities and restrictions of caste, status and so on do not apply to the physician, because what he does no one else in the society can do:

This was said by Mitakshara, the commentator of the famous law-giver Manu, who held that the

चिकित्सको यत्कुरुते तदन्येन न शक्यते ।
 तस्माच्चिकित्सकः स्पर्शं शुद्धो भवति नित्यशः ॥

physician was always pure, and among the elite. Charaka says that a physician is superior to a twice-born, for he is a thrice-born one: he acquires the third birth after he completes his medical education:

विद्यासमाप्तौ भिषजस्तृतीया जनिरुच्यते

Charaka, however, classifies physicians into two categories: the right ones and the wrong ones.

द्विविधास्तु भिषजो भवन्त्यग्निवेश प्राणानामेकेऽभिसराः हन्तारो
 रोगाणां, रोगाणामेकेऽभिसराः हन्तारो प्राणानामपि ॥

The former remove diseases and assure life, while the latter produce illnesses and remove life itself (Sutra 29,5). He also explains that the former hail from respectable families, are adequately educated, have served diligently competent and elderly physicians as apprentices and are themselves competent and sincere. They have self control, are well-equipped, and are free from defects. They look upon every patient as their own mother, father, brother or other relative. They are essentially kind-hearted, and are solely interested in relieving the patients of their suffering.

There were quacks and fakes even in the ancient times. They have been termed 'prati-rupakas', 'ku-vaidyas', 'bhishak-chhadmacharas'. Even the law of the land laid a heavy hand on them. Manu, the law-giver, enjoins that a fake-physician must be severely punished:

चिकित्सकानां सर्वेषां मिथ्यां प्रचरतां दमः ।
दुश्चिकित्सां कुर्वतां दण्डः कर्तव्यः ॥ (*Manvartha-Muktavali*)

Yajnavalkya - Smriti lays down that a quack is to be fined heavily :

भिषङ् मिथ्या चरन् दण्ड्यः ।

Kautilya's Artha-Sastra, which is both normative and descriptive concerning the social life and polity of ancient India, suggests that the punishment (sahasa-danda) meted out to a false physician must be mild or severe according to the damage that he has caused and the suffering that the patient has experienced because of his treatment:

The false physicians have their eyes on the fees: they are greedy and exploit the gullible folk with

भिषजः प्राणाबाधिकमनाख्यायोपक्रममाणस्य विपत्तौ पूर्वः साहसदण्डः
कर्मोपरोधेन विपत्तौ मध्यमः मर्मवैगुप्यकरणे दण्डपारुष्यं विद्यात् ।

their tall claims and superior air. The well-known literary work *Visva - gunadarsa*, describes

मिथ्यौषधैर्हन्त मृषाकषायै-
रसह्यलेह्यैरयथार्थतैलैः ।
वैद्या इमे वञ्चितरुग्णवर्गाः
पिचण्डभाण्डं परिपूरयन्ति ॥

how the charlatans pretend to be competent physicians, administer drugs about which they do not know anything, and make a big show of their expertise, all only to fill their own enormous belly :

Sometimes quacks do succeed in their sham treatment; the patient does get better and recover his health. But the cure has been effected not at all by the medicine given but by the fast and other healthy procedures which the patient follows. The quack however rushes forward to take the credit and extract a large fee

Charaka blames the administration for the presence of such dishonest physicians and quacks :

कषायैरुपवासैश्च कृताप्युल्लाघतां नृणाम् ।
निजौषधिकृतां वैद्यो निवेद्य हरते धनम् ॥

and "Such are the pretenders who masquerade as efficient physicians and roam about the country, as veritably thorns, owing to the negligence of the administrators" (Sutra, 29, 8). The quacks are not in fact physicians at all, although they pretend to practice medicine. They are self-seekers, and value only monetary rewards. They are entirely devoid of ethics in their lives as in their practice. They have no commitment to cure and have no obligations to the patient. They are by no means kind-hearted, sincere or honest as a true physician should be.

Charaka mentions another class of charlatans along with the quacks mentioned above. They are the ones who practice medicine on very slender and improper credentials. They would have acquired some celebrity owing to factors not connected with medicine at all. Charaka calls them 'siddha-sadhita', or those who exploit patients on the basis of their ill-gotten repute and false claims. They may be eminent in some other calling, but they enter the field of medicine to make money. They would not really be interested in healing the suffering folk, nor for that matter capable of doing so.

Charaka also warns that some of the cures effected by these quacks and charlatans should not mislead us. "The quack who cures accidentally some patient who is destined to live longer, may soon kill many patients whose longevity is not previously determined!" (Sutra 9, 17). He comes down heavily on the physicians who take a casual attitude while treating patients (ibid 11, 126-1333), and on those who take to the profession only as a means of livelihood, for

धर्मार्थं नार्थकामार्थमायुर्वेदो महर्षिभिः ।
प्रकाशितो धर्मपरैरिच्छद्भिः स्थानमक्षरम् ॥

according to him, the great sages gave us this art of healing not to make money but to do good to . the people :

3.5 Since very early times, and until our own day, medical profession has been lucrative; the art of healing and the science of curing have been easy avenues to acquire wealth and celebrity. A verse in *Rigveda* admonishes, ten thousand years ago, the physician who sets out to sell his precious magical gem of wish-fulfilment (Chintamani), viz. his medical expertise, for but a few trinkets of trash (viz. money) (RV, 10,97). The Buddha also chides the physician who is keen on monetary gains.

The physician should be a benefactor, according to Charaka, inasmuch as he facilitates people to attend to the three main objectives of life, viz. virtuous living (dharma), wealth and security (artha) and pleasures of life (Karna), for all the three depend on health. The physician in this sense is looked upon as a 'donor' (dāta), for he gifts bodily health and well being. He lends a helping hand to those who are sinking in the quagmire of disease; what other service could be more valuable? *Yogaratanakara*, a medieval work on medicinal preparations, says that the physician is most virtuous on this account, and worthy of all honour:

रोगपङ्कणवे मग्नं यः समुद्धरते नरम् ।
कस्तेन न कृतो धर्मः कां च पूजां न सोऽर्हति ॥

As we all know, monetary considerations play an increasingly important and enormous role in modern society. A large number of young and brilliant aspirants take to medical practice only for the rich rewards that it entails. And the social fabric has become so complicated and tangled that one does not readily distinguish the competent and honest doctor from the commercial minded doctor who merely puts on airs. Ethics in this context gets terribly out of gear. The old and honoured concepts of service, propriety, efficiency, integrity, honesty, commitment and sincerity in medicine do not seem to be applicable to the modern times.

The code of conduct, even when one has a notion of it, seems impracticable. It is economics, and not ethics, that seems to rule the roost.

4. Ideals to Be Pursued

But an inquiry into what constitutes the best physician is not only relevant but necessary at any time. An ethical consideration cannot be avoided and the ideals must always be kept before us, however difficult they are to be achieved. According to Charaka, "one wants to become a physician must previously become thoroughly knowledgeable and cultivate virtues. He must work hard, for he is a saver of lives (pranada) of human beings. A good physician is one who frees patients from their distress" (9,134). It is only the serious-minded and knowledgeable physician that can restore the lost health of the patient and bring him back to an active and purposeful normalcy.

Vagbhata's Ashtanga-Samgraha suggests that the physician must regard all his patients as his own dear children who need his attention, and that he must proceed to treat them in the light of his wisdom and being aware of the virtuous path.

भिषगत्यातुरान् सर्वान् स्वसुतानिव यत्नवान् ।
अबाधेभ्योऽभिसंरक्षेत् ज्ञानं धर्ममनुस्मरन् ॥

Mahabharata, the great Indian epic, tells us that we must cultivate the physician who is wise, virtuous, pleasant, friendly, honest and compassionate. Adequate medical education is no doubt “a light jyoti or pradipa)” that will extend

प्रज्ञोपसेविनं वैद्यं धार्मिकं प्रियदर्शनम् ।
मित्रवन्तं सुवाक्यं च सुहृदं परिपालयेत् ॥

the horizon of ones vision and refine ones native talent. The education, according to Charaka, should enable the student of medicine to hold this light and enter into the inner life of the patient, so that he can treat him effectively; otherwise the education is wasted.

योगमासां तु यो विद्योद्देशकालोपपादितम् ।
पुरुषं पुरुषं वीक्ष्य स ज्ञेयो भिषगुत्तमः ॥

The above citation brings out the fact that in traditional Indian medicine (which alas very few practice today), the individual is more important than the disease he may be suffering from. The patient is not merely a case or illustration of a specific disease category; he is a person to whom a disease has occurred. Charaka points out that the same disease will appear in different patients differently; hence the expression “purusham purursham vikshya”.

It is important that study of texts should go hand in hand with practice; otherwise competence will elude the prospective physician. And besides the medical knowledge and skill Charaka speaks of an intuitional understanding of the patient-and-the disease as a total picture, and he calls it ‘vijñana’.

प्रयोगज्ञानविज्ञानसिद्धिसिद्धाः सुखप्रदाः ।
जीविताभिसरास्ते स्युर्वैद्यत्वं तेष्ववस्थितम् ॥

This is basic to all effective treatment.

ज्ञानप्रदीपेन यो नाविशति योगवित् ।
आतुरस्यान्तरात्मानं न स रोगांश्चिकित्सति ॥

Charaka describes this ability as an intuitional and spiritual approach, a ‘Yoga’. But this is a not a supernatural or magical skill; it can be acquired during the course of medical education and training. So, says Charaka himself, and he points out that this ability will enable the physician to treat each patient as an independent entity. Treatment must necessarily be individual oriented:

Sushruta insists that the physician should not confine his studies to the medical field only, but must get acquainted with several other disciplines. This will make his mind open and alert, and his approach will be broad based. He need not be proficient in other disciplines; proficiency must be aimed at in his own field, but he must not be a stranger to other branches of knowledge. Medical knowledge alone will not give him the expertise that the physician needs to have, nor the renown that he aspires to acquire:

एकं शास्त्रमधीयानो न विद्याच्छास्त्रनिश्चयम् ।
तस्माद् बहुश्रुतः शास्त्रं विजानीयाच्चिकित्सकः ॥
स्वतन्त्रकुशलोऽन्येषु शास्त्रार्थेष्वबहिष्कृतः ।
वैद्यो ध्वज इवाभाति नृप तद्विदपूजितः ॥

In the medical curriculum must be included medical ethics, not as a normative discipline but as a practical course with its own problems and considerations. The role of ethics is certainly vast and varied, from treating a common cold to the controversy on euthanasia, from the simple obligations of a family doctor (grha-vaidya) to the specialist services in the high cost and high-technology Medicare units that are springing up in our cities. The medical programmes are now in the nature of an elaborate and sophisticated industries and sharp business enterprises. Ethical considerations become all the more urgent and relevant; also more difficult and almost utopian .

However, all ethical considerations are essentially human in orientation, and need to be accorded a place of importance in the Medicare services. The Indian writers on medicine (like Charaka, Sushruta and Vagbhata) uniformly indicate that the physician must cultivate the qualities of friendliness (maitri), kindness for the suffering folk ('karunyam arteshu'), and eagerness to do his best to alleviate the suffering ('sakye pritih') (Charaka, 9,26)

Sushruta adds that the physician acquires just renown when his instructions are clear and firm (ajna), when he is ready to sacrifice for the sake of the patient's well-being (tyaga), when he is patient and forgiving (kshama), when he is steadfast when confronted with difficulties (dhairya) and when he is uncommonly courageous (vikrama) (Sutra, .34, 10).

Vagbhata's Ashtanga-samgraha indicates that an efficient doctor is friendly towards all, compassionate to the patients, happy when he sees healthy people, and composed when he finds that his patient is unlikely to be saved; his good conduct is what distinguishes him.

सर्वत्र मैत्री करुणाऽऽतुरेषु
निरामदेहेषु नृषु प्रमोदः ।
मनस्युपेक्षाऽपकृतिं व्रजत्सु
वैद्यस्य सद्दत्तमलं तनोति ॥

Finally, the advice given by Charaka may be pertinent for the practitioners even today: "He who practices not for money nor for caprice, but out of compassion for living beings (bhuta-daya) is best among all physicians. The physicians who set out to sell their skill like merchandise only lose sight of the gold and acquire

heaps of dirt. Hard is to find a conferrer of spiritual blessings comparable to the physician who snaps the snares of death for his patients and proffers renewed lease of life for them. The physician who regards compassion for living beings as his. Highest religion fulfils his mission in life and obtains the highest happiness" (Sutra, 1, 58, ft).

सर्वत्र सुखिनः सन्तु सर्वे सन्तु निरामयाः ।
सर्वे भद्राणि पश्यन्तु मा कश्चिदुःखभागभवेत् ॥

"May all beings be happy; may all beings be free from ailments;
May all good occur to all people; and may no one be troubled with misery."

Notice

Charaka-samhita, which is a text prepared nearly a thousand years before Christ, was in fact a redaction of an earlier classic, viz. *Agnivesa-tantra*. This Charaka samhita was redacted in turn by Patanjali in the second century B.C. The present form of the text is traced to 175 B.C.

If Charaka is famous as a physician, Sushruta is celebrated as a surgeon. His Samhita is referred to in a work called *Katyayanavartika* in the 4th Century B.C. According to Hoernle, the samhita was prepared about 600 B.C. The present form of the text is ascribed to the century preceding the Christian era.

Vagbhata, the author of *Ashtanga Samgraha* is said to have lived in the fifth century A.D. (according to Gananatha Sen).

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THE ART OF POSITIVE THINKING ANCIENT INDIA'S CONTRIBUTION

By Dr. V. Parameshvara¹

Thinking means exercising the mind in an active way. Positive thinking or explicit or definite way of conceiving notions of doings brings up an important word namely mind, which is a seat responsible for thinking.

A mind is in some sense reflected in such occurrences or sensations, perceptions, emotions, memory, desires, various types of reasoning, motives, choices, traits of personality and the unconscious. The task of the philosophy of mind is to examine and analyse these concepts in order to discover their nature, the relations between them, how they are to be classified and how they relate to such concepts as matter and energy and the body in particular to the central nervous system.

Our most difficult problem in discussing consciousness through memory and learning is that we do not know the neural mechanism of a thought. Each thought almost certainly involves simultaneous signals in portions of the cerebral cortex, thalamus, limbic system and reticular formation of the brain stem. A thought probably results from momentary pattern of stimulation of many different parts of the nervous system at the same time. This is known as "Holistic Theory" of thought. The stimulated areas of the cerebral cortex, thalamus, limbic system and reticular formation perhaps determining the general nature of the thought - pleasure, displeasure, pain, comfort and modalities of sensation etc. However, positive thinking is variable from circum stances to circumstances, time to time and governed by context and environment.

Mind in Indian Thought

Mind (Antahkarana) in Indian thought is an organization of four factors:- 1) thoughts (manas), 2) resolutions (buddhi), 3) ego (ahankara) and 4) memories (Chitta). Thoughts are associated with sense-functions (Indriya Vritti) and thus rely on the outside world. They are usually intentions and desires to get What is pleasurable and avoid What is painful. This is What is called Kamaraga. Thoughts such as these are reinforced by resolutions (Planning, decision-making), ego (the notions of 'I', 'Mine', 'For me' etc) and memories.

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In order to have wholesome thoughts, it is necessary to restrain the sense-activities to their minimum. Excessive indulgence in any sense-organ is likely to vitiate the thoughts. Indriya-nigraha means monitoring the sensory channels of self-expression. Unless one is careful about what he transacts with, and how much his involvement should be, he is sure to come to grief sooner or later, for his mind becomes wayward.

Peace of Mind

Peace of mind is the nearest approximation to the final goal namely liberation or mukti, in Indian way of thinking. Liberation is difficult of attainment, at any rate, in this life. It presupposes strenuous discipline, wisdom and several un-seen influences. Very few can indeed attain it. But peace of mind is within easy reach and can be attained by a large majority of people, irrespective of caste, vocation, knowledge of philosophical truths and so on. Therefore, Indian books like the Gita, Ramayana and Mahabharata plead that everyone must aspire to secure peace of mind. The Gita recognises that happiness is sought after by all human beings, but argues that the pre-requisite for the happiness is peace of mind (2,66). Its prescription for peace of mind is meditation (bhavana), which is impossible without an integration of thoughts, feelings and action (Yukta) without such integration, even intelligence (buddhi) cannot be there.

अशान्तस्य कुतः सुखम्

Peace of mind is related to contentment. The exact meaning of the Sanskrit word 'santosha' is not happiness but contentment. Patanjali's Yogasutra (2, 32) includes santosha under the necessary observances (niyama), and lists it immediately after bodily and mental purity (saucha). Santosha is defined here as 'not to covet more than what can be got from the means at hand'. It is the opposite of over-much desire, or greed. The person who is interested in higher things of life should carefully consider (a) his physical capacity for work, pleasures and stress, (b) financial resource (c) responsibilities to the family and community, (d) attitudes of mind, and (e) the ultimate destiny. He should then delimit his commitments to work, to the family and community and should curtail his involvement in pleasures. He plans out his life in all its details in a manner that fits in with the resources at his disposal, that suits his attitudes and outlook, and that gives him most satisfaction in the circumstances. He accepts the limitations without regret, envy or churning. This is explained by - the commentators on Yogasutra - (like Vyasa vachaspathi and Bhoja). Contentment leads to the ability to bear with fortitude the opposites like joy and misery, heat and cold, success and defeat. This is technically called 'tapas' and is defined as quiet endurance of opposites (dvandvasahana) Life is a package deal: it comes in all colours and

shapes. There are good things and bad things coming to us, and it is not always that we are responsible for what we get or do not get. Things go wrong with the best of careful planning; and things come off alright with no effort on our part. Realizing that there is a limit to our knowledge, effort, desires, plans and occurrences, we should learn to take things as they come, with as much of a smile as possible. Without this, life can be one round of misery, suspense, anxiety and regret as the poet said "We look before and after and pine for what is not". This attitude of not losing one's head in pleasure or in pain is called in Indian thought "Santosha".

Motivations in Life

There are three main motivations in life 1) desires (raga) 2) fears (bhaya) and 3) aversions (krodha, anger) (Gita 2, 56). Because of fears (anxieties about security, health, death etc.) we have desires. When fears are great, desires are also many And When desires are not fulfilled, anger results and When one is angry his mind is clouded, When the mind is clouded one does not resolve properly, for his thoughts are not collected and inability to make right decisions leads to ruin. This is explained in getha 2, verses 62 and 63.

Doshas

In Ayurveda, health is the balance of the three doshas, related to the three gunas Sathva, rajas and tamas (Vata, pitta and kapha). Mind by its constitution is of the nature of sattva it is pure, transparent, clear and perceptive. But it is conjoined with ragas (desires, greed, anger, envy, remorse, fear, excitement etc) and tamas (ignorance, indolence, sloth, disinclination to work, aversion to knowledge etc.) Thus the states of mind play an important role in the causation of physical and mental imbalances.

Three-fold are the causes of illness, according to Ayurveda: (a) improper employment of organs (असात्म्येन्द्रियार्थ) (b) errors of judgement, (प्रज्ञापराध) and (c) factors outside the control of the individual (like changes, seasons, accident etc.) (परिणाम) of these three errors of judgement figure prominently (Charaka- samhita, Sharira sthana, 1/109). An intelligent man must take care how, how much and When his organs (sensory as well as organs of action) must be employed, and should also consider the changes (in his own body and outside himself), seasonal variations, exigencies of circumstances. Excessive, deficient or improper activity leads to illness.

Peace of Mind - A therapeutic aid

Therefore, as a therapeutic aid, peace of mind is prescribed. It is technically called 'mastery over the vagaries of the mind.' (Sattvavajaya) by eliminating or avoiding the impact of rajas and tamas. The Ayurvedic term for peace of mind is prasada, tranquility, equipoise. It is an attitude of mind that is cultivated in order to preserve and promote health, and to prevent ill-health.

We find in texts like Mahabharata (moksha dharma parva, Shanti parva) And Gita, methods prescribed for the cultivation of this attitude of undisturbed peace of mind. All the methods involve a certain independence of the individual from outside crutches his involvement with the world needs to be minimal, his love of money and material comforts also minimal, and his reliance on other human beings for personal satisfactions also reduced to bare necessities. Withdrawal from the multitude, renunciation of luxuries, disinclination for wrong living, restraint from exciting the world and from getting excited with the world, and an absorbing interest in understanding one's own real nature.

The texts also suggest that no man can change the world to suit his conveniences, ideas or ideals. There is greater need to change oneself, so as not to be troubled by the world. A Subhashitha says "For one who wears a pair of slippers. The Whole earth is covered with leather. For him who is content, all the riches of the world are his".

Contentment is thus key to peace of mind, and peace of mind is the only gateway of happiness. Contentment does not mean a passive helpless resignation in the face of odds. It is the preservation of one's exposure in happiness as well as in distress, in profit and in loss, in success as, in defeat. Peace of mind is described in the Gita as the Characteristic trait of 'Sthithaprajna' or the liberated soul whose mind is steadfast. Such a one is not troubled With whatever happens to him, good or bad, and Will not allow his mind to be soured or spirit flagged by unpleasant events (calamity, ill will of others, slander etc.) Beside, there is a positive aspect to it. He is clear in his thoughts correct in his judgements. Firm in his resolves, and active in his environment He does whatever he does, in the spirit of doing his duty without fear or favour, without the fever of excitement or anxiety concerning how it will turn out or what people will say. He is indifferent like to public opinion and personal profit.

Peace of mind will give a better perspective in daily life and the right measure of initiative, energy and involvement. It will enable one to avoid extremes in any undertaking. An old advice is to avoid excesses. The man can live his life more normally and meaningfully.

In the Sankhya school of thought man's misery is ascribed to sequence of five stresses (called kleshas): fundamental ignorance of reality (avidya), ego-

feeling (asmita), attachments (raga), aversions (dvesha) and involvements in the world outside (abhinivesha). The only way, the actual and possible misery of man can be eliminated is to develop an understanding of things as they really are, devoid of our prejudices, preconceptions, emotional involvements and expectations. This is called *Viveka*, the purpose of all philosophical study. This is achieved by a deep, sustained introspective investigation (prasankhyana). Viveka manifests it so as tranquillity (shanti) or peace of mind.

Happiness - vs - Peace of Mind

The highest value held out in Indian thought is not happiness or sukha, because happiness necessarily presupposes its invariable concomitant, unhappiness the two constitute a pair one cannot be there without the other. On the other hand, shanti (peace of mind) is freedom from all opposite, and therefore, the highest objective. It results when there is no longing, and thus no stress.

In happiness there is a hierarchy. A happy man wants to be happier, getting one measure of happiness, getting one kind of happiness, he longs for other kinds of happiness. A person who is content thus it eliminates rivalry. Strife and stress, shanti is defined as that, obtaining which one does not seek to obtain anything else.

Yoga

The **योग** important and useful art that has been universally employed over ages is the practice of yoga. Yoga itself is regarded as four-fold aim is to dissolve one individuality by concentrating, attention on tip of nose or between eye brows or by devoting oneself to musical strands or by contemplating on the void. Employment of body towards release from worldly disabilities. Principally it is postures and breathing exercises (Especially retention of breath) Aim is to prevent and cure diseases and to attain occult powers. The system taught by patanjali, in yoga-sutra, also called Rajayoga (a) so called because it shines among the yogic methods as the king. (b) Expression not found in patanjali's yoga-sutra or in early texts. it is a later nomenclature. (c) it is principally a method of reaching through discriminative wisdom and renunciation of passions.

- (a) It rejects the violent practices of and does not aim curing diseases or making the body strong (as does). Thus it is closer to and inside on knowledge as equally important in obtaining.
- (b) it distinguishes between two states of or one pointedness of mind-body complex:

(I) Where the individual's mind is concentrated but he is aware of this state of concentration (II) Where the individual's mind is so fully concentrates that he is no longer aware of his body: his mental state or his existence in space and time. The latter is regarded as the same as jivan-mukti or liberation while still alive

The method ad vocation is the eight-fold praxis or graded steps:

- 1 Yama: Control of sense-organs and
- 2 Niyama: Observances for purity (internal and external) contentment introspection and devotion to
- 3 Asana: Assuming postures that are firm and pleasant.
- 4 Pranayama: Breathing exercise, especially restraint of breath within the body after inhalation the purpose is to control the mind which is association closely with breathing processes.
- 5 Pratyahara: Withdrawal of inclinations (sensory as well as mental) so as to minimise actual and possible distractions.
- 6 Dharana: Holding of attention steadfastly on the chosen object to the exclusion of distraction.
- 7 Dhyana: Intent and deep contemplation when all efforts at eliminating distraction is unnecessary. It is natural absorption of consciousness in the object of contemplation.
- 8 Samadhi: Total absorption or one pointedness of body mind complex.

The idea underlying this practice is the suppression of primordial inclination to worldly involvement, know as which is born out of ignorance of reality the practice is said to provide wisdom that is called. This is a possibility for all human beings provided they make sincere efforts.

Raja yoga insists on the twin procedures (a) constant unremitting and earnest practice and (b) development of an attitude of dis-passion and equanimity hence the yoga sutra prescription.

Raja Yoga

The expression raja yoga was made popular by swami vivekanande in the sense of a 'royal' approach to spiritual awakening in man. He translated and explained patanjali's yoga-sutra under this title (1927). by yoga he meant the integrated personality () where the lower aspects of the physical plans were united in effect with the higher aspects of psychological functioning. He also sought to involve the ideas of Karma-yoga, Bhakti-yoga and Jnana-yoga in Rajayoga.

THE ART OF POSITIVE THINKING ANCIENT INDIA'S CONTRIBUTION

Yoga has the following definitions: yoga is suppression of all processes of individuated consciousness or mind in general. It is beyond mere control of mind, for it is said to work at a deeper level. At the level of the 'mind-stuff'.

(in Gita) yoga is skill in one's work. Whatever one does is done very well, When the individual approaches it in an integrated manner () When his thoughts, or attention are not distracted by conceding thoughts, feeling, consideration etc. It is in the sense of work as dispassionate duty, without worrying about the outcome or effects.

Equanimity is called yoga. To take things as समत्वं योगमुच्यते they come, without exceptions or involvements is the teaching of Gita

Success or failure should not loom larger in the mind of the doer: he must also look upon all things alike. It is an attitude that is objective and wholesome.

Thus the first definition is relevant for the yoga practice and is involved in raja-yoga. The second definition refers to personal efficiency and is described as karma-yoga. The third definition describes the enlightened attitude, and refers to Jyana-yoga.

The application of an institution of this ancient wisdom as a model should impart systematic training of mind in moral ethical and spiritual values within one's personal life in particular and the community as a whole.

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BRIEF BIOGRAPHIES OF FEW EMINENT CONTRIBUTORS TO AYUSH

By Dr. Galib, Associate Professor, AIIA, New Delhi

Prof. Ashok DB Vaidya

Prof. Ashok DB Vaidya, a leading clinical scientist, had his undergraduate and postgraduate medical education at Seth GS Medical College, Mumbai. He is a physician-scientist and is known as the father of Reverse Pharmacology. He belongs to the fourth generation of Medicine and Ayurveda. His ancestor- Aryavaidya Mayaram Sunderji was a renowned Ayurvedic scholar, author and an expert vaidya. Dr. Vaidya has inherited his archives and notes.

Over half-a-century of career in drug development, he has pioneered phase 1 to 4 clinical trials with new drugs. He has trained many scientists in drug research. He was the Merck International Fellow in Clinical Pharmacology at Yale Medical School, USA. Later, he was at the CIBA Research Centre and KEM Hospital, Mumbai for Phase I, II and III clinical trials on new molecules, and for research on natural products at Podar Ayurvedic Hospital. He was the first who did GCP clinical trial of Benazepril. He has been in academic activities in the planning and execution of the GCP training courses like Clinical Pharmacology and Therapeutics Courses conducted by the Indian Council of Medical Research at Seth GS Medical College, courses in Clinical Trials Methodology with Association of Medical Advisors to the Pharmaceutical Industry of India and the courses organized by the Government of India.

He retired from CIBA as Medical Director and dedicated himself to scientific research in Ayurveda and new drugs, at Bhartiya Vidya Bhavan's SPARC. Dr. Vaidya has pioneered the new discipline of Reverse Pharmacology for new drug development from Traditional Medicine. Currently, he is in charge of the ICMR Advanced Centre of Reverse Pharmacology at MRC-KHS, Mumbai. His research in Ayurveda has contributed new modalities in Parkinson's disease, diabetes, hepatitis, arthritis and cancer.

Dr. Vaidya has received several honours and awards including Lifetime Achievement Award and Sir Ramnath Chopra Award by Indian Pharmacology Society, Prof. UK Sheth Oration Award in Clinical Pharmacology, Shri BV Patel Memorial Award, Dr. SL Bhatia Oration, Rotary Distinguished Service Award, Dr. KN Udupa Award for scientific research in Ayurveda and Aryavaidyan Warrior award etc.

He has been the President of the Indian Society of Clinical Pharmacology and Association of Medical Advisors to the Pharmaceutical Industry. He has been on the editorial boards of several journals. He has been a consultant to WHO, CSIR, ICMR, DBT, CCRAS and several industries and research councils. Dr. Vaidya has traveled extensively nationally and internationally, as he has been a much-sought speaker at scientific conferences and meetings on Ayurveda/ Medicinal plants. He has more than 250 research publications to his credit. His students and colleagues, trained by him in clinical drug research and Ayurveda, occupy important positions in academia and industries.

Dr. Nitya Anand

Dr. Nitya Anand, a legendary figure in the Indian Drug Research, was born on 1st January 1925. He completed his M.Sc. in Chemistry (1943-45) from Delhi and then to the University Department of Chemical Technology (UDCT), Bombay for research in organic chemistry where he was awarded PhD in 1948. This was followed by yet another PhD from St. John's College, Cambridge University. After returning back to India, he joined the Medicinal Chemistry Division of Central Drug Research Institute in March 1951 and continued there until his retirement in 1984. His stay in CDRI first as a Scientist, then as Head of the Medicinal Chemistry Division (1963-1974) and later as a director (1974-1984) has been of great significance in shaping and directing the Institute. He undertook a post-doctoral training under a Rockefeller Foundation Fellowship at Harvard Medical School, Boston, USA. He left his impressions in the field of bacteriology through his pioneering observations and the mechanism of action of streptomycin. Under his leadership, the Division of Medicinal Chemistry became the leading school in the field and achieved international recognition. He was first to initiate the era of synthetic peptides in the country and synthesized muramyl-peptide analogs as cell wall antagonists and a number of nucleosides as potential purine antagonists. He has published more than 400 research papers, been granted about 130 national and international patents, and jointly authored two books. He has also edited two books, around 30 book chapters in medicinal chemistry textbooks, and many review articles. He has supervised about 90 students for their Ph.D. degree and many post-docs.

Dr. Anand's contribution to the growth and development of the Central Drug Research Institute has been monumental. He propelled its advancement to a world-class center for drug discovery and development especially for tropical diseases (malaria, filaria), contraception and drugs from medicinal plants, areas of special national relevance.

He was associated with different drug policy formulating bodies of the Government of India for almost four decades. He has been an adviser and consultant to many scientific bodies and institutions. He was a member of the

Scientific Advisory Committee to the Cabinet of GOI (1981-83), a Member & Chairman of the Steering Committee for Chemotherapy of Malaria of WHO, a Member of the Scientific and Technical Advisory Committee for Tropical Diseases and for Human Reproduction of the WHO. He has been the Chairman of the Indian Pharmacopoeia Committee of the Govt. of India.

He has received many honours and awards. He is a Fellow of the Indian National Science Academy, New Delhi, the National Academy of Science, and the Allahabad and Indian Academy of Sciences, Bangalore. He has been a President of the Indian Pharmaceutical Congress. He received the Amrut Mody Research Award (1971), the KG Nayak Gold Medal, Baroda University (1972), the Vishwakarma Medal, INSA (1982), the JB Chatterji Gold Medal, Tropical School of Medicine, Calcutta (1982), the Acharya PC Ray (1972) and Sir JC Ghosh (1976) Medals, Indian Chemical Society, the National Nehru Science Award of MP (1996) and the Vigyan Gaurav Award (2000). The Government of India awarded him, the Padma Shri, the fourth highest civilian award, for his contributions. He is endowed with a huge number of orations.

Dr. Sharadini Arun Dahanukar

In early 1970s Dr. Sharadini Dahanukar joined the Department of Pharmacology after completing her internship in Gynecology-Obstetrics in the USA. She was trained under both conventional as well as Ayurveda physicians of her days. Ms Dahanukar was good at Sanskrit language that assisted her referring to the classical texts of Ayurveda.

Dr. Dahanukar's love for plants and her knowledge about them was exemplary. She was associated in studies with *Tinospora cordifolia* that reported significantly to reduce the mortality comparable to that of a combination of metronidazole and gentamicin. Her studies on the efficacy of *P. longum* in childhood asthma showed an excellent response. She was also associated in the challenging work of trying to find if there are any good scientific correlates in modern medicine to classification of individuals by the well-known concept of "Prakriti." This was possibly one of the earliest studies in this area. She is pivotal in establishing Ayurveda Research Center (ARC) at KEM Hospital, where she studied extensively on various aspects of medicinal plants. Efficacy of *Azadirachta indica* in second degree burns; *Emblica officinalis* as a health boon; leech therapy for complicated varicose veins; anti-endotoxin effect of *Tinospora cordifolia*; effect of *Terminalia chebula* on gastric emptying; effect of *Embelica officinalis* in acute pancreatitis; activity of *Tinospora cordifolia* in liver damage etc. are a few studies to refer.

At ARC, she also initiated education and service programs in methodology and techniques for experimental work. Organizing Ayurveda Update, every 4 years, with a view to keep continuity was a laudable effort. She

created a good set up for offering "*Panchkarma*" as a well-accepted modality and an integral part of Ayurvedic therapeutics.

Dr. Dahanukar wrote good review articles on Pharmacology in Ayurveda, including adverse reactions to Ayurvedic drugs. She wrote many books, devoted to a wide array of subjects. Her book "Ayurveda Revisited" is very well acclaimed. Her views were thought provoking and enthused young researchers to commit themselves to scientific research in Ayurveda. Subsequently, she was part of the Council of Scientific and Industrial Research project, New Millennium Indian Technology and Leadership Initiative for drug discovery from Ayurveda. Dr. Mashelkar had heavily banked on her expertise for the project.

Prof. Sukhdev Swami Handa

Prof. SS Handa, a Pharmaceutical scientist, academician, well known for Quality control and Standardization of medicinal plants and their products; completed his education from London School of Pharmacy, London and University of Illinois, Chicago, USA; served in different capacities at Institute of Pharmaceutical Sciences, Panjab University, Chandigarh and as Director, Indian Institute of Integrative Medicines (IIIM), CSIR. Post retirement, he contributed immensely to the herbal sector in various industries including Ranbaxy Herbal Drug Research, Zandu Pharmaceutical Works, Emami Health Care, Glaxo Smith Kline etc. In different capacities, he closely associated with Ministry of AYUSH since 1999, particularly in Pharmacopoeia Commission for Indian Medicines wherein he supervised publishing of various Ayurvedic Formularies and Pharmacopoeias. Besides, he contributed immensely in different capacities to DBT, ICMR, CSIR and CIMAP. Noteworthy to mention is his contribution to Medicinal Plants Division of ICMR, who supervised publication of 550 monographs on Quality Standards of Indian Medicinal Plants in 17 volumes & Reviews on Indian Medicinal Plants. His role under CDRS (Composite Drug Research Scheme on Traditional AYUSH Medicinal Plants) and later in Disease oriented Approach to Validate Traditional Medicines at ICMR is exceptional where he associated in clinical evaluation of AYUSH products in anal fistula, mild diabetes, and Filariasis. His contributions in the United States Pharmacopeia (USP), USP South Asia Herbal Medicine Compendium and British Pharmacopoeia Commission (Herbal & Complimentary Medicines) are enormous. Because of continuous efforts, Quality Standard monographs of Indian Ayurvedic Plants have been included in USP and BP.

Prof. SS Handa has received several honors and awards including Ranbaxy Research Award, IDMA - APA Eminent Pharmaceutical Analyst Award, Dr. KM Parikh Award of IASTAM, Life time award by the Indian Society of Pharmacognosy, Schroff Memorial National Award, Bisheswar Saha Memorial Award by the Indian Society for Ethnopharmacology etc. He

delivered lectures in his field of specialization in various developing, emerging and developed countries such as UK, USA, Germany, Austria, North Korea, Kazakhstan, Thailand, China, Nepal, Malaysia, Myanmar, Iran, Spain, Italy, Hungary, Turkey, South Africa, West Africa, Nigeria, Panama, and Trinidad & Tobago. He is credited with more than 100 publications including research articles, reviews, book chapters etc. About 44 patents are in his credit. Professor Handa has supervised 10 Ph.D. theses. He is currently, Chairman, Special Scientific & Technical Appraisal & Advisory Group (STAG) on Anti-SARS-CoV-2 virus studies using Botanical Ingredients & Traditional Formulations (2020-2023).

Dr. GV Satyavati

Dr. GV Satyavati is one of the former Director Generals of Indian Council for Medical Research. She represents a unique combination of independent doctorates in both Pharmacology and Kayachikitsa. Her interest in Ayurveda, desire to prove its scientific aspects and commitment are unique. Her pioneering work unraveled through the hypolipidemic activity of *Commiphora mukul* that led to the discovery Guggulipid. After about two decades of further research at the Central Drug Research Institute, Lucknow, the product was marketed in India and few European countries. Her work on uterine activity of *Saraca indica* has also received high commendation. Under the aegis of ICMR, she coordinated multi-disciplinary research studies, with disease-oriented approach, in selected thrust areas of traditional medicine. She was first to initiate such disease oriented multi-centric clinical trials on anal fistula, bronchial asthma, diabetes, viral hepatitis, urolithiasis, filariasis etc. adopting multidisciplinary and reverse pharmacology approaches. This approach helped in validating efficacy of Ksharsutra in the management of anal fistula and Hepatoprotective activity of *Picrorhiza kurroa*.

Dr. Satyavati has authored several scientific articles and reviews in national and international journals and contributed chapters in Monographs and Books. As the Editor-in-Chief of Indian Journal of Medical Research, her efforts resulted in terms of the impact factor and the citation. She also initiated pioneering studies on scientometric analysis of biomedical research. Her most significant contribution for the AYUSH sector is to undertake developmental work and publication of the three volumes of the Monographs on Medicinal Plants of India. Dr. Satyavati, with her ability to develop integrated approaches in research in the traditional medicine contributed to WHO Expert panel on Traditional Medicine for 18 years. She served as a WHO Consultant on Traditional Medicine (Herbal Drugs) on several occasions. She was invited as a consultant to UNICEF (India) to develop a global film on Herbal Medicine. She is an elected member fellow of many academic bodies like the New York Academy of Sciences, the National Academy of Sciences (India) etc. She has served as a member of the Research councils of CSIR, NIHF. As Director

General of ICMR with her commitment to Ayurveda, she helped create better awareness and interest amongst the authorities for healthcare through the indigenous systems of medicine. Even after her retirement, she has continued her scientific interest in biomedicine and Ayurveda. She is the recipient of RN Chopra Memorial Oration Award of the Indian Pharmacological Society, Prof. KN Udupa Award for Biomedical Research of IASTAM.

Dr. Sukh Dev

Dr. Sukh Dev, born in 1923 is an Indian organic chemist; academican and researcher secured his master's degree from Punjab University in 1945 and joined the Indian Institute of Science, Bangalore as a research associate. Further, obtaining his PhD in 1948 under noted natural products chemist Praphulla Chandra Guha at the IISc. Later, he conducted post-doctoral research at the Massachusetts Institute of Technology with John D. Roberts. He joined the National Chemical Laboratory, Pune as the Head in the Organic Chemistry (Natural Products) Division, with a promotion to deputy director and then appointed as director of the Malti-Chem Research Centre, Nandesari, Gujarat. Later he joined the Indian Institute of Technology, New Delhi as the INSA SN Bose Research Professor, shifting to the Dr. BR Ambedkar Centre for Biomedical Research, Delhi University.

He has conducted advanced research in biomedical science and natural products chemistry and is familiar for his works on medicinal plants particularly on *Cedrus deodara* and *Commiphora wightii*, and well-known for his contributions in the development of Guggulsterone, a plant-derived steroid used as a therapeutic agent. He holds 55 patents for his researches. His researches have earned him 55 patents. His work has been documented in over 290 scientific articles and he has published 10 books. He has also mentored 92 research scholars.

He is recipient of several honors including Shanti Swarup Bhatnagar Prize, the highest Indian award in science and technology. In 2008, the Government of India awarded him the Padma Bhushan, the third highest civilian honour of India, for his contributions to science and technology. The other awards include Sudborough Medal of the Indian Institute of Science, Acharya PC Ray Award of Indian Chemical Society, Vishwakarma Medal of Indian National Science Academy, Ernest Guenther Award of The American Chemical Society, Distinguished Alumnus Award of the Indian Institute of Science, VASVIK Industrial Research Award, FICCI Award of the Federation of Indian Chambers of Commerce and Industry, Professor TR Seshadri Seventieth Birthday Commemoration Medal, Meghnad Saha Medal, TWAS Prize, Srinivasan Ramanujan Birth Centenary Award of the Indian Science Congress Association, Lifetime Achievement Award by the Indian Chemical Society and the Chemical Research Society of India.

Dr. Chandra Kant Katiyar

Born on 27th September 1954, Chandra Kant Katiyar is MD and PhD in Ayurveda, specialized in Rasa Shastra and Pharmacology from Institute of Medical Sciences, Banaras Hindu University, Varanasi. This unique blend of qualification has given him proficiency of interpreting ancient wisdom of Ayurveda in modern scientific context and terminology. Dr. Katiyar has more than 30 years of Industry experience in research and development of products spanning across the categories from Ayurvedic medicines to nutraceuticals, as well as Pharmaceutical products. Dr. Katiyar is currently CEO Health Care (Technical) for Emami Ltd. at Kolkata, who introduced State of the Art technologies in Ayurvedic drug development in the Research and Development at Emami. Before Emami, he has served at Dabur India Ltd. and at Ranbaxy Research Labs, where he contributed in the field of drug discovery from plant sources besides developing several Ayurvedic/Herbal products including products for Oncology and Neurology.

His contributions in research have been recognized by various International and National Journals by including him on editorial boards of Journals like Journal of Ethnopharmacology, Frontiers in Pharmacology, Journal of Ayurveda and Integrative Medicine etc. Dr. Katiyar has edited five books latest being 'Ayurveda at the turning' point published from UK in 2018. He has contributed more than 25 book chapters, more than 50 research papers and has about 20 patents to his credit. He has made important contributions in quality control of Ayurvedic/ Herbal drugs being member of Ayurvedic Pharmacopoeia Committee, Herbal Committee for Indian Pharmacopoeia and South East Asia Expert Panel on Dietary Supplements for United States Pharmacopoeia. He has played significant role in introducing Phytopharmaceuticals under the category of new drugs in the Drugs and Cosmetics Act and Rules and is one of the very few experts on the subject. He is member in all the Phytopharmaceutical Missions on CSIR, ICMR and DBT. Dr. Katiyar is a reputed researcher, academician and expert in regulatory policies for Traditional Medicines including Ayurveda. He has received several accolades including Sir Col. RN Chopra Oration in International Conference on Translational Pharmacology at AIIMS, New Delhi. Dr. Katiyar is also recipient of Dr. C Dwarakanath IASTAM Award for contributions to Contemporary Interpretation or Application of Ayurvedic Principles. Probably, Dr. Katiyar is the only person with Ayurvedic background who has been awarded the membership of the National Academy of Sciences, India (NASI) and Fellowship of Indian Pharmacological Society.

Prof. Malati G Chauhan

Late Prof. Malati Gulabsinh Chauhan is an outstanding example of a young lady who came from a humble background and became a lifelong teacher. Fifth amongst eleven children to an Education inspector as a father

and a primary school teacher as a mother, Malati Chauhan joined the LM College of Pharmacy as an undergraduate student and retired from her alma mater as Head of the Pharmacognosy Department, after an illustrious career spanning of 39 years. Post retirement, she went on to head the Medicinal Plant Sciences Section for 15 years at Gujarat Ayurved University, Jamnagar. Prof. Chauhan has published two volumes on Microscopic Profile of Powdered Drugs used in Indian Systems of Medicine featuring Bark and Leaf drugs and two volumes on Microscopic Profile of Drugs Used in Indian Systems of Medicine exclusively on Seed drugs.

A doyen in the field of Pharmacognosy, Late Prof. Malati Gulabsinh Chauhan was associated with a number of organizations like ICMR, ICAR, CCRAS, IASTAM, FIHI, GTU(Gujarat Technological University), Ahmedabad, SRISTI(Society for Research and Initiatives for Sustainable Technologies and Institute), SMPC (State Medicinal Pharmacy Council), Ahmedabad, GSMPB (Gujarat State Medicinal Plant Board), Ahmedabad, ICTA(Indian Cosmetic Technologists' Association), Pondicherry, SFTRRD(Science Foundation for Tribal and Rural Resource Development), Bhuvanesar, AADAR(Academy of Ayurveda Development and Research), Ahmedabad etc.

A lady driven with immense passion and dedication for her research work, Prof. Chauhan believed that if your endeavor is driven and fueled by purpose, then giving up is never an option. You'll find the courage and persistence to look past the problems and difficulties along your path and instead focus on finding solutions. Till the very end, she continued her work, one of the last being the revision of the entire Ayurvedic Pharmacopoeia of India. Always a teacher, Professor Malati Gulabsinh Chauhan continues to be remembered by students, academicians, industrialists, friends and well-wishers.

Prof. Shibnath Ghosal

Shibnath Ghosal, a researcher and professor of pharmaceutical chemistry, a former UGC-National Professor and head of department of pharmaceutics, Institute of Technology, Banaras Hindu University, Varanasi, is the research adviser to Natreon Inc, India and USA. He is a reputed Phytochemist of eminence. A Fulbright Scholar and a post-doctoral fellow at the school of chemistry, University of Minnesota, USA has traveled far and wide, namely as a visiting professor/ professorial scientist at Pharmazeutisches Institute, Bonn, Germany; department of chemistry, University of Hull, UK, and Schools of chemistry and pharmacy, University of Minnesota, USA. His work in Phytochemistry established Siterosides and withanolides as major chemical compounds responsible for biological activity in Ashwagandha and Humic and Fulvic acids in Shilajit. Professor Ghoshal probably for the first time established that though Shilajit is found as rock

exudate but actually it comes from a plant source residing inside them, therefore, actually it is a product of plant origin as against earlier convictions. Before this research, Shilajit was considered to be a mysterious origin product. It was Professor Ghoshal, who reported that Amla (Indian gooseberry) does not contain Vitamin C, but it still remains one of the most potent anti-oxidant fruit. The responsible compounds for this activity are found to be ten small molecular weight polyphenolic compounds. Professor Ghosal has guided the researches of over 50 M. Pharm. and 38 Ph.D. researchers to their degrees in chemical and pharmaceutical sciences. He has to his credit over 400 research papers published in international journals of chemical and pharmacological sciences and 15 US and international patents on natural drug products and bio-informatics.

Prof. Shiv Dayal Seth

Professor Shiv Dayal Seth was born in Agra in 1937, did his MBBS from SN Medical College, Agra, and his MD in Pharmacology from the All India Institute of Medical Sciences (AIIMS), New Delhi. After a brief stint as an Assistant Professor in Ludhiana at Dayanand Medical College, he joined AIIMS as an Assistant Professor in 1965. He became Professor and later the head of the department in 1993. He was also elected unopposed as the President of the Indian Pharmacological Society. He was a member of several prestigious committees such as the Scientific Advisory Committee of the Drugs for Neglected Diseases Initiative, Geneva, Drugs Technical Advisory Board, Investigational New Drug Committee, National Pharmacovigilance Steering Committee, and other committees of the Indian Council of Medical Research (ICMR), Council for Scientific and Industrial Research, Department of Science and Technology, Department of Biotechnology, and the Ministry of Health. He founded the National Poisons Information Centre at AIIMS, and was also the Chairman of the Forum for Ethical Review Committee of India, Institutional Ethics Committee of ICMR, and Ethics Committees of National Institute of Medical Statistics, ICMR, Sir Ganga Ram Hospital, and National Dope Testing Laboratory, New Delhi.

Professor Seth is one of the most prominent Pharmacologists of India. His contributions in the modern medicines are very well known but his contribution in Traditional Medicines are little known. Probably he was the first person to conduct Pharmacological study on Arjuna Bark for its cardio protective activity on isoproterenol model long ago. Still, it is one of the most commonly used models for such studies. Being expert in Cardio-vascular Pharmacology, Professor Seth guided development of an Ayurvedic Cardio protective product as well as Hypolipidemic agent based scientific studies. Prof. Seth also guided regulatory studies of Ginger extract for Chemotherapy induced vomiting. It is one of the only three herbal drugs approved as modern drug by Drugs Controller General of India.

Post superannuation from AIIMS, New Delhi, Professor Seth continued to contribute in the development of Traditional Medicine during his tenure at Indian Council of Medical Research. It was during his tenure that National Innovation Foundation got approval for major product development on Traditional Medicine based on folklore use. Professor Seth was instrumental in establishment of National Institute of Traditional Medicine at Belgaum in Karnataka under ICMR. Professor Seth also played a major role in developing Good Clinical Practices (GCP) for ASU drugs through Central Council for Research in Ayurveda and Siddha where he was member of the Scientific Advisory Committee for a long time. He is credited with more than 350 publications including research articles, books, and monographs.

Prof. Pratip Kumar Debnath

Born in 1946 in a traditional Ayurveda family with outstanding heritage; was a retired Professor of Kayachikitsa from JB Roy State Ayurvedic Medical College & Hospital, Kolkata. He was trained under Prof. YN Upadhaya during his post-graduation period and shifted to the Department of Pharmacology for Ph.D. under Prof. AK Sanyal. In his 47 years of professional carrier, he served different institutions in various capacities including CCIM, CCRAS, ICMR, AYUSH, UGC, DST, BHU, and UPSC. He was also a member of Academic Committee, School of Natural Product Studies, Jadavpur University.

His clinical researches with Ayurveda formulations on gastric pharmacology, as add-on therapy with anti-tubercular drugs, immunomodulatory activity of Ayurveda Rasayana formulations on stress adaptation etc. have helped him to work on HIV/AIDS project with NACO, Ministry of AYUSH and ICMR. He had worked with more than 50 medicinal plants and published more than 150 research papers.

He was member of several International and National scientific organizations, visited European and African countries including London, Malaysia, Italy, Cameroon, Nepal, Bangladesh etc. and involved in scientific deliberations. Elected President, Indian Science Congress Association (Medical & Veterinary), appointed as expert by Government of India on Traditional Medicine for WHO. Parallel to Ayurveda researches, Prof. Debnath exclusively contributed in the field of Sports Medicine. He was nominated during ASIAD games (1982), SAF games (1986), Santosh Trophy, National Volleyball, National Kabbadi, National aquatic meet, Asian Archery Competition, Asia Cup Football, World long distance swimming etc.

He is recipient of Uvna's Prize, Fellowship of National Ayurvedic Academy, Fellow of Indian Pharmacological Society.

Acharya Priya Vrata Sharma

Prof. Sharma, a great academician and researcher, born in 1920 in a small village near Patna, in the family of traditional Vaidyas, completed his Ayurveda education in BHU in 1940. Besides, he was proficient in Sanskrit, Hindi and English along with Grammar, Literature, History, and Philosophy. Prof. Sharma was also awarded Saahityaacharya in Sanskrit. Before joining as Professor in department of Dravyaguna at BHU, he served at various places in different capacities. Later he became Director, Post Graduate Institute of Indian medicine (PGIIM), BHU. After a span of time, he was made Dean, Faculty of Ayurveda. Prof. Sharma superannuated from his services in 1980.

Prof. Sharma worked in three major areas viz. Dravyaguna, Itihasa (history) and Ayurvedic Manuscripts. He always thought that the contemporary modern medical knowledge should be imparted to Ayurvedic students and to fulfill the same he actively encouraged the experimental and clinical research in the field of Dravyaguna. He made notable contributions in Dravyaguna like standardization of single drugs and finished products. Vision of Prof. Sharma was accepted and made him member of various Ayurveda committees by Government of India. He was invited to participate in conferences and symposia across the country and globe.

The scientific contribution of Prof. Sharma is outstanding and amazing. He was a pioneer in creation of new authentic ayurvedic literature in 20th century. He was the one who considered publications as the foremost in disseminating the knowledge and published his first article on Santata and Vishamajwara (malarial fevers) in 1941 and published about 395 research papers in the life time. Prof. Sharma authored various books including Dravyagunavijjanana, Introduction to Dravyaguna, Fruits and vegetables in Ancient India, Dalhana and his Comments on Drugs, Priya Nighantu, Dravyagunasutram, Classical uses of Medicinal Plants, Dravyagunakoshah, Pushpaayurveda, Namarupajnanam, Susruta Samhita – Saptaadhyayee mein Vanaspatiyam aur anya dravya. Prof. Sharma made outstanding and unchallengeable publications in the field of History of Ayurveda too. To refer a few are Vaaghbhatavivechans, Charakachintana, Indian Medicine in Classical Age, Ayurved ka vaijnanik Itihas etc. Books on Ayurvedic Physiology including Sarirkriyaavijnana, Rogiparikshavidhi, Shodasanghrudayam, Essentials of Ayurveda are also his important contributions. Prof. Sharma edited History of Medicine in India, which is the prestigious publication of Indian National Science Academy. He also wrote a book on Ayurvediya Anusandhana Padhdhati (research methodology for Ayurveda) in 1976, which is first of its kind. He edited a number of Sanskrit Medical Manuscripts, which were hitherto unknown in the Ayurvedic world. His command on Sanskrit Language is unparallel. He proved this by publishing Sriramavataracharitam and Vasanta Shatakam.

He was a voracious reader, prolific writer, orator, teacher, researcher, leader, administrator and above all a good human being, which was accepted equally by his admirers and adversaries. His dedication, hard work and conceptual thinking, simplicity, dutifulness and discipline made him unique and incomparable. He created new path not only for his ownself but also for many others to follow.

Prof. Krishna Chandra Chunekar

Prof. Krishna Chandra Chunekar, an Ayurvedic scholar, practitioner and writer, known for the books he published, born in 1928. He completed his Ayurveda education from Banaras Hindu University and served in the Department of Dravyaguna of the same university for about 30 years. He supervised theses of several scholars during the period. He also served as a visiting professor at the Gujarat Ayurveda University, Jamnagar.

Prof. Chunekar is considered by many as an authority in the identification of ayurvedic herbs. His experience helped many research scholars in their researches and doctoral studies while his service was hired by the World Health organization to supervise preparation of Herbal Formulary of Essential drugs of Ayurveda in Nepal. He has served on the scientific advisory committee of the Indian Council of Medical Research and was a senior expert advisor for the Traditional Knowledge Digital Library Project of the Council for Scientific and Industrial Research. He contributed immensely as member, Scientific Advisory Committee (Indian Medicine), CDRI, Lucknow; member, ICMR Expert Committee on Illustrated Manual of Herbal Drugs Used in Ayurveda; member, Ayurveda Pharmacopoeia Committee, Ministry of AYUSH. He also rendered his services as expert teacher of National Academy of Ayurveda, Ministry of Health & Family Welfare, Govt. of India. He has contributed in several books on Ayurveda.

Prof. Chunekar, was awarded the fellowship by the National Academy of Ayurveda. He was also awarded the title of Guru by the Government of India, was a recipient of Sri Gyaana Kalyaana Award, and The Government of India awarded him, the Padma Shri in medicine, the fourth highest civilian award, for his contributions.

Prof. SP Thyagarajan

Prof. SP Thyagarajan, Professor of Eminence has made extraordinary contribution in the field of Medicinal Plant Research and Ethnopharmacology. He is a D.Sc. in Microbiology in addition to his Ph.D. He is forerunner for standardization and development of scientific validation protocols of the Indian System of Medicine. He has also been conferred with several fellowship titles including those by National Academy of Sciences and National Academy

of Medical Sciences. He has put in 37 years of teaching and research experience, supervised more than 100 students during the period. He has completed about 57 research projects funded and published 320 research papers, 16 books in the area of infectious diseases especially hepatitis, STDs and HIV/ AIDS. He had conducted international collaborative projects with scientists from 26 countries including USA, UK, Australia, New Zealand, Japan etc., with mutual visits to these countries.

His research contributions have been recognized by 21 international and national awards. The awards of excellence include the Consultant Epidemiologist award of Glasgow University, UK; ICMR award in Virology and Kamal Kumari National award in Science and Technology; Dr. SC Agarwal Prize; IAMM Endowment Award; Dr. HI Jhala Award of Indian Association of Medical Microbiologists; DrPran Nath Chhuttani Oration Award of the National Academy of Medical Sciences; the Italian Chavelier-Order of Merit of Italian Republic Award; SFE Lifetime Achievement Award-2017, by Society for Ethnopharmacology, India. He is the inventor of a drug for the treatment of Hepatitis-B from the Indian medicinal plant, *Phyllanthus amarus*. He has also awarded various patents in USA, UK, South Africa and North Korea for this discovery on the name of University of Madras. He additionally holds three more Indian patents. He was the member of expert committees of UGC, ICMR, DST, DBT, Ministry of Health, WHO etc.

Prof. Thyagarajan has served the Madras University in several administrative positions. Prof. SP Thyagarajan, on completion of his term as Vice Chancellor of University of Madras, has taken over the position of Pro Chancellor (Research) at Sri Ramachandra University. He has set up the Central Research Facility as a unit to cater for basic medical research leading to Translational medical research in the University under one umbrella with an University Industry Interaction Centre to facilitate R&D projects and clinical trials for biotechnology and pharmaceutical industries.

Prof. CK Atal

Professor CK Atal, an internationally reputed research scientist, is renowned all over for his outstanding original contributions and pioneering work in the field of plant and medicinal plant-based disciplines. He has achieved the feat of being one of the uncommon but truly multidisciplinary research scientists whose contributions have had major global impact in a wide variety of fields. Prof. CK Atal has been a pioneer in Pharmacognosy in India, who revolutionized Pharmacognosy as a subject, as a teacher, researcher and scientist. He is one of the first Pharmacognosists of India. The multidisciplinary range and vast depth of his work can be seen in more than 550-600 scientific research publications in national and international journals, an uncommon occurrence. He is an award-winning scientist, researcher,

BRIEF BIOGRAPHIES OF FEW EMINENT CONTRIBUTORS TO AYUSH

discoverer, teacher, author, writer, administrator, historian, artist, art patron, critic, and collector all combined in one.

Born on 4th November, 1928, Dr. CK Atal was a brilliant student completed his M.Pharm under the able guidance of renowned Botanist, Prof. PN Mehra, gaining teaching and research experiences. With the support of Tata endowment fellowship (Tata Foundation), he travelled to USA in September, 1954; completed his PhD in 1957, in Pharmacognosy and Phytochemistry based on the works on *Withenia somnifera* under the eminent Pharmacognosist of USA, Prof. AE Schwarting. *Withania* later came to be internationally highlighted for its medicinal properties. He was exposed to a variety of subjects such as Plant physiology, Biosystematics, Experimental taxonomy, Statistics, Genetics, Plant breeding, identification of structures of new compounds from plant microbiology, plant tissue culture and submerged culture in fermenters etc. Joined a teaching assistantship at the University of Connecticut, USA, became President, International affairs at the same University. Held many key positions including Chairman, Department of Bio-Sciences, the Creighton University, Omaha, Nebraska, USA; Dean, Head, Department of Analytical chemistry Creighton University. He was involved with research on pharmacognosy, natural product chemistry, pharmacology, analytical chemistry and standardizations.

Armed with the latest technology and broad-based knowledge gained in USA, Dr. Atal returned to India and was appointed as the Head, Department of Pharmacognosy and Phytochemistry at Punjab University, Chandigarh. He was involved in teaching students introducing latest techniques and instrumental methods of research which he had acquired in USA. He worked under the ICMR multidisciplinary research units, and also continued the process of publishing research papers in scientific journals, which grew in numbers with the passage of time. He became the youngest assistant director in CSIR at Regional Research Laboratory, Jammu. Soon, was promoted to become Director, which he held as a record longest serving Director in CSIR. Dr. Atal formed a team of multidisciplinary task force that produced several significant and major breakthroughs in research. A large number of departments were created to pave way for multidisciplinary research, while old departments were revamped and modernized. Time bound programmes, well defined targets, induction of young talent and modern technology was employed that started yielding goal-oriented results. This resulted in introduction of many turn key projects. He was invited by United Nations as chief technical advisor to United Nations, Vienna, Austria for implementing UNDP projects in South East Asia. He handled five UN projects.

He is recipient of innumerable awards, honors, internationally recognized discoveries, member of various governing bodies under Government of India. Dr. Atal has been invited by various international

agencies as a mission consultant to their various projects. He has written many books, some of them world reference books and also officially recommended in the Pharmacy colleges of India. His two volumes book on cultivation and utilization of medicinal and aromatic plants is used officially in curriculum in Pharmacy colleges of India and is in demand all over the world.

Prof. Gurdip Singh

Born in Rayatpur, Bhind district Madhya Pradesh in 1941; completed his basic Ayurveda education from Gwalior, post-graduation and PhD (in Kayachikitsa) from Banaras Hindu University. Joined as lecturer in the department of Kayachikitsa, Gujarat Ayurved University, Jamnagar, Gujarat in 1977 and served there until his retirement. Post retirement, he continued his services as honorary director of PG studies and Research at Sri Dharmasthala Manjunatheshwara (SDM) College of Ayurveda, Hassan, Karnataka.

While serving at Jamnagar, he made many revolutions in Ayurveda education. He introduced statistics in Ayurveda researches while keeping the essence of Ayurveda intact, by inventing the symptom score at Jamnagar. He set convention of reading classical texts of Ayurveda in Sanskrit by Sandhi-Vicheda that provided confidence in their Sanskrit knowledge and now adopted by many scholars across the country. Sensing the need of globalizing the Ayurveda knowledge across the sea; he initiated conducting short-term orientation courses in Ayurveda for foreigners at Jamnagar. Besides, he initiated conducting re-orientation programs for Ayurveda physicians and teachers to improve and upgrade their clinical skills and knowledge. He designed and supervised the construction of Trigarbha Kuti based on the Vaidik concept for undertaking Kayakalpa Rasayana therapy. Recognizing the importance of providing scientific basis for traditional wisdom, he planned and established experimental laboratories including pharmacology and a well-equipped Vajikarana laboratory. He is the first one to initiate experimental and clinical research for proving Immunity promoting effects of Ayurveda Rasayana drugs in Ayurveda institutes.

His Ayurveda career is enriched with 54 years of experience in different capacities including teaching, research, clinical and administrative aspects. During the period, he supervised more than 100 students. He has published about 150 research papers authored and coauthored many books and monographs.

Dr. Singh has closely associated in establishing Ayurveda College for Israel students at Reidman College for Complementary and Integrative Medicine at Tel Aviv. He stayed three months in UK to supervise establishing MSc (Ayurveda) course at Ayurveda College of Middlesex University, London. He visited France to provide guest lectures, conducted seminars for general

public and organized certificate courses in Ayurveda at Tapovan University. He visited Germany on the invitation of Berlin Medical Association and Hungary to deliver lecture on Ayurveda to modern doctors, Ayurveda professionals and public as well.

Considering his outstanding contributions to the field of Ayurveda; he received many awards including Rashtriya Dhanvantri Award, from the Department of AYUSH; Fellow award (RatnaSadasya) by Rashtriya Ayurveda Vidya Peetha, Ministry of AYUSH; Hari Om gold medals for contributions in Ayurveda clinical research; Gold medal by Ayurveda Academy, Andhra Pradesh; Sunderlal Joshi Puraskar, Gujarat; Best teacher award, from All India Ayurveda Teachers Association, Delhi etc..The Government of India awarded him, the Padma Shri in Medicine, the fourth highest civilian award, for his contributions. Dr. Singh's contributions to Ayurveda are inspiring and noteworthy.

Vaidya PR Krishna Kumar

Vaidya PR Krishna Kumar, an embodiment of Ayurveda was born in 1951. After completing his schooling in Coimbatore, he moved into a traditional form of education in Ayurveda. He has always stood for scientific validation of Ayurveda, and incorporation of the best of modern science in clinical practice, without compromising traditional standards. It was with this intention that he supported the creation of the AVT Institute for Advanced Research (AVTAR) to conduct clinical, literary, field and drug researches and to train aspiring Ayurveda scholars. He had always felt that only a scientifically validated Ayurveda could achieve global acceptance. He has successfully implemented a number of projects approved by the Department of Science and Technology and Department of Environment in various areas and topics related to Ayurveda.

One of his noteworthy contributions included the initiation and setting up of a clinical trial on rheumatoid arthritis at Coimbatore between sponsored by WHO and ICMR. In recognition and honor to that, National Institutes of Health (NIH), USA, funded a clinical trial project through University of Washington which was a great success. The second and perhaps most important contribution of Vaidya Krishna Kumar was to conceive, organize, establish and run a seven and a half year Ayurveda degree course (Ayurvedacharya) recognized by the CCIM and affiliated to the Madras University, which ran as a successful pioneering and path breaking Ayurveda degree program where students and teachers lived together in a 70-acre forest campus, where students were introduced to the classical Darshanas, Kalaripayattu, Yoga, Meditation, Sanskrit grammar and ancient Sanskrit literature by experienced teachers and professionals. The interest of Vaidya Krishna Kumar was not only in Ayurveda but also in India's cultural heritage

in toto. In association with Prof. Prema Pandurang, he established the Kshetropasana Trust to revive old temples, bring back temple rituals and culture attached to them. To revive the Indian visual and performing arts, he established Bharatamuni Foundation for Asian Culture. "Sharanagathi" an old age home for unattended parents was another contribution of his. To orient Ayurveda graduates to clinical practice, he started 'Tatvaprakashini' and 'Karmaprakashini', annual programs for theoretical and practical training in clinical Ayurveda. All over India, thousands of students have benefited from these programs. The International Institute of Ayurveda (IIA) was established by him in 1980 which has given a significant outcome of "Ancient Science of Life" an international popular journal. He also started an informal school "Divyam" for learning the Indian sciences in traditional ways.

The AVP foundation launched a clinical documentation program, called RUDRA, to promote practice-based evidence in Ayurveda. He was the chancellor of the Avinashilingam University, and the chairman of Confederation for Ayurvedic Renaissance, Keralam. For his remarkable contributions, The Government of India awarded him the fourth-highest civilian honour, Padma Shri in the field of medicine in 2009. Shri PR Krishna Kumar, a man with multiple personalities, who contributed immensely in several domains, will be remembered eternally.

Dr. PK Warriar

Dr. PK Warriar born in 1921, is a distinguished scholar of Ayurveda who represent everything authentic and pristine about the science. He played a historical role in invigorating the traditional practices of Ayurveda by his significant contributions to research and innovative experiments. He also took this holistic science to distant shores of the world ever since he assumed charge as Managing Trustee in 1954. As the Managing Trustee and Chief Physician of the 116-year-old Charitable Trust, the Kottakkal Arya Vaidya Sala (AVS), he has rendered significant service for the upgradation and expansion of Ayurveda by modernizing its clinical, pharmaceutical, educational and research domains. Added to all that, he is an illustrious clinician of international repute and have healed many thousands of people across the globe, including most respected dignitaries like Sri AB Vajpayee, Sri Pranab Mukherjee, Sri KJ Yesudas and many more renowned persons.

He brought some revolutionary changes in the pharma industry by incorporating the principles, methods and tools of industrial technology in drug manufacturing. Three manufacturing units under his able guideship all together produce about 530 classical formulations and 37 "new generation formulations" which are all recognized as "golden standards" of authentic Ayurveda. Another most significant contribution was to introduce patient compliant Kashayam tablets, dose regulated Bhasma capsules into the market. These innovations have endeared Ayurveda to the younger generation.

Research is another area where he has rendered his remarkable contribution, which includes a vigilant study on 7000 cancer patients and evolving a unique package of formulations to deal with different types of cancer; setting up of Centre of Medicinal Plants Research at Kottakkal etc. It undertakes research in the areas of photochemistry, taxonomy, pharmacognosy and tissue culture on behalf of national bodies like ICMR, DBT, DST, AYUSH, NMPB, etc. It is now recognized as a Centre of Excellence by the Ministry of AYUSH. The five-volume treatise "Indian Medicinal Plants - A Compendium of 500 Species", which he co-authored, amply represents his dedication to scientific research and documentation in Ayurveda.

He held prestigious positions in Pharmacopoeia Commission for Indian Medicine, Central Council of Indian Medicine, Central Council for Research in Ayurveda and Siddha etc. Adding to the glory of his commendable work, he has received many national and international recognitions. Govt. of India conferred him with the honor of Padma Shri in 1999 and Padma Bhooshan in 2010. He was awarded with Doctor of Medicine by Copenhagen University, Denmark. He has been recognized for his literary excellency with Kerala Sahitya Academy Award for his autobiography 'Smritiparvam' in 2009. Pandit Shiv Sharma Oration Award was presented to him by IASTAM. Vaidya Yadavji Trikamji Award for Best Statesmanship in Ayurveda. Bhoopalmansingh Korki Award from Katmandu, Nepal; Sevanaratnam Award by National Association for Science and Arts, Thiruvananthapuram.

Prof. Madhaw Singh Baghel

Prof. MS Baghel is born in 1953, is a renowned clinician, academician and researcher with an experience of about 35 years. He is specialized in the areas of Kayachikitsa, Panchakarma and Roganidana. He is the former Director, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, India. He also served as in-charge Vice Chancellor, Gujarat Ayurveda University. Recognizing the importance of Pharmacovigilance; he recommended Ministry of AYUSH to extend the program to AYUSH drugs also. He was the first Director, Pharmacovigilance Program for ASU Drugs. He also served as Director, International Centre of Ayurvedic Studies, Jamnagar where he contributed significantly in the global propagation of Ayurveda.

He has supervised about 100 theses, many of whom are holding top positions in the country today. He published about 149 Research papers and authored various books and monographs. As the Editor-in-Chief of the prestigious AYU Journal, his efforts achieved significance in terms of citations. One of his main contributions includes Researches in Ayurveda (A Classified Directory of All India PG & PhD Theses) A Searchable directory of titles of all India Ayurvedic PG and PhD theses that include about 20000 titles.

His played a pivotal role in designating IPGT & RA as the WHO Collaborating Centre for traditional medicine (Ayurveda). Developing Standard life style guidelines under the activities of WHO Collaborating Center; Standardization of clinical terminologies of Ayurveda; Manual on simple Ayurvedic herbal formulation for common ailments; International Catalogue of Ayurvedic publications; Model recruitment rules for AYUSH personal under an APW Project of WHO, India-Country Office are his contributions. He is on the boards of various journals like AYU, JAIM etc. as advisor. Dr. Baghel has delivered more-than 180 lectures on national as well as international platforms, invited for attending WHO consultation meetings and represented Government of India at multiple levels. He had served as Chairman, Ayurveda Chair in Medical School, University of Debrecen, Hungary. Travelled across the globe to deliver lectures, attend consultation meetings and represented Government of India at various instances in different countries including London, Srilanka, Florida, France, Netherlands, Hungary, China, Switzerland, Germany, Russia, France, South Korea, Italy.

He has received many awards including Ayurveda Martanda by All India Ayurvedic Specialist (PG) Association, New Delhi; Vishva Ayurveda Ratna by International Academy of Ayurvedic Physicians; Ayurveda Bhushana, by All India PG (specialist) Association; Ram Narayan Sharma Best Teacher Award by All India Ayurvedic Teachers Association of India; Fellow of Rashtriya Ayurveda Vidyapeetha, Ministry of AYUSH, New Delhi; Dhanvantari Award by Hungarian Ayurveda Medical Foundation, Budapest.

He was nominated by CSIR as member of Advisory Board of Institute of Genomics & Integrative Biology, New Delhi. He also served as member of Scientific Advisory Body of CCRAS, New Delhi. He was an active member at various committees including PAC, Ministry of AYUSH; National AYUSH Mission; Governing Body & Executive Body of All India Institute of Ayurveda; Scientific Council, Zandu Foundation for Health Care. Currently, he is Chief Ayurveda Consultant, Emami Limited since 2018. He has created new path not only for his own self but also for his students through his dedication and quest for learning.

Prof. Marthanda Varma Sankaran Valiathan

Dr. MS Valiathan is an Indian cardiac surgeon. He was an erstwhile President of the Indian National Science Academy and National Research Professor of the Government of India. He has made great contributions to medical sciences and technology through developing Chitra-TTK, valveoxygenator and cardiotomy reservoir. Currently, Dr. Valiathan is engaged in promoting research in basic sciences, based on clues from Ayurvedic concepts and procedures. He has pioneered various scientific studies in the field of Ayurveda and authored several books on the subject. He has also been

serving as the Chairman of the Task Force in Ayurvedic Biology of the Department of Science and Technology.

In 1994, Dr. Valiathan became the Vice-Chancellor of the newly set up Manipal University. In 1999, he was awarded a Senior Fellowship by the Homi Bhabha Council to pursue a study of Charaka, which culminated in a book entitled Legacy of Charaka published by Orient Longman in 2003. The companion volumes on the Legacies of The Great Three of Ayurveda - Susruta and Vagbhata were released by the same publisher in 2006 and 2009. Another book An Introduction to Ayurveda has also been released by the same publisher in 2013. He has also given a course of video lectures on The Ayurvedic Inheritance of India.

He is a recipient of many Awards for Science, Technology and Education, which include the RD Birla Award; OP Bhasin Award; Jawaharlal Nehru Award; Dhanwantari Prize; Aryabhata medal; Basanti Devi Amirchand Prize; JC Bose medal; Kerala State Science and Technology Award; BC Guha Award; Pinnamaneni Foundation Award; Sat Pal Mittal Award; GM Modi Award; MV Pylee Award; HK Firodia Award and the Sastra Puraskaram of the Kerala Government etc. He received the Dr. Samuel P Asper International Award from the Johns Hopkins University, USA for his contributions to medical education. For his remarkable contributions, The Government of India awarded him, Padma Vibhushan in 2005 for his contributions to health technology in India. His works have always been setting new grounds for integration of sciences.

Vaidya Chandrakant Prabhushankar Shukla

Dr. Chandrakant Prabhushankar Shukla was an educationist and teacher. He is known as Charaka Vaidya for his profound knowledge of Charaka Samhita, and his expertise in putting it into practice. He has been considered as an 'encyclopedia' in Ayurveda. In 1944, Vaidya Shukla has joined Gulab Kunvarba Ayurved Society, Jamnagar for the translation of Charaka Samhita and joined as professor in Ayurvedic College, Jamnagar. There he worked in the domains of teaching, as a physician, head of the clinical research and administrator too. His principles of education include patient-based learning, consideration of psychological aspects in the management and inclusion of modern techniques for understanding the disease, ayurvedic principals and diagnosis.

His literature contributions include Charaka Samhita translation published by Shree Gulabkunveraba Ayurveda Society, Jamnagar; Home and domestic medicines published by Central Council of Research in Ayurveda and Siddha (CCRAS) New Delhi.

He has been awarded Fellowship of Rastriya Ayurveda Vidyapeeth; Ayurved Martanda, Maharshi Award, Ayurveda Chudamani, Shree Jagatram Vaidya Award for excellence in ayurvedic teaching. Though past 80, he still worked as an Ayurveda physician. He was very forward thinking and underlining the need for instituting programs of research and development in Ayurveda. He has also served as an advisor to the Public Service Commission, Gujarat Public Service Commission; Service commission, BHU; Madhya Pradesh PSC; Rajasthan PSC.

Prof. Ram Harsh Singh

Prof. Ram Harsh Singh is a life time Distinguished Professor in Faculty of Ayurveda at Banaras Hindu University. He has played commendable role in revival and development of Ayurveda and its scientific validation which has accelerated the process of its mainstreaming in India and its globalization. His work has helped setting trends in Contemporary Ayurveda.

Prof. Singh born on Jan.10, 1942 graduated in Ayurveda from Banaras Hindu University, did Ph.D. and D.Litt. He is Fellow of National Academy of Indian Medicine and is a Jewel Member of All India Ayurveda Academy. Professor Singh has produced over 80 MDs and 40 Ph.Ds under his guidance, many of whom are holding top positions in the country. He has published 20 books and 200 research papers in National and International Journals. He is on the Editorial board of several National and International Journals.

Prof. Singh joined the Faculty of Ayurveda at Banaras Hindu University in 1964 and served for 40 years in the capacity of Professor and Dean of the Faculty after which he joined the Rajasthan Ayurved University of Jodhpur as its First and Founder Vice Chancellor.

Prof. Singh is the Member of National Commission on History of Science, INSA. He is the recipient of the prestigious Triguna Award; Ram Narayan Sharma National Research Award; Hari Om Ashram Award; IASTAM Award of Asian Medicine; Life-time achievement Award of AIIMS; Kasturba Oration Award; Platinum Jubilee Oration Award of Indian Science Congress and Distinguished Alumnus Award of Banaras Hindu University. Prof. Singh has been honored by the President of India with prestigious civilian award Padma Shri in 2016. He has widely traveled all over the world to promote Ayurved globally.

Prof. Singh has been the Chair Professor at Wonkwang Digital University, Republic of Korea and a Visiting Professor at Mount Madonna Institute of Creative Science and Arts, USA. He has been working as Emeritus Professor and now is the Life-time Distinguished Professor at Banaras Hindu University. He is designated as Ayurved Guru by RAV under the Ministry of

AYUSH, Govt. of India and has been the Chairman of the Scientific Advisory Board of CCRAS. He has been the Chairman of AYUSH sector Innovation Council constituted by Govt. of India.

Prof. Singh is an extremely popular Ayurvedic Physician practicing Ayurvedic medicine on classical lines with scientific temper. He is a successful and extremely popular teacher and a researcher in his field of specialization. He has been seriously engaged in revival and development of Ayurved on scientific lines as an evidence-based system of Medicine and has extended commendable help at National level in educational reform in AYUSH sector.

The research interest of Prof. Ram Harsh Singh has been the chronic disease management and Geriatric health care including Mental health with attempts to evaluate the safety and efficacy of Ayurvedic drugs and therapies specially Rasayana Therapy. Through his teachings, deliberations in innumerable national and international forums and publications, Professor Singh has extended commendable help in bridging the gap between traditional and conventional systems of medicine promoting Medical Pluralism and its mainstreaming.

Prof. Prabhakar Janardhan Deshpande

Prof. Prabhakar Janardhan Deshpande, born on in 1925, is an outstanding alumnus of Banaras Hindu University, Varanasi. He joined BHU in 1941 in AMS course, completed it with Gold Medal. Further, he obtained special training in Medicine and Surgery at KEM Hospital, Mumbai. He joined at BHU as lecturer in Anatomy and also served as lecturer in Clinical Surgery and as Emergency Medical Officer in SS Hospital, BHU till 1951. Later, he pursued post graduate studies at Vienna Academy of Medicine, Austria and joined back to his services at BHU. With the support of United States Public Health Scholarship, he served for two years at the University of Oregon Medical School, Oregon, USA, where he extensively contributed in the field of Surgery. On returning to India, he joined Department of Shalya-Shalaky Tantra, BHU became professor and later served as Dean, IMS, BHU and superannuated in 1985. Dr. Deshpande is known for his revolutionary contribution in the field of Kshara Sutra, a classical technique for the treatment of Fistula-in-ano and developed standard methods of its preparation.

Besides being a surgeon; Dr. Deshpande was a reputed athlete of the University. He won championships in Wrestling, Weight lifting and Boxing. He completed the Indian Air Training Corps Examination, Conversion Course at AFMS.

He was the recipient of many honors for his extraordinary contributions. He received Gold medals by Central Council of Ayurveda, Ministry of Health, GoI, New Delhi (1966) and by Academy of Ayurveda,

Vijayawada (1967); Honorary Fellowship of International Academy of Proctology, USA (1972); Gold medal by Gujarat Ayurved University, Jamnagar, (1975); Hari Om Ashram Trust Award (1976); Fellowship of Royal Asiatic Society, London (1976); Sushruta Oration Award by National Integrated Medical Association (1981); Ayurveda Martanda by Akhila Bharatiya Ayurveda Mahasammelan(1981). He was offered visiting professorship at Medical School, San Francisco University of California, USA (1972); University of Oregon Medical School, USA (1972); at University of Wisconsin, Madison, USA (1972); at Gujarat Ayurveda University, Jamnagar, Gujarat, India (1974 to 1985). Dr. Deshpande was member in different associations, societies and bodies in India and abroad. He was the member of the International Board of Proctology, USA; Member, Royal Asiatic Society, London, UK; International Polypathic Society; International Board of Ragants of Proctology. Dr. Deshpande has published about 235 research papers and supervised about 100 theses.

Prof. Vinayak Jayanand Thakar

Prof. VJ Thakar, born in 1920, was a great teacher of his times, said to be National Professor for Charaka Samhita considering his profound knowledge of the classic and his expertise in putting it into practice. Completed his education at Banaras Hindu University, Varanasi and held various teaching, clinical, research and academic positions at Gujarat Ayurved University, Jamnagar. Prof. Thakar completed Sanskrit courses of Sahitya Shastree, Kayva Tirtha and was proficient in Sanskrit. He had a good command over three languages (Hindi, English and Gujarati) and published eight books. Anupana Manjari, Ayurvediya Manulika Siddhantah, Purusha vichaya, Research Methodology in Ayurveda, Diagnostic methods in Ayurveda, Srotovijnana, Aushadh karma vigyana are the books that are familiar among Ayurveda professionals. He served academic dean and two terms as Vice-chancellor at Gujarat Ayurved University, Jamnagar.

He was the recipient of many awards including National Research Award (1996); Gold Medal from Hari om Asharm; Gold Medal from Academy of Ayurveda, Vijaywada; FRAV, Rashtriya Ayurveda Vidyapeeth; Bruhatrayi Ratna Award from Arya Vidya Ramavariar Memorial Trust, Coimbatore; Ayurveda Kesari; Ayurved Martanda from Ayurveda Mahasammelan etc. He published about 70 research papers and supervised about 75 theses.

His dedication, hard work and conceptual thinking, simplicity, dutifulness and discipline made him unique and incomparable. He created new path not only for his own self but also for many others to follow.

Dr. Hanmanthrao Sambaiah Palep

Born in Polasa, Telangana, in the year 1938, **Hanmanthrao Sambaiah Palep**, completed his school education in 1955, graduated in Ayurvedic Medicine from RA Podar Medical College, Mumbai in 1962. Thereafter he completed MBBS and MD in Modern Obstetrics and Gynecology from Grant Medical College, Mumbai in 1973. He is the pioneer of modern scientific researches in Ayurveda and a leading consulting obstetrician and gynecologist with a large clinical and surgical experience. Currently he is the National Professor and visiting scientist to Haffkine institute of research & testing, Parel, Mumbai. He is the founder chairman of Dr. Palep's Medical Research Foundation Pvt. Ltd. and Dr. Palep's Medical Education & Research Trust, Mumbai.

Dr. Palep has spent a major part of his prolific years in imparting knowledge both in India and abroad. Dr. Palep has held the post of Hon. Professor at Grant Medical College and Professor at RA Podar Medical College for more than two and half decades. He is a pioneer in integrative approach in medicine. He is instrumental in starting a first integrative medicine department at KJ Somaiya Medical College, Hospital and Research Centre in Mumbai. His zeal and vision led him to decipher the language of Ayurveda into modern scientific language resulting into authoring a book titled, Scientific Foundation of Ayurveda in 2005. He is the founder chairman of Dr. Palep's Medical Research Foundation Pvt. Ltd. and Dr. Palep's Medical Education & Research Trust, Mumbai. Dr. Palep is a well-known educationist. He has cofounded a library in 1967, named Vivek Granthalaya in Mumbai. Dr. Palep has presented and published many research papers in conferences, seminars and journals, both national and international spreading the message of scientific base of Ayurveda. He is working on Panchagavya, microbiome and involved in a RCT on Covid-19 with AYUSH Interventions at BYL Nair Hospital, Mumbai. Currently Dr. Palep is the working president of Indian National Fellowship Center, which has dedicated itself for the service of North East states.

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AN OVERVIEW OF CONTRIBUTIONS OF MINISTRY OF AYUSH TO RESEARCH IN AYURVEDA

Dr. Rajeshwari Singh, Research Officer (Ayurveda), CCRAS

The Indian System of Medicine (ISM) has a long tradition of usage. Many thoughts came together to develop a way of healthy living esteemed with protracted and distinctive cultural history, as conjointly amalgamating the best of impacts that rolled in from contact with other civilizations like inculcating the Unani and Homeopathy in our healthcare system. These antiquated systems of healthcare have evolved over centuries blessed with a plethora of traditional medicines and practices.

An independent Department of Indian Systems of Medicine and Homoeopathy (ISM&H) was established in 1995 to ensure the peerless growth and propagation of AYUSH systems of health care. It was rechristened as the Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy with acronym as AYUSH in November, 2003; Sowa Rigpa was added further in acronym in 2011. Further on, the department of AYUSH was granted as Ministry of AYUSH under government of India on 9th November, 2014 to ensure the optimal development, propagation and popularization of AYUSH systems of health care not in the country but also at global platform.

Genesis of formation of Department

The development of AYUSH systems was a part of 5- year plan process since 1951. The progressive growth could be noted by reviewing these 5 years plan. The development was not so noteworthy until 8th five year plan. A separate department was created in 1995 during 8th five year planning (1992-1997) to ensure the growth, development and propagation. This plan suggested that ISM and H practitioners can play an important role in primary health care delivery. This plan also advocated the strengthening of the infrastructure, capacity building, training of teachers, research and development, standardization and enforcement of Drug and Cosmetics Act,1945. However there was a notable growth of AYUSH practitioners from 4.5 lakhs at the beginning to 6lakhs at the end of 8th five year plan. These points were also were accounted in the 9th five year plan (1998-2002) wherein there was a mention of AYUSH in various segments. This plan is mainly focused on the improvement of the healthcare facilities at primary, secondary and tertiary care, quality of services rendered by AYUSH practitioners, promotion and cultivation of medicinal plants, pharmacopoeia, encouraging good manufacturing practices to ensure quality control of drugs.

Apart from these, there was also an emphasis on research and development through strengthening of the central research councils and interfaces with other research agencies. Mainstreaming and revitalization was also proposed for the first time during this five year plan. Apart from the issues which were accounted in the 9th five year plan were also extended to 10th five year plan (2002-2007). The plan suggested the accreditation system of ISM&H education for the first time in AYUSH, revival of continued medical education (CME) for periodic updating of knowledge and skills and AYUSH practitioners and inclusion of AYUSH professional at the all level of healthcare. It was noticed that these healthcare professional were also not involved in national disease control programs or family welfare programs during the 10th plan. This issue was further taken up during the 11th 5-year plan (2007-2012) which was envisaged about the mainstreaming of AYUSH through specific strategic intervention for wider utilization of AYUSH along with a vision for a globally accepted system. National Rural Health Mission (NRHM) was introduced in 2005 which was mainly focused on the strategic provisions like co-location, intersectoral convergence and provisions for AYUSH drugs in pursuance of mainstreaming of AYUSH and revitalization of local health traditions. National AYUSH Mission was also launched by then, Department of AYUSH during 12th plan (2012-2017) which envisaged on providing affordable, sustainable and accessible care. 2014 onwards, Department of AYUSH was granted Ministry of AYUSH status was a noteworthy policy decision for overall growth of AYUSH systems.

The various committees have been formed for institutionalization of AYUSH and they really worked far in shaping the present AYUSH system. The Chopra Committee (1948) envisaged the research component and Central Research Institute for Ayurveda was established at Jamnagar in 1953 and furthermore post graduate training course was also started there in 1956. The Udupa Committee (1958) also emphasised on research and four-fold strategy for clinical trials. To take this forward, the government established Post Graduate Institute of Indian Medicine at Banaras Hindu University Varanasi in 1963, Central Council for Ayurvedic Research and Composite Drug Research Scheme to facilitate researches in Indian system of medicine. The Vyas Committee (1966) was much focused on vital role of Ayurvedic physicians in research domain. The Central Council for Research in Indian Medicine and Homeopathy (CCRIMH) was established in 1969 to look the researches in Indian Systems of Medicine and major institutes and projects for research in Ayurveda, Siddha, Unani, Yoga and Homeopathy were taken in the various parts of the country. The utilization of indigenous doctors for delivering vertical healthcare programs are recommended by Mudaliar Committee.

Policy Support

The National Health Policy of our nation aims to achieve Universal health coverage by and delivering quality healthcare at reasonable cost. The policy comprises comprehensive primary health package which incorporates major communicable, non-communicable and chronic diseases, geriatrics, palliative and rehabilitative care. The adoption of National Policy on Indian Systems of Medicine and Homeopathy was embraced in 2002 which led the phased integration of these systems into the main healthcare delivery system and enabled the expansion of AYUSH. The various expert groups and committee recommended the utilization of Indian system of medicines with or in absence of the conventional health system to strength the comprehensive primary health care. The National Health Policy (1983), National Education Policy in Health Sciences (1989) and National Health Policy (2002) are based on the same thought. National Rural Health Mission was envisaged for the revival of local health traditions and mainstreaming of AYUSH for further strengthening the Public Health System at all levels. Apart from this, there are several other policy provisions for mainstreaming of AYUSH at various levels of health care delivery system. The Central Council for Health and Family Welfare responsible for laying down policy for all sectors covered under the health portfolio in 1999 recommended a presence of one physician of Indian Systems of Medicine and Homoeopathy at every primary health centre in every state and the vacancies caused by non-availability of allopathic personnel should be filled by ISM&H physicians. The National Health Policy (NHP) 2017, Situation Analyses - Backdrop to NHP 2017, Ministry of Health and Family Welfare, Government of India; and Three-Year Action Agenda 2017–2020, NITI Aayog, Government of India are also emphasised on prevention through lifestyle advocacy, health care delivery through integration, collocation, and medical pluralism. The National Health Policy-2017 encompasses various component related to AYUSH system. It talks about the Pluralism, Primary Care Services and Continuity of Care, Preventive and Promotive Health, Promotion of healthy living and prevention strategies from AYUSH systems and Yoga at the workplace, in the schools and community, urban health care, prioritize the utilization of AYUSH personnel in urban health care. This policy recommends the integrated medical care for non communicable disorders for mainstreaming AYUSH, access to AYUSH services through co-location in public facilities and leveraging digital tools for AYUSH. Digital tools would be used for generation and sharing of information about AYUSH services and AYUSH practitioners, for traditional community level healthcare providers and for household level preventive, promotive and curative practices.

Ayurveda is categorized under industries as per Ministry of Statistics and Programme Implementation (MoSPI)'s National Industrial Classification (NIC). Ayurveda is categorized into two groups viz; first group is the production of 'Ayurveda' or 'Unani' pharmaceutical preparation (code 21003

under division 21, manufacture of pharmaceuticals, medicinal chemical and botanical products) and the second group comprises of Ayurveda physicians (code 36901 under division 86, human health activities). Ayurveda is also considered under 'Wellness' industry as per the Indian Government's Make in India initiative which was launched in September, 2014. Over the years however, the wellness industry has evolved to include other dimensions of physical, emotional and mental well-being. The Government has been undertaking steps to promote the Indian Ayurveda Industry and other wellness services, particularly at the administrative level.. Health is a part of 12 Champion Services Sectors identified by the Department of Commerce, Government of India. There is an existence of various policy supports which would certainly help to boost the growth of Indian traditional system based industry.

Institutional Framework of Ministry of AYUSH

A broad institutional framework has been developed over the years to carry out the various activities of the Ministry of AYUSH. There is a wide spread of AYUSH infrastructure across the country which incorporates various educational institutes, research organizations, hospitals, dispensaries, licensed drug manufacturing units and registered practitioners providing health care. Central Council of Indian Medicine (CCIM) and Central Council of Homoeopathy (CCH) are the two statutory regulatory bodies, laying down the regulations of medical education and practice. Recently, National Commission for Indian system of Medicine (NCISM) Act, 2020 and National Commission for Homoeopathy Act, 2020 repealed the Indian Medicine Central Council Act, 1970 and Homoeopathic Central Council Act, 1973 respectively. There are five research councils of each respective system viz; Ayurveda (CCRAS), Siddha (CCRS), Unani (CCRUM), Homeopathy (CCRH) and Yoga and Naturopathy (CCRYN) for undertaking, coordinating, formulating, developing and promoting research in respective system on scientific lines. The core research activities comprise of clinical research, medicinal plant research (medico-ethno botanical survey, pharmacognosy and tissue culture), drug standardization, pharmacological and literary research. These activities are carried out through wide spread more than 100 peripheral units located across the country. There are so far, eleven National Institutes for Ayurveda (NIA, Jaipur), (RAV, New Delhi), (AIIA, New Delhi) & (IPGTRA, Jamnagar), Siddha (NIS, Chennai), Unani (NIUM, Bangalore), Yoga (MDNIY, New Delhi), Naturopathy (NIN, Pune) and Homoeopathy (NIH, Kolkata), (NEIAH, Meghalaya), (NEIFM, Pasighat) are existing at national level for teaching, research and clinical practices. Very recently, National Research Institute of Sowa Rigpa, Leh is also being under process. The National Medicinal Plants Board (NMPB) was established in November, 2000 to promote and coordinate the activities pertaining to conservation, cultivation, marketing, export and policy making for the development of the medicinal plants sector.

A Drug policy section is dealing the matters pertain to regulation of drugs, pharmacovigilence and AYUSH industry. There are four different Pharmacopoeial Committees which are responsible for uniform standards required in the preparation of Ayurveda, Siddha, Unani and Homeopathy drugs in the form of official formularies and pharmacopoeias. The responsibility of harmonization and development of Ayurveda, Siddha, Unani & Homeopathy pharmacopoeial standards is on Pharmacopoeia Commission for Indian Medicine & Homeopathy (PCIM&H). Pharmacopoeial Laboratory for Indian Medicine (PLIM) and Homeopathic Pharmacopoeial Laboratory (HPL) are Drug-testing Laboratories for Indian Medicines and Homeopathy respectively under the ambit of PCIM&H. The Ministry is also associated with Indian Medicines Pharmaceutical Corporation Ltd. (IMPCL), a public sector undertaking which is responsible for manufacturing the classical Ayurveda and Unani drugs.

Since the creation of a separate Ministry, there has been a substantial increase in the infrastructural facilities under AYUSH systems in the country. There are 799879 AYUSH medical practitioners; 4035 AYUSH hospitals with 58851 bed capacity; 27951 dispensaries; 498 co-located district hospitals; 2776 co-located CHCS; 7623 co-located PHCs and 8954 Drug Manufacturing Unit; 702 AYUSH educational institutions with admission capacity of 46835 and 5885 undergraduate and postgraduate seats respectively according to AYUSH in India, 2018, publication by Ministry of AYUSH.

The paradigm shift has been evident in all spheres of Ministry's activities, viz., health care activities, policy matters, execution of policies/schemes, budgetary allocation & utilisation, education matters, research related activities, promotional activities, regulatory activities, activities related to medicinal plant, liaisoning with the foreign governments and international organisations, expansion of facilities etc. Consequently, the Ministry of AYUSH has been able to infuse new energy into the practice of AYUSH system of healthcare since 2014, after the formation of independent Ministry of AYUSH. The noteworthy significance can be categorized under various headings.

Major achievements of Ministry of AYUSH since its formation

Budgetary allocation and its utilization

A budget of Rs 2,122.08 crore was allocated during 2020-21 which was three times to budget allocated in 2013-14 i.e Rs. 771 crores.

Educational activities and reforms

The demand for quality education has been steadily growing. There is corresponding boom in the number seats accessible to students in range of various AYUSH streams. The demand for qualified doctors is met adequately by increasing the number of institutes' conveyance education in AYUSH. In order to ensure that human resources engaged in various activities are equipped with appropriate knowledge & skills and to further ensure that a proper control and monitoring is in place, continuous reforms are a sine qua non. Several reform measures in different human endeavours and processes e.g. procedure for filling up seats in different under-graduate and post-graduate courses in medicine, course curriculum, skill up-gradation training, regulatory measures for standardization of drugs etc. Various reforms have been introduced viz; National Level Test, ie. National Eligibility cum Entrance Test (NEET) and All India AYUSH Post Graduate Entrance Test (AIAPGET) for under-graduate and post graduate courses respectively. Further fostering research capacity in AYUSH scholars, AYUSH –NET, a fellowship program for doctoral courses is initiated.

The establishment of central institutes for quality education are expedited viz; All India Institute of Ayurveda, New Delhi; North Eastern Institute of Ayurveda and Homoeopathy, Shillong; and North Eastern Institute of Folk Medicine, Pasighat. National Institute of Homoeopathy (NIH) Narela, Delhi, National Institute of Unani Medicine (NIUM) Ghaziabad, UP, National Institute of Naturopathy, NISARG GRAM, Pune, National Institute of Ayurveda, Yoga and Naturopathy (NIAYN), Panchkula, Haryana and National Institute of Sowa Rigpa, Leh etc.

All the National Institutes are involved in quality academia, research and health care services. They are also in imparting several skill related jobs in the field of health services. Few of these institutes have upgraded their services, technological and infrastructural facilities which attracted many foreign countries for educational courses. A national international interface has been created by entering into collaboration with other countries. The monthly stipend for Post Graduate courses has been significantly raised to Rs.42,560, 45,600 and Rs.48,640 per month for the first, second and third year respectively. Similarly, the stipend for Ph.D. programme has been raised to Rs.50,315 and Rs.51,990 per month for the first year and second year respectively. The teachers of the National Institutes have been extended the Dynamic Assured Career Progression Scheme during these times.

Research

The Ministry of AYUSH has five autonomous Research Organizations, namely, Central Council for Research in Ayurvedic Sciences (CCRAS), Central Council for Research in Yoga and Naturopathy (CCRYN), Central Council for Research in Unani Medicine (CCRUM), Central Council for Research in Siddha (CCRS) and Central Council for Research in Homoeopathy (CCRH) are responsible for deciphering the research activities, These Councils apart from conducting research activities also running outreach activities in certain privileged areas to take care of the health of the people in the village and also to promote knowledge and awareness about health all around. During COVID-19 pandemic, these Research councils have initiated various research studies to check the efficacy of these systems in the mitigation and management of COVID-19. AYUSH research portal is a repository of more than 30000 researches for disseminating the current researches in various AYUSH streams.

COVID-19 related Research

The Ministry of AYUSH took Covid -19 pandemic as an opportunity not only to create awareness about the AYUSH systems but also for dissemination of the AYUSH researches on the scientific parameters for generation of scientific evidences too. Apart from this, AYUSH extends its full support through contributing as COVID warriors and by infrastructure being used as COVID care centres in the fight against COVID 19. Many advisories deciphering the self advocacies based on preventive health measures were issued for improving immunity. The Guidelines for Registered Practitioners of AYUSH systems were also issued for a uniform guidance for AYUSH practitioners. A dedicated chapter on National Clinical Management Protocol based on Ayurveda and Yoga for management of Covid-19 is also included in National Clinical Management Protocol: COVID-19.

The Ministry of AYUSH has constituted an Inter-disciplinary AYUSH R&D Task Force to ascertain the potential of various AYUSH Interventions in COVID-19 to generate tangible evidence ensuring the robustness of scientific designs of study. This taskforce comprise with representation from scientists from ICMR, DBT, CSIR, AIIMS which is headed by Prof. Bhushan Patwardhan, Vice Chairman, University Grant Commission. Various clinical research protocols and guidelines for practitioners are formulated by this taskforce. AYUSH has also taken four candidates viz; *Withania somnifera* (L.) Dunal, *Glycyrrhiza glabra* L., combination of *Tinospora cordifolia* (Thunb.) Miers and *Piper longum* L. and a poly herbal formulation AYUSH- 64 developed by Central Council of research in Ayurvedic Sciences (CCRAS) as prophylactic and add-on therapy in the management of COVID-19 at various sites across the country in collaboration with Council for Scientific and Industrial Research (CSIR). The robust Research Protocols for this study has been developed by an eminent

clinician Dr Arvind Chopra, CRD Pune in association with this R&D Task Force. More than 80 research studies at 112 centres are taken up through different Research Councils and National Institute. These studies includes Prophylactic intervention studies, stand alone and add-on AYUSH intervention studies and retrospective studies of AYUSH interventions in COVID 19 as well as observational studies and survey studies over a large cohort, as intra mural and in collaboration with reputed organisations like DBT, AIIMS, Delhi, AIIMS Jodhpur, MGIMS KGMU Lucknow, Medanta Gurugram etc. Population based studies are taken up on more than 100000 participants which also includes All India Institute of Ayurveda has taken up population based prophylactic studies on 80000 Delhi Police personnel. These informations are also captured at the dashboard developed by Ministry of AYUSH.

AYUSH Sanjivani mobile app is developed to assess the impact of effectiveness, acceptance and usage of AYUSH advisories and measures in prevention of COVID-19. It has covered more than 1 crore population so far and usage of *Samshamani Vati* has shown very positive response as prophylactic management in COVID-19 among respondents.

Clinical Practice & Public Health Care Activities

National AYUSH Mission (NAM) was launched during the 12th five year plan to promote AYUSH systems with a vision to promote cost effective and equitable AYUSH services across the country through States and Union territory. Basically the mission is based on the strengthening the AYUSH services, AYUSH educational institutions through co-location of AYUSH facilities at Primary Health Centres (PHCs), Community Health Centres (CHCs) and District Hospitals (DHs). It also focuses to provide quality and constant supply of Ayurveda, Siddha, Unani and Homoeopathy (ASU & H) drugs by supporting States in for setting up of Drug Laboratories and sustained availability of quality raw materials. The Ministry has been able to co-locate 11,172 PHCs and CHCs and 495 District Hospitals (DHs) with AYUSH facilities through National AYUSH Mission (NAM). This is fulfilling the aspiration of people to have a choice of treatment.

The Ministry of AYUSH is also a part of AYUSHMAN Bharat scheme and committed to set up 12,500 AYUSH Health and Wellness Centres (HWCs) by the year 2023-24. The AYUSH health services may also expanded to at central government health scheme (CGHS), employees' state insurance hospitals, state level dispensaries, AIIMS, Ministry of Railway's hospitals; Ministry of Defence's hospitals and other primary and tertiary setups.

There are 799879 registered AYUSH doctors/ practitioners on 01.01.2018 who are extending their services for the community. Total number

of IPD and OPD Patients who visited Government Health Care Facilities during 2017-18 was 19,57,921 and 17,73,75,226 respectively.

Standardization and Quality Assurance

The Ministry has made considerable investments through NAM to enhance/improve the quality of Drugs. There is a consistent increase in the number of pharmacies and Drug Testing Laboratories almost tenfold and 13.5 fold respectively in the states for continuous supply of quality AYUSH medicines. More than 60 Drug Testing Laboratories have been approved for the purpose of quality assurance.

NABH accreditation is an effective tool towards improving quality in health care service. All India Institute of Ayurveda, New Delhi, National Institute of Ayurveda, Jaipur and Institute of Post Graduate Teaching & Research in Ayurveda (IPGTRA) got their hospitals NABH accredited. More institutes are in the process to obtain accreditation.

Insurance coverage

Ayush treatment has been covered under medical insurance with the efforts of Ministry of AYUSH. The Insurance Regulatory and Development Authority (IRDA) has issued necessary notification in this regard. Ministry of AYUSH in consultation with the Insurance Regulatory Development Authority of India (IRDAI), Insurance companies, AYUSH Hospitals Associations and other stakeholders has developed guidelines for coverage of Ayurveda, Siddha, Unani, Yoga & Naturopathy under Insurance coverage. The guidelines contain information regarding indicated therapies, duration of treatment and benchmark rates for information and guidance of AYUSH industry and insurance companies. Very recently, a new a vertical structure has been formed in Central Drugs Standard Control Organization with creation of 12 regulatory posts to control quality of Ayurveda, Siddha, Unani & Homoeopathy (ASU&H) Drugs.

The Ministry of AYUSH has envisaged Pharmacovigilance Initiative for ASU&H Drugs in 2017 to document adverse drug events pertaining to ASU&H drugs, surveillance of misleading advertisements related to these systems and development of an institutional mechanism for safety monitoring of AYUSH drugs. One National Pharmacovigilance Coordination centre is established for collecting reports on quality aspects from 05 intermediary and 43 peripheral centers across the country. Ministry of AYUSH is also closely working with Bureau of Indian Standards (BIS), New Delhi to develop the standards on AYUSH Health Informatics.

SKILL INDIA

HSSC sub council on AYUSH is created by Healthcare Sector Skill Council to develop National Occupational Standards for AYUSH Sector to enhance the skill competency of the AYUSH manpower. Skill competency is one of the pre-requisites for Standardisation. The Ministry of AYUSH has made it an obligation upon AYUSH hospitals for their accreditation to NABH standards with a view to enhance the quality and safety aspects. An Accreditation Standards for Certificate Course for Panchakarma Assistant to produce skilled manpower in Panchkarma has been developed. A Voluntary Scheme for evaluation and certification of Yoga professionals in association with QCI to fulfil the demand of skilled Yoga Experts at National as well as International level has also been started. The Establishment of AYUSH Health Care Super Specialty Day Care / Hospital and Skill Development under the Champion Sectors in Services are also underway.

DIGITAL INDIA

As a part of Digital India campaign, the AYUSH GRID was conceptualized for digitalization of the entire AYUSH Sector which aims to bring onboard all AYUSH facilities including hospitals and laboratories and to promote traditional systems of healthcare. AYUSH Hospital Information Management System (A-HMIS), Tele-Medicine, YogoLoctaoor Application, Bhuvan Application, Yoga Portal, Case Registry Portal, etc. are few projects which are co-opted under AYUSH GRID. National AYUSH Morbidity and Standardized Terminologies Portal (NAMSTP) informatics initiative for centralised collection of morbidity statistics pertaining to various systems of medicine was launched by Hon'ble Prime Minister on 17.10.2017. The portal provides information about Standardized Terminologies and Morbidity Codes along with dedicated data entry module for updating morbidity statistics in consolidated form as well as on real time basis.

YOGA- A MASS MOVEMENT

International Day of Yoga (IDY) was adopted by UN General Assembly's Resolution A/Res/69/131—which declared 21st June as the International Day of Yoga (IDY) in 2014 due to the initiative and efforts of Shri Narendra Modi, Prime Minister. The country has been successfully organizing the function from 2015 onwards. During the celebration of 1st IDY, which was organized in India and in 192 other countries of the world two Guinness World Records were achieved. Prime Minister's Yoga Awards are being given away each year for exemplary contribution in the field of Yoga towards the development and promotion of Yoga. The Ministry is observing the International day of Yoga every year on 21st June through its wide-ranging initiatives, strives to reach out to all individuals and institutions - including educational institutions,

government bodies, business firms, industries and cultural organizations to join IDY for the benefit of themselves and /or their family members, employees, members or other stake-holders. Ministry has initiated many promotional initiatives to create awareness like "Yoga Goes Green"- Promotion of eco-friendly Yoga Accessories. Two mobile technology-based applications deployed by the Ministry, namely BHUVAN-YOGA (developed by ISRO) to assess the magnitude of participation at different venues and Yoga Locator helped the public to locate events near them.

Yoga certification Board (YCB) was established in an effort to popularize Yoga and as a career skill and to bring standards and uniformity in the teaching and practice of Yoga across India and Globe. YCB is providing Certification of Yoga Professionals and Accreditation of Yoga Institutions across the globe. This will certainly increase the acceptability of the YCB and will help to reach out to more Yoga Professionals and Yoga Institutions. It proposes to introduce certification of Yoga Professionals under 2 categories: Yoga Education & Training and Yoga Therapy. Under Yoga Education & Training there would be 4 levels of certification and under Yoga Therapy there would be 3 levels of certification as per the competencies of Yoga Professionals. In addition to this, new concept of Continuing Yoga Education program will be introduced which aims at supporting certified Yoga Professionals and orient them to development in the field of Yoga.

5-minute Yoga module is also designed to practice at workplace to help professionals to de-stress, refresh and re-focus also known as Yoga protocol, Y-Break or Yoga Break. It consists of a few 'light' but very effective Yogic practices that can be done by taking a 5 minutes break from work. Y-Break is a very brief introductory capsule or a teaspoon to taste the benefits of Yoga.

Domestic Market of Ayush Products

The domestic market for AYUSH sector has been increasing steadily over the past decade. According to Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, domestic pharmaceutical market turnover reached Rs.129.01 Crore (USD 18.12 billion) in 2017, growing 9.4% year on year. Currently market size of Ayurveda pharma industry is estimated to be around Rs. 30,000 Crore per annum. At national level, as on 01.04.2018, there are 8954 AYUSH drug manufacturing units (licensed pharmacies) in the country. Out of these, 99.5% of the licensed pharmacies were controlled by non-government bodies, and only 0.5% licensed pharmacies were in Government sector.

International Co-Operation

Ministry of AYUSH was created with a view to providing focused attention to development of Education & Research in Ayurveda, Yoga and other

Traditional System of Medicine. This ministry ensures the optimal development and propagation of AYUSH systems of health care in the field of AYUSH education, practices and research at national as well as at international level. Ministry of AYUSH undertakes various activities and measures at international level with the mandate to promote/ popularize Ayurveda, Yoga and other Indian Traditional System of Medicine across the globe.

The Ministry of AYUSH is also provided with the mandate of liaison with foreign countries and international bodies as regards matters relating to Indian System of medicine and Homoeopathy. In pursuant to this objective, 11 country to country Memorandum of Understanding (MOUs), 14 institute to institute MOUs have been signed for cooperation and collaborative research activities etc. Ministry of AYUSH has also entered into collaborative agreements with World Health Organization (WHO). Further, 10 MoUs have been signed with Universities for setting up of AYUSH chair.

As of now, Ayurveda is recognised as System of Medicine in India and has become integral part of national health care delivery system in India. It is also recognised as System of Medicine in other countries like- Nepal, Sri Lanka, Bhutan, Bangladesh, UAE, Oman, Saudi Arabia, Bahrain, Malaysia, Mauritius, Hungary, etc. and in other countries such as Cuba, Brazil etc., it is in process for getting official recognition. In Romania, Hungary, Latvia, Serbia and Slovenia, treatment of Ayurveda is regulated in these countries however profession is not regulated. Ayurveda are practiced under the benefit of health Freedom Laws in five States in USA viz., California, New Mexico, Minnesota, Idaho and Rhode Island. In the most of EU Countries, Ayurveda gained popularity as a wellness system that uses natural medicines and there is huge demand for Ayurveda in the whole Europe and it developed fast and gained good clientele for minor ailments and for general wellness. UK, Germany, Switzerland, France are the developed countries where Ayurveda flourished well. Many Indian Ayurveda Doctors are practicing in these countries. The traditional medicine system of Myanmar, Cambodia, Indonesia etc. are based on Ayurveda and Anthroposophic medicine is well established and recognized especially in Central Europe like Germany, Netherlands, Italy, Latvia, Switzerland etc. which is also similar or based on Ayurveda or Indian Philosophy. Agni karma, is an important procedure described in Ayurveda, is being practice in UK, Ireland, Greece and Egypt as Thermal Micro-Cautery for the treatment of severe chronic pain.

Ayurveda products are being exported to more than 100 countries and these products are exported as medicines to countries where it is recognized as system of medicine and where Ayurveda is not recognized, the products are suitably modified and exported as per the requirements and classification of the importing country and sometimes under the chapter 30, and 21 alternatively, and Dietary supplements, Nutraceuticals, health supplements.

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AN OVERVIEW OF CONTRIBUTIONS OF CENTRAL COUNCIL FOR RESEARCH IN AYURVEDIC SCIENCES TO RESEARCH IN AYURVEDA

Background

The science of Ayurveda has been in vogue in this country from the earliest times and serving the medical needs of most of our people. These systems were developed by ancient scholars on the basis of their own philosophy, oriental methodologies and practices prevalent in that era and have popularized as a system of medicine. The advent of foreign invasions and cross cultural interactions had definite impact on these systems. The beginning of twentieth century saw efforts to revive these systems. The members of the Imperial Legislative Council got the resolution of investigations and recognition of these systems was accepted in the year 1916. The Indian National Congress also passed similar resolution in 1920. This led to establishment to number of colleges of Ayurveda.

In the post-independence era, the efforts to develop research gained momentum. As per recommendation of the various committees, grant-in-aid projects were sanctioned to selected colleges. The Central Council for Ayurvedic Research as an Advisory body was established in 1962 and finally the Central Council for Research in Indian Medicine & Homoeopathy (CCRIM&H) was established in 1969. This Council initiated research programs in the Indian Systems of Medicine & Homoeopathy in different parts of the country and started coordination at the National level for the first time.

The Central Council for Research in Ayurveda & Siddha (CCRAS), an apex body for the formulation, coordination and development of research in Ayurveda & Siddha on scientific lines was established in March 1978 after reorganization of CCRIM&H.

The Central Council for Research in Ayurvedic Sciences is a Registered Society under Societies Registration Act XXI of 1860 on 29.07.2011 (formerly registered as Central Council for Research in Ayurveda and Siddha on 30th March, 1978). The Minister of AYUSH is the President of the Governing Body of the Council while the Joint Secretary chairs the Standing Finance Committee. The Scientific/ Research programs are supervised by the respective Scientific Advisory Board/Groups chaired by eminent scholars of the system.

Research Areas

The Central Council for Research in Ayurvedic Sciences (CCRAS), an autonomous body under Ministry of AYUSH, Govt. of India is an apex body in India for undertaking, coordinating, formulating, developing and promoting research on scientific lines in Ayurvedic sciences. The activities are carried out through its 31 Institutes/ Centres/ Units located all over India and also through collaborative studies with various Universities, Hospitals and Institutes. The research activities of the Council include Medicinal Plant Research (Medico-ethno Botanical Survey, Pharmacognosy and Tissue culture), Drug Standardization, Pharmacological Research, Clinical Research and Literary Research & Documentation. Besides this, Council has conducting outreach activities viz., Tribal Health Care Research Program (THCRP) under Tribal Sub-Plan, Ayurveda Mobile Health Care Program under Scheduled Castes Sub Plan (SCSP), Ayurvedic Health Centres under North East Plan, Swasthya Rakshana Program (SRP) 2 VOLUME-VII and National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS).

Summary of notable achievements of CCRAS at a glance

- Generated scientific evidence of safety efficacy of approximately 100 classical Ayurveda formulations of 36 disease conditions.
- Developed an automatic working prototype model for preparation of Kshara sutra.
- Developed and launched National AYUSH Morbidity and Standardized Terminology Portal (NAMSTP) for uniform centralized collection of AYUSH morbidity statistics.
- Successfully launched and initiated Integration of AYUSH (Ayurveda) with NPCDCS (National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases & Stroke) in three districts to demonstrate the feasibility of integration of Ayurveda.
- Set up Digital Centralized Herbarium at Regional Ayurveda Research Institute (RARI) Jhansi for wider utility by industry, academicians and researchers.
- Herbariums at four Institutes have got international recognition and accredited with acronyms by the New York Botanical Garden, USA.
- Contributed in development of monographs in different volumes of Ayurvedic Pharmacopoeia of India (API) and Monographs on medicinal plants for "Quality standards of Indian Medicinal plants" in different volumes published by Indian Council for Medical Research (ICMR), New Delhi.
- Generated safety of 14 commonly used Ayurvedic metal based / Herbo mineral medicines and published.

- Repository of manuscripts of Ayurveda, Siddha and Unani manuscripts at Preserved National Institute of Indian Medical Heritage (NIIMH) Hyderabad.
- A web based portal for Research publication in AYUSH "Ayush Research portal" functional since 2011.
- Successfully conducted feasibility study for integration of Ayurveda in RCH at selected districts of Himachal Pradesh.
- Introduced Ph.D fellowship and Ayurveda Award Scheme.
- 12 technologies transferred through NRDC.
- Successfully launched online version of Journal of Research in Ayurvedic Sciences (JRAS) and Journal of Drug Research in Ayurvedic Sciences (JDRAS).

1. Clinical Research

The Council undertakes validation of classical Ayurvedic formulations already in the healthcare system through clinical studies to generate evidence on clinical efficacy and safety and scientific validation of new combinations (coded drugs) under drug development. The classical Ayurvedic formulations are already in the healthcare system and coded Ayurvedic drugs are made available into the healthcare system through systematic process of drug development viz. drug standardization and quality control, preclinical safety/toxicity studies and biological activity studies (as appropriate) and clinical trials as per requirement. The details are as under:

I. Validation of classical Ayurvedic formulations for clinical efficacy and safety

The Council has undertaken validation of classical Ayurveda formulations for identified disease conditions referring to Ayurveda classics, Ayurvedic pharmacopeia /Ayurvedic Formulary of India, Essential Drug list of ASU medicines (2013), Ministry of AYUSH. These formulations are being validated through Council's institutes engaged in clinical research in a phased manner. Some of the formulations are clinically validated for different disease conditions and some are used in different combinations for the same or different disease conditions.

- Generated scientific evidence on safety and efficacy of approximately 100 classical Ayurvedic formulations on 36 diseases/conditions viz. Allergic Conjunctivitis, Dry Eye Syndrome/Computer Vision Syndrome, Bronchial Asthma, Chronic Bronchitis, Cognitive Deficit, Dyslipidemia, Type II Diabetes Mellitus, Essential Hypertension, Irritable Bowel Syndrome (IBS), Duodenal Ulcer, Jaundice, Diarrhoea, Fistula-in- ano, Iron Deficiency Anemia, Menopausal Syndrome, Osteoarthritis, Sciatica, Hemiplegia/Paraplegia, Filariasis, Obesity, Osteoporosis/Osteopenia,

Rheumatoid Arthritis, Rasayana for healthy ageing(Geriatric health), Dysmenorrhea, Psoriasis, Gout, Polycystic Ovary Syndrome, Hemorrhoids, Malaria, Generalized Anxiety Disorder, Mental Retardation, Epilepsy, Schizophrenia, Refractory errors, Urolithiasis, and Heart disease . The research outcomes are being published in reputed journals.

- Further, validation of 35 classical Ayurvedic formulations is continuing for generation of scientific evidence on safety and efficacy on 14 diseases/conditions viz. viz. Psoriasis, Urolithiasis, Uterine Fibroids, Rheumatoid Arthritis, Haemorrhoids, Osteoarthritis, Gout, Osteopenia/Osteoporosis, Obesity, Iron Deficiency Anaemia, Menopausal Syndrome, Cervical Spondylosis, Cognitive Deficit and Chronic Allergic Conjunctivitis in various institutes of the Council engaged in clinical research.

The research outcomes of these studies are being published in journals for wider dissemination. The evidence on clinical efficacy and safety of Ayurvedic formulations which are vogue and available in the market is highly useful to practitioners and consumers for their rational use. The evidence of their safety and rational use will also strengthen integration of Ayurveda with other systems of medicine and also help in convincing scientific community across the world which may also improve its market in the country and world at large.

II. Scientific validation of new formulations/drugs:

Besides validation of classical Ayurveda formulations, the council is engaged in drug development of new/coded formulations based on leads from classical texts, contemporary scientific and pharmacological leads for important diseases of National importance based on strength of Ayurveda.

- Till date, 12 technologies such as Ayush 64 for malaria, Ayush SG for Rheumatoid Arthritis, Ayush 82 for Diabetes mellitus have been developed and commercialized through National Research Development Corporation (NRDC) for wider public utility.
- CCRAS has undertaken the development of the various coded formulations for different disease conditions viz. AYUSH Manas for Mental retardation/cognitive deficit, AYUSH QOL 2C for improving Quality of Life of Cancer patients, AYUSH Rasayan A & B in geriatric health ,AYUSH C1 Oil for wound healing, AYUSH PJ-7 for Dengue fever, AYUSH M-3 for Migraine, AYUSH SL for Filariasis, AYUSH A for Bronchial Asthma ,AYUSH D for Type II Diabetes Mellitus, Carctol S for Cancer , AYUSH K1 for Chronic Kidney Diseases, Ayush coded drug for non alcoholic fatty liver disease and Ayush coded drug for hepato-protection as adjuvant to ATT which are at different phases of drug development. These studies are being conducted in

collaboration with reputed institutes like AIIMS New Delhi, NIMHANS Bengaluru, BHU, ICMR, St.John's Medical College Bengaluru etc.

III. Other Collaborative projects:

Besides this clinical research has also been undertaken to develop Bio-medical instrumentation for Ksharasutra with IIT, New Delhi and for Development & validation of Prakriti Assessment Questionnaire/Scale with reputed organizations

2. Medicinal Plant Research Programme:

Medicinal plants are the major natural bio resource for Ayurvedic Drugs. For preparation of Ayurvedic formulation, the basic key is the availability and correct identification of the raw material. Under Medicinal plant research major components covered are Medico Ethno Botanical Survey Programme, Demonstrative cultivation of Medicinal plants and study of propagation techniques including in vitro methods and Pharmacognosy research mainly two programmes, they are Medico-Ethno Botanical Survey programme and Cultivation of medicinally important plants in the Demonstrative gardens.

Under Medico-Ethno Botanical Survey Programme , the survey has been conducted through its 5 peripheral Institutes, namely RARIMD Bengaluru, RARIGID Guwahati, RARI Itanagar, RARI Jhansi and RARI Ranikhet. The Council has surveyed part of every phyto-geographic region across the country including the Andaman & Nicobar Islands and Lakshadweep. conducted 974 survey tours, covered more than 976 Forest areas across the country and collected more than 1lakh,50 Thousand (Approximately) Medicinal Plants, collected more than 10,000(Approximately) folk claims, preserved 19,000 (Approximately) Museum samples and Documented more than 1 lakh (Approximately) Herbarium sheets.

The Council is having Herbarium and Museum containing samples of medicinal plants and crude drugs at most of its peripheral Institutes. Herbariums at four Institutes have got international recognition as these are accredited with acronyms by the New York Botanical Garden, USA viz. **(i)** Regional Research Institute of Himalayan Flora, Tarikhet – **'RKT'**; **(ii)** National Vriksha Ayurveda Research Institute, Jhansi– **'JHS'**; **(iii)** National Ayurveda Dietetics Research Institute, Bangalore–**'RRCBI'** and **(iv)** Ayurveda Regional Research Institute, Itanagar – **'ARRI'**

Further, extensive field explorations resulted in finding 10 new species to plant kingdom. The research findings were published in book form like Flora of Chikmangalur, Flora of Coorg, Medicinal Plants of Karnataka, Medicinal

Plants of Tamil Nadu (Volume 1 & 2) and Monograph of Tribal Pockets of Nilgiris (Ooty).

Cultivation of medicinal plants under Medicinal Plant Research Programme is being carried out mainly in four gardens located at different climatic zones, viz., Regional Ayurveda Research Institute (RARI), Jhansi (Uttar Pradesh), Regional Ayurveda Institute for Fundamental Research (RAIFR), Pune (Maharashtra), RARI Itanagar (Arunachal Pradesh), and RARI, Ranikhet (Tarikhet) (Uttarakhand).

Totally, 533 species of medicinal plants are maintained in these four gardens, out of which, 332 plant species were maintained by RARI, Jhansi; in which 4 species are critically endangered, 20 species are least concerned and rare. In RAIFR, Pune, 159 species of medicinal plants were maintained; out of which 12 species are least concerned and 1 species is vulnerable. In RARI, Itanagar, 126 plant species of medicinal plants were maintained; out of which 4 species under cultivation are critically endangered, 6 species least concerned, 2 vulnerable and threatened. In RARI, Ranikhet, 119 plant species of medicinal plants were maintained; out of which 8 species under cultivation are rare, 4 species critically endangered and vulnerable. Saffron (*Crocus sativus* L.) is successfully cultivated in the Institute (RARI, Ranikhet) gardens situated at Ranikhet and Chamma.

Under development of agro techniques of medicinal plants, 30 protocols were prepared for conservation of these highly valued medicinal plants viz. *Aconitum heterophyllum*, *Acorus calamus*, *Mucuna pruriens*, *Digitalis purpurea* etc.

- *The live plants act as specimen for referencing and correct identification of the medicinal plants. Experimental application of agro techniques and adaptable practices are carried out to study the growth of corms and plants, yield of saffron, etc.*
- *These gardens work as reference centers for researchers/ students/academicians for identification of their plants/plant parts, and the genuine materials collected from the gardens are used as a reference material for herbarium and museums.*

Further, under plant tissue culture, In vitro propagation trial was conducted on 14 plants species and in vitro propagation trial of 7 plants species is under pipeline.

3. Drug Standardization:

Standardization is an essential step to ensure the quality of Ayurvedic drugs. Exploration of Ayurvedic drugs for chemical studies and quality

assessment was initiated in the form of Chemical Research Studies and Standardization Studies with an approach plan to lay down analytical values and to identify the presence or otherwise of main ingredients in the preparation. Confirmation of identity, quality, purity, and detection of adulterants are the major objectives of standardization. One of the prime activities of the Council is Quality assessment of the single drugs and compound formulations and their method of preparation (standard operating procedures) through its Drug Standardization units.

Initially, the Drug Standardization Units were Chemistry departments of reputed Institutes and Colleges *viz.* National Chemical Laboratory (NCL), Poona (Now Pune); University College of Sciences, Osmania, University, Hyderabad; Delhi University, Delhi; University of Kerala, Trivandrum; University College of Science, Calcutta and Banaras Hindu University, Varanasi in 1969 while three Preliminary Standardization Units- 1. Capt. Srinivasamurthy Research Institute, Madras; 2. Department of Modern Pharmacy, Gujarat Ayurvedic University, Jamnagar; 3. Department of Dravyaguna, Institute of Medical Science Banaras Hindu University, Varanasi in 1970. In view of the application of Drugs and Cosmetics Act, 1940, as amended in 1964 it has been decided that preliminary standards are to be worked out for formulations as well as the ingredients (single drugs) for entering into the official pharmacopoeia. All this work was published as Pharamcopoeial Standards for Ayurvedic Formulations. This book consists of 431 formulations divided in 21 categories of dosage forms.

Since inception, the following activities were carried out:

- 2520 samples of single drugs.
- 1369 samples of the formulation/finished products has been standardized
- 356 samples were considered for analytical standardization.
- 512 samples of 392 Ayurvedic plants for chemical studies
- Self-life studies of 20 formulations.
- HPTLC/TLC studies of 256 drug samples.

At present, council has Drug standardization units *viz.* Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute (CSMRADDI), Chennai (NABL accredited lab); Central Ayurveda Research Institute for Drug Development (CARIDD), Kolkata; Central Ayurveda Research Institute for Respiratory Disorders (CARIRD), Patiala; Regional Ayurveda Research Institute for Drug Development (RARIDD), Gwalior and National Ayurveda Research Institute for Panchakarma, (NARIP) Cheruthuruthy etc.

Under Drug Development Programme, the Council has developed various formulations *viz.* Ayush 64, Ayush-56, 777 Oil, Ksharsutra, Ayush Ghutti, Balarasayan, Ayush 82. Besides, Council has coordinated Reproductive and Child Health Care Programme with 17 formulations for pre and post natal

care viz. Ayush Candy, Ayush Ark Pudina, Ayush BL Oil (Bala Taila), Ayush Bala Rasayana Tablet, Ayush PK Avleha (Panchakola avaleha), Ayush Bala Rakshak Leham, Ayush PG Tablet (Punarnavadi yoga), Ayush SDM Tablet (Arogya sutika), Ayush SS Granules (Payaswini), Ayush KVM syrup (Vasadi panak), Ayush BC Tablet (Balamrita yoga), Ayush AG Tablet (Shatamuli mandoor), Ayush GG Tablet (Gokshura ghanavati), Ayush LND Tablet (Laksha durvadi yoga), Ayush VRG Tablet (Rajahpravartan yoga), Ayush KD ointment (Khadiradi malahara) and Ayush UT ointment (Rakshoghni malahara). Under new drug development programme 15 new formulation has been developed.

In order to provide third party certification, the concept of laboratory accreditation was developed and the Council got NABL accreditation for Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, Chennai in 2008. Besides NABL accreditation this lab has authority to test drug samples from State Licensing Authority, Government of Tamil Nadu and has been declared as Drug Testing Laboratory (DTL) for ASU (Ayurveda, Siddha and Unani) drugs, Govt. of Tamil Nadu. Under the programme 59 samples were tested for various parameters.

The same institute, Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, Chennai was recognized as a centre for pursuing Ph.D. by different Universities. Total 39 scholars have been awarded Ph.D. and four candidates are pursuing their Ph.D. work. Presently the Institute is recognised by University of Madras as a research centre for Ph.D.

A considerable work has been done by CCRAS in evaluation of Pharmacopoeia and Formularies. CCRAS remains member of Ayurvedic Pharmacopoeia of Committee (APC) since its beginning in 1969 to prepare and finalization the main task to bringing out Ayurvedic Pharmacopoeia in convenient installments on single and compound formulations and Ayurvedic formularies effectively. Director General, CCRAS was nominated as Member Secretary of APC in 2005. The Council has contributed a lot in finalization and publication of Ayurvedic Pharmacopoeia of India (API) and Ayurvedic Formulary of India (AFI). So Far, CCRAS has contributed 48 monographs in different volumes of API and 8 monographs in Siddha Pharmacopoeia of India (SPI).

Monographs on 95 plants have been contributed to the book "Quality standards of Indian Medicinal plants" in different volumes published by Indian Council for Medical Research (ICMR), New Delhi.

13 guggulu, 28 churna/kwath churna, 11 tablets/vati/gutika, 18 taila/ghrita, 4 arishta/asava, 8 avleha and sveta parpati, apamarga kshara, yashad bhasma under clinical research projects of IMR-PEMC- CCRAS have been examined.

4. Pharmacological Research

Pharmacological studies determine biological effect, effective dose range and overall effectiveness of the optimized lead. It is very important to perform all pharmacological studies in relevant *in-vivo* and *in-vitro* test system, which has closest resemblance to human disease condition. These studies give a further understanding into the mechanism of action and an in depth understanding of the drug action. While, toxicity studies support toxicity profiling evaluation for the drug candidate which includes a battery of *in-vivo* and *in-vitro* studies. The results eventually help to determine no adverse effect level (NOAEL) and maximum tolerated dose (MTD) for the drug which ultimately helps in calculation for a safer and potentially effective start up dose regimen for human studies.

Under pharmacology research, Ayurvedic drugs are studied for their safety evaluation and biological activity in various areas such as diabetes mellitus, bronchial asthma, anti-cancer, immunomodulation, wound healing, anti-urolithiatic, Anti-arthritic, migraine, dengue etc and toxicity study such as acute, sub-acute, chronic, dermal, ocular etc. Besides conducting studies through its own institutes viz. Central Ayurveda Research Institute for Drug Development, Kolkata; Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, Chennai; Regional Ayurveda Research Institute for Drug Development, Gwalior; National Ayurveda Research Institute for Panchakarma, Cheruthuruthy; Regional Ayurveda Institute for Fundamental Research, Pune and the Council collaborates /outsources through institutes of national repute.

Approx. 636 studies have been carried out for toxicity evaluation/biological activities since inception. Approx. 50 medicinal plants have been studied out for toxicity evaluation/biological activities since inception. Screening of medicinal plants for their biological activity/pharmacological action and /or safety/toxicity study which may provide leads for further drug development viz. *Premna integrifolia* for anti-atherosclerosis, *Cardiospermum halicacabum* for hypolipidemic, *Nyctanthes arbor-tristis* for hypoglycemic, hepatoprotective and anti-dislipidaemia, *Ficus lacor* Buch Ham, *Callicarpa macrophylla* Vahl, *Thespesia populnea* Soland ex Corr, *Ficus bengalensis* L, *Ficus religiosa* L, *Holoptelia integrifolia* (Roxb.) Planch, *Albizia lebeck* Benth, *Balanites aegyptiaca* (L.) Del, *Sesbania grandiflora* L, *Cissampelos pareira* (L.) Poir, *Solanum xanthocarpum*, *Glycyrrhiza glabra*, *Berberis aristata*, *Piper longum*, *Zingiber officinalis*, *Picrorhiza kurroa*, *Tinospora cordifolia*, *Embelia ribes*, *Cedrus deodara*, *Withania somnifera*, *Phyllanthus emblica*, *Phyllanthus amarus*, *Acorus calamus*, *Bauhinia variegata*, *Terminalia chebula* for *in-vitro* anti-cancer activity.

Safety profile of most commonly used classical Ayurvedic herbomineral formulations viz. Rasamanikya, Naga Bhasma, Hridyarnava Rasa, Swarna Bhasma, Tamra Bhasma, Trivanga Bhasma, Makaradhwaja, Arogyavardhini Vati, Mahalaxmi Vilasa Rasa, Mahayograj Guggulu etc. was established.

Biological activity and/or Safety studies of Ayurvedic classical formulations viz. Jatyadi Grita for wound healing, Arogyavardhini Vati for hepatoprotective activity, Laghu Vishagarbha Taila for arthritis, Yograj Guggulu for arthritis, Vaisvanara Churna for rheumatoid arthritis, Gokshuradi Guggulu for urolithiasis, Panchagavya Ghrita for immunomodulatory activity, *Sveta parpati* for urolithiasis have been conducted.

Under new drug development, screening of 10 formulations for biological activity/efficacy and safety studies of Ayush QOL-2C for improvement of quality of life for patients receiving chemotherapy/radiotherapy, Ayush-Manas for mental retardation, Ayush-SL for filariasis, Ayush rasayana- A&B for immunomodulation, Ayush-D for diabetes, Ayush-A for asthma, Ayush M-3 for migraine, Ayush PJ-7 for dengue, Ayush SG for rheumatoid arthritis and Ayush AGT for wound healing have been completed. Further, 17 Ayurvedic formulations for RCH were evaluated for their safety. 16 Intra mural research projects have been completed and 10 Intra mural research projects are ongoing.

5. Literary Research and Documentation

The Council's literary research and Documentation programme broadly relates to medico-historical studies, transcription, translation and publication of classical treatises, important/ rare works, unpublished texts and their commentaries in to Hindi, English or other languages. This work has been carried out by the Headquarter along with selected peripheral Institutes. National Institute of Indian Medical Heritage (NIIMH), Hyderabad with the objective of literary research additionally focuses on medico-historical survey, preparation of biography of eminent scholars, preparation of e-books on classics etc.

National Institute of Indian Medical Heritage (NIIMH) is actively engaged in the tasks of revival and retrieval of manuscripts and rare books since from its establishment. NIIMH, Hyderabad maintains repository of manuscripts of Ayurveda, Siddha and Unani manuscripts. The collection includes palm leaf and paper manuscripts in different languages: Sanskrit, Telugu, Tamil, Malayalam, Urdu, Arabic, Persian etc. The manuscripts are housed in the Institute are periodically subjected to curative and preventive conservation to reduce and prevent the deterioration. These manuscripts are retrieved in digital form too. The Institute has taken up of editing, translation and publication of several books/ works based on original manuscripts and

rare books which are published from time to time. Apart from manuscripts, the Institute's library contains very rare and valuable collection of books on History of Medicine of different Systems and medical journals. NIIMH, Hyderabad is a great resource Institute for scholars engaged in the Medico-historical & Literary research in AYUSH Systems of medicine as well as Biomedicine.

Besides, CCRAS has surveyed and digitized more than 5000 Ayurveda, Yoga Unani, Siddha, Sowa Rigpa etc., manuscripts/ rare books from Odisha, West Bengal, Bihar, Andhra Pradesh, Telangana, Tamilnadu, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Assam and Jammu & Kashmir (Leh) etc. Out of 5000 collection, more than 4000 digitized manuscripts are catalogued and the descriptive catalogues are published.

Further, the Council made continuous efforts to survey, collect, edit and publish the Ayurveda books mentioned in Schedule I of Drugs and Cosmetics Act, 1940. CCRAS, by extensive surveys, out of 54 books (of Schedule I, Drugs and Cosmetics Act 1940), manuscripts and published books/works of different editors/publishers/editions and in different languages pertaining to 48 books are collected and retrieved in print and digital form. Among these 48 books, the following 11 books viz. Abhinavacintamani, Astanga Hridayam, Astangasamgraha, Basavarajiyam, Bhelasamhita, Cakradatta (residual portion of Ratnaprabha), Rasacandansu, Rasapradipika, Sahasrayoga, Vaidyaka cikitsa sara , Visvanathacikitsa based on original manuscripts/ rare books are published by the Council for wider accessibility and utility. These works are widely referred by students, researchers, practitioners, industries, indologists, linguistic experts etc.

Apart from editing and publication of manuscripts and rare books, the Council has taken major initiative to create a **Centralized Digital Repository of Medical Manuscripts of AYUSH Systems of Medicine** with an objective to conserve and preserve rich cultural and medical heritage of India for posterity as well as to provide easy access.

Under the "Survey, cataloguing and digitized inventory of medical manuscripts" program, about 5000 manuscripts are digitized from manuscript libraries, museums, educational and cultural institutions, private collections etc. across the country. Among the 5000 manuscripts, metadata of 2086 Ayurveda, 598 Siddha, 542 Unani, 628 Sowa-Rigpa, 49 Yoga and 179 other manuscript's prepared under 44 fields. Apart from manuscripts, the metadata of 1336 rare books is presented in 18 fields. The entire data is published in 9 descriptive catalogues.

A web based portal has been created to provide comprehensive metadata of manuscripts of Ayurveda preserved in various Government

Oriental Institutes, Libraries, museums, institutions related to education and culture as well private collections across India. The data in the portal include the details of Descriptive Catalogues of Ayurveda manuscripts published by CCRAS and descriptive catalogues/ Institute catalogues are published / available. *This portal facilitates scholars to identify and locate desired manuscripts for their studies and also to bring out critical editions (the work is in progress)*

Apart from revival and retrieval of manuscripts and rarebooks, the Council has taken major initiative in bringing out electronic version of important treatises (Samhita) and compendia/lexicons (nighantu) and Pharmacopeia and Formularies of Ayurveda and Siddha. These ebooks are designed and developed by using in house technology at National Institute of Indian Medical Heritage, Hyderabad. Apart from being used as a Search tool, the User can read the text of Carakasamhita, Susruta samhita, Madhavanidanam and 25 Nighantu in eight Oriental languages. These e books are widely referred by students, research scholars, and faculty of Ayurvedic teaching/ Research Institutions.

The Council publishes books, monographs, technical reports and also the outcome of intramural researches, sponsored research projects, compilation of research related data, medico-historical data, which are useful and informative for researchers, academicians and students as well as public.

CCRAS has published several periodicals viz. Journal of Research in Ayurveda and Siddha, Journal of Drug Research in Ayurveda & Siddha and Journal of Indian Medical Heritage. Besides, a quarterly News Bulletin of CCRAS has also been published periodically.

6. Extension activities: CCRAS informed that it has also been engaged in several extension activities. The major activities are listed below:

6.1 Health care services:

- i. Health care services were extended to approximately 1,29,56,841 patients through OPD/IPD
- ii. AYUSH Wellness Clinic was established in President Estate in July 2015. The Health care services were provided through OPD and Panchakarma therapy. A total 12694 patients ere treated in OPD and Panchakarma therapy was given to 7688patients

6.2 Public Health Oriented Research activities

- i. **Tribal Health Care Research Programme:**
Tribal Health Care Research Program (THCRP) was initiated by the Council in 1982 with the core objectives encompassing to study the

living conditions of tribal people including health related demography, documentation of folk claims and Local Health Traditions and use of common medicinal plants in the area, availability of medicinal plants in the area, propagation of knowledge about hygiene and prevention of diseases besides extending medical aid at their door steps. The program has been continued at 6 States Madhya Pradesh, Maharashtra, Bihar, Assam Arunachal Pradesh and Andaman & Nicobar from 1982 to till 2014. During this period, 5 independent Tribal Health Care research Units have been relocated through reorganization which came into force in the year 2000.

Further during the year 2014-15 and 2016-17 the program has been extended in 10 more States viz. Rajasthan, Jammu & Kashmir, Himachal Pradesh, Karnataka, Tamil Nadu, West Bengal, Odessa, Andhra Pradesh, Sikkim and Telengana. Currently, the Tribal Health Care Research Program is being executed in 14 States through 15 Peripheral Institutes of CCRAS under Tribal sub-Plan (TSP). The gross physical achievements including the beneficiaries of health care services, details of villages, tribal's pockets covered, documentation of disease prevalence and local health traditions during period 1982-2017 were compiled summarized and presented based on the information available in the published monographs, technical reports and annual reports of CCRAS.

A critical appraisal reveal that from 1982 up to March 2017 CCRAS has extended Health Care Services at 1737 Villages/Tribal pockets across 16 States covering a population of 1065957 while medical aid and counseling was offered to 377945 seekers and 929 Folklore Claims and Local Health Traditions (LHTs) were documented.

ii. **Swasthya Rakshan Programme:**

Council had initiated Swasthya Rakshan programme by undertaking outreach health care services through its 21 peripheral research institutes at 19 states viz. Kerala, Odisha, West Bengal, Punjab, Uttar Pradesh, Maharashtra, Rajasthan, Madhya Pradesh, Andhra Pradesh, Karnataka, Bihar ,Assam, Sikkim, Arunachal Pradesh, Jammu & Kashmir, Himachal Pradesh, Gujarat and Tamil Nadu rendering clinical services. This programme has been executed by the concerned CCRAS institute by adopting at least 5 large colonies located in urban areas or 5 villages if the institute is located at Tehsil (Block level) per institute. It is a type of mobile community Health Care services through which health care services are provided to people. The Programme is linked with Swacch Bharat Mission. This programme has been initiated during the month of November, 2015. A total 165 villages/colonies covered through 4601 tours in 19 states and medical aid was provided to

137572 patients. During these tours, awareness about hygiene was also provided to the people.

iii. **Ayurveda Mobile Health Care Programme under Scheduled Castes Sub Plan (SCSP):**

The Council implemented "Scheduled Caste Sub Plan (SCSP)" in 19 State through its 20 peripheral institutes. Through this programme special emphasis is giving on collection of the demographic information of the particular area. The focus is on socio-economic information, food habits, lifestyle, etc. of people and patients of that particular region. In addition, the OPDs and Camps are being organized in each village/ selected area on a weekly basis where qualified doctor assess the patient and provide suitable treatment/ medicine for various disease conditions. During the survey Health Camps are organized where Medicines are distributed at free of cost and people are advised for hygiene and prevention of diseases and Ayurveda concepts on preventive health in relation to Pathya-apathya and Sadvritta.

This programme has been initiated during the month of November, 2015. A total 277 villages/colonies covered through 3713 tours in 19 states and medical aid provided to 134801 patients. During these tours, awareness about hygiene was also provided to the people

iv. **Integration of AYUSH(Ayurveda) in National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases & Stroke (NPCDCS):**

The Council in collaboration with Directorate General of Health Services, Ministry of Health & Family Welfare has implemented and executed a programme viz. Integration of AYUSH (Ayurveda) component with NPCDCS (National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases & Stroke) programme in the identified districts of 3 states viz. Bhilwara (Rajasthan), Surendranagar (Gujarat) and Gaya (Bihar) to cater health care services and to reduce the burden of NCDs by combining the strength of Ayurveda and Yoga. The programme was launched during 2015.

The aforesaid programme is now successfully functional in 52 centres (49 CHCs and 3 District Hospitals) of the all 3 identified districts, through AYUSH- NPCDCS Clinic/Lifestyle modification Clinics, established for prevention and management of selected NCDs by Ayurvedic intervention, Lifestyle modifications and Yoga Advice.

An interim analysis has revealed that the dosage or components of conventional medicines/ prescription were either reduced or discontinued, in consultation and supervision of Modern doctors after

integrating the intervention of Ayurveda medicines, lifestyle modification & Yogic practices in patients of Diabetes, Hypertension and Dyslipidemia. Ayurveda - Modern medicine integrative health care services seems to be successful attempt of functional integration through delivering in the context of Non-communicable diseases with encouraging benefits of stand-alone Ayurveda therapies as well as benefits as add-on therapies. Till January, 2018, 301102 patients have been screened and, out of which 59107 patients have been enrolled for selected NCDs under this programme.

v. **Ayurvedic Health Centres under NE Plan:**

CCRAS has set up Ayurveda health centres in 20 districts of North-East states during 2015-16, viz. 10 OPD in Assam state, 6 OPD in Arunachal Pradesh state and 4 OPD in Sikkim state. In **Arunachal Pradesh**, 6 Ayurvedic Health Centres viz. District Hospital, Bomdila; District Hospital, Namsai; District Hospital, Tezu; District Hospital, Seppa; CHC, Likabali and CHC, Ruksin/General Hospital Pasighat are continuing under the supervision of RARI, Itanagar and a total 3910 patients were attended in these Centres. In **Sikkim** - 2 Ayurvedic Health Centres viz. Gayzing, South Sikkim and Jorethang, South Sikkim are functioning under the supervision of RARI, Gangtok and a total 880 patients were attended in these Centres. Besides this, the remaining 2 Ayurvedic Health Centres viz. Mangan, North Sikkim and Singtham, East Sikkim will be opened shortly. In **Assam**, extended OPD at 5 centres viz. Kamrup, Nalbari, Morigaon, Darrang, Barpeta have been started and process for opening of remaining 5 centres is in progress.

A total 5964 patients were attended at 4 Ayurvedic Health Centres through RARI, Gangtok and in Arunachal Pradesh a total 8631 patients were attended at 6 Ayurvedic Health Centres through RARI, Itanagar.

7. AYUSH Research Portal

To disseminate the merits of AYUSH systems across the globe, a web based portal for Research publications in AYUSH was launched in 2011 which is being maintained by NIIMH Hyderabad. The portal is successfully continuing and the information is being updated periodically.

8. Memorandum of Understanding (MOU)

62 Memorandum of Understanding (MoUs) for collaboration in the field of academic, drug development and research have been signed with reputed institutes, organizations at national and international level, out of which 21 Memorandum of Understanding (MoUs) are operational at present.

9. Technologies Patented & Commercialized

Total No. of Patent Awarded: 17

Total No. of Technology Transferred to Industry: 12

S. No	Product Name	Process
1.	AYUSH-64	A process for the preparation of a therapeutically active anti-malarial preparation.
2.	*777 Oil	A process for the preparation of a medicated oil from <i>Wrightia tinctoria</i> for Psoriasis
3.	BAL RASAYAN	A process for the preparation of a herbo- mineral preparation for general immunity and strengthening of children
4.	AYUSH Ghutti	A herbo-mineral formulation for cough and cold
5.	AYUSH-56	Process for preparation of therapeutically active anti-epileptic preparation
6.	AYUSH –SS granules	A process for preparation of an Ayurvedic herbal compound preparation for post natal care (to enhance the quality and quantity of breast milk in mother having deficient lactation)
7.	AYUSH AG Tablet	A process for preparation of an Ayurvedic herbal compound preparation of AYUSH AG Tablet (Shatamuli Mandura) for Ante natal care
8.	AYUSH PK Avleha	A process for preparation of an Ayurvedic herbal compound preparation of AYUSH Panchkola Avleha for post natal care to enhance the process of recovery after delivery and other complications of puerperal period
9.	AYUSH PG Tablet	A process for preparation of an Ayurvedic herbal compound preparation of AYUSH PG Tablet for Ante natal care
10.	AYUSH BR Leham	A process for preparation of an Ayurvedic herbal compound preparation AYUSH Bala Rakshak Leham for paediatric care
11.	AYUSH 82	An Anti Diabetic Ayurvedic Formulation
12.	AYUSH SG	An Anti-Rheumatoid Arthritis preparation.

NB: - * Transferred to CCRS, Chennai.

CCRAS has developed and commercialized the following three drugs which are readily available in the market:

1. AYUSH 64 An Anti Malarial Formulation.
2. AYUSH 82 An Anti Diabetic Ayurvedic Formulation
3. AYUSH SG An Anti-Rheumatoid Arthritis preparation.

Premia/Royalty obtained from Patents and Commercialization of Technologies (Since Inception): Approximately three crores twenty lacs obtained through commercialization of technologies developed by the Council

10. Research Publications: 3746 Research papers and more than 250 books/monograph/technical report were published by CCRAS scientists.

11. Other important Research outcomes:

- **Healthcare seeking trends in Ayurveda:** The OPD data (app.62 lac patients) available in annual report of 24 CCRAS institutes for the period 1991-2012 was analyzed to present the healthcare seeking behaviour. The analysis showed that majority of patients (16.17%) suffered from diseases of digestive system followed by musculo-skeletal system (15.88%) and nervous system (11.55%). The data was suggestive of patients inclination towards Ayurveda treatment for chronic and lifestyle related diseases. A Report "**Healthcare seeking trends in Ayurveda A CCRAS Perspective**" was published in 2015.
- CCRAS published "Evidence based Ayurvedic Practice" in 2015 on 18 disease conditions based on the several research studies conducted at CCRAS institutions for the last three decades. The document is an effort to translate research into practice.
- Some articles published in journals reported the toxicity, presence of heavy metal contents of certain classical/proprietary preparations which created misconceptions regarding the safety of Ayurvedic Rasa Kalpas and Bhasmas. Recognizing the therapeutic importance and safety concerns of such formulations, CCRAS compiled experimental studies conducted by CCRAS and other institutions on safety profile of 15 metal/herbomineral formulations and published a document "**Evidence based Safety of Ayurvedic Herbo-Mineral Formulations**" in 2015.
- The Council-WHO India country office conducted ***an operational study to explore the feasibility of integrating Ayurveda with modern system of medicine in a tertiary care hospital (Safdarjung Hospital***

New Delhi) for the management of Osteoarthritis (Knee) in 2007. The Ayurvedic treatment provided to 201 patients was found effective in the management of Osteoarthritis Knee with respect to reducing the symptoms, improving the quality of life and reducing the intake of rescue medication (analgesics). The project established a cross referral system and revealed a shift in service seeking behaviour of the patients. A Technical report of the study was published by CCRAS in 2007.

- **Feasibility of integration of Ayurveda in RCH programme:** The Central Council for Research in Ayurvedic Sciences (CCRAS) carried out the study in a pilot mode for introducing Ayurveda health care system in the conventional system for Antenatal, postnatal and neonatal care with technical support from Indian Council of Medical Research (ICMR), Government of India. It was implemented in some selected areas viz. Ladbhadhol & Chauntra blocks of Mandi District; and Mahakal & Panchrukhi blocks of Kangra District of Himachal Pradesh. Total 2465 participants were enrolled in the study. Significant improvement in various outcome indicators such as improvement in Hb%, minimal complications such as vomiting, Edema etc. during pregnancy, achievement of full term pregnancy and nil still birth and neonatal death were observed in the study. Whereas in Himachal Pradesh, Neonatal Mortality Rate (NMR) was 31 per 1000 live births and Infant Mortality Rate (IMR) were 40 according to Sample Registry survey (SRS-2010). Further, there was no mortality of women in the registered cases. No adverse drug reaction (ADR) or adverse event (AE) was reported during the study period. The responsiveness of study participants and the outcome of core indicators reveal the acceptability of study participants for Ayurveda during pregnancy. A paper has been published "Effectiveness of Ayurvedic interventions for Ante-natal Care (Garbhini Paricharya) at Primary Health Care level - A multi-centre operational Study" in Journal of Research in Ayurveda and Siddha published by Central Council for Research in Ayurvedic Sciences, Ministry of AYUSH, New Delhi (2015).
- The Central Council for Research in Ayurvedic Sciences (CCRAS) has conducted scientific studies in collaboration with reputed institutes to establish safety profiles of most commonly used Ayurvedic Medicines viz. **Rasamanikya, Naga Bhasma, Hridyarnava Rasa, Swarna Bhasma, Tamra Bhasma, Trivanga Bhasma, Makaradhwaja, Rasa Sindoor, Arogyavardhini Vati, Mahalaxmi Vilasa Rasa, Vasanta Kusumakara Rasa, Yogaraja Guggulu, Mahayogaraja Guggulu and Kasisa Bhasma.** The Ministry of AYUSH, Govt. of India brought out the document "Evidence Based Safety of Ayurvedic Medicines" (2016) focusing on safety of Ayurvedic metal and mineral based formulations

to present the scientific aspects, relevance and rationale of unique interventions in the public domain.

- Under Golden Triangle Partnership (GTP) programme, SOPs for preparation, chemical characterization and safety/toxicity studies of 8 Rasayogas (Herbo-mineral formulations) viz. *Rasa Manikya, Kajjali, Rasa Sindura, Basant Kusumakara Rasa, Arogya vardhini vati, Maha Yogaraja Guggulu, Makardhwaja, Mahalaxmivilas Rasa* were carried out in collaboration with CSIR. The articles/monographs are being published in reputed journals. Research protocols have also been developed in partnership with ICMR.
- CCRAS also contributed to TKDL in the matter of collection of published material on Ayurveda, compilation of formulations and generation of Traditional Knowledge Resource Classification (TKRC).

12. Recent Initiatives

i. Development and Validation of Prakriti Assessment Questionnaire/Scale

The individualized treatment of diseases is the unique approach of Ayurveda which recognized every individual with a specific constitution vis-a-vis *Prakriti*. Ayurveda classifies all individuals into specific types of 'Prakriti' based on the theory of *Tridosha* (Three humours as functional entities of the body) i.e. *Vata, Pitta & Kapha* and their relative ratios. The determination of Prakriti has significant importance in healthy / unhealthy states of an individual. This information can be successfully applied clinically in diagnosis, treatment (for deciding appropriate drug, dose, duration, diet and life style) and prognosis of the disease. Even the daily and seasonal regimens adopted for promotion of health also vary according to Prakriti.

For the determination of Prakriti, the characteristic features mentioned in Ayurvedic texts are subjective in nature and the clinicians/Ayurvedic experts apply their own wisdom and experience to capture these features. Considering the need to develop a uniform method for capturing these predictors for assessment and reliability of the data, CCRAS has undertaken the initiative to develop the 'Prakrit Assessment Scale' with rationality, reliability, validity and reproducibility. The project comprises of (i) Development of a comprehensive questionnaire/ Scale for assessment of Prakriti, (ii) Development of Sops for the application of questionnaire/ scale in the form of User Manual (iii) Validation of the questionnaire/scale and

(iv) Development of Software for the validated prakriti assessment tool. The standard Operative Procedures (SoPs) for capturing each predictor have been developed and the same has been elaborately discussed in '**National Consultative Expert Group Meet**' comprising of learned experts from various fields of Ayurveda and other contemporary sciences for content validity. For construct validity the developed scale has been given to 20 Ayurvedic physicians, already trained on User manual, at 10 centers situated at different geographical regions of the country for a sample size of 500. Online Data capturing Form also been developed for easy collection of the data and its day to day monitoring.

After data analysis and inputs from the investigators, necessary changes as required will be made in the prakriti Assessment questionnaire to make it more comprehensive & user friendly making further reductions which will be subjected for final validation. After standardization of Prakriti Assessment Scale, the study on correlates of Prakriti with genomes and other relevant factors may be planned to establish the concept of Prakriti on scientific footings.

ii. **National AYUSH Morbidity and Standardized Terminologies Portal (NAMSTP)**

National AYUSH Morbidities and Standard Terminologies Portal (NAMSTP) is a web based portal exclusively dedicated to the centralized collection of morbidity statistics of various health care provider institutions under the all AYUSH systems spread over the country. This portal was formally launched by Shri Narendra Modi, the Hon'ble Prime Minister of India on the occasion of 2nd Ayurveda Day (17th October 2017). This portal has the potential to revolutionize morbidity statistics data collection and may have a huge impact on the future policy making decision by bringing to light the contributions of various AYUSH systems in the healthcare delivery system of the country. The core objective of this portal is to accurately project the contribution of various AYUSH systems in the healthcare sector of the country through centralized data pooling into a common portal.

The Major Benefits of this portal are Real time morbidity data collection; Identification of areas of strengths of the various systems under AYUSH; Electronic Health Record (E.H.R.) systems integrated with morbidity codes; helpful in regulating the healthcare delivery system in AYUSH systems by providing standardizing diagnostic terminologies, thus overcoming the barrier of the diagnosis being written in Sanskrit-Arabic-Tamil languages in case of A-S-U systems and the diagnostic codes can serve as a tool for documentation in various other programmes such as outreach activities.

iii. Validation and reliability testing of Ayurveda Diagnostic Tools

Diagnosis forms the most important part of any medicine as this directly influence the outcome of any treatment. Diagnosis in Ayurveda can be grouped into Roga Pareeksha and Rogi Pareeksha. The examination of disease is done through nidana panchaka (Nidana, Purvarupa, Rupa, Upasaya- Anupasaya and Samprapthi) and Rogi Pareeksha is done through Astasthana and Dasavidha Pareeksha commonly. Ayurveda has dealt with these examination methods in depth but attaining a uniform diagnosis encompassing all these factors after detailed examination still remains difficult. Bio-medicine has come up with excellent tools of case recording for the purpose of diagnosis. Current Ayurveda graduates are exposed to both systems and though there is an arbitrary system in place to achieve the objective of clinical case recording, the reproducibility in terms of measurable parameters is non-uniform and hence the diagnosis comes out vague. Keeping in view, it's the need of the hour to "prepare standardized diagnostic protocol(s)/tools" which are aptly integrated with latest Information Technology tools such as *Internet of things* (IoT) to aid Ayurvedic Physician in proper diagnosis and assessment of roga, rogibala and achieve the objective of "*Anapayi Chikitsa*".

Considering this, CCRAS has undertaken a project on reliability testing and validation of Ayurveda diagnostic tools focusing on development of Standardized Ayurvedic Case Taking Protocol(SACTP) in consideration with elements of diagnosis/Case recording from Ayurveda and current Standard health record format(s) ,developing standard diagnostic protocols for selected diseases frequently managed is considered in conjunction for uniform diagnosis and development of an interface for integration/ Customization and development of diagnostic gadgets which are integrated with latest information technology tools for accurate and easy diagnosis.

For this purpose, a Standardized Ayurvedic Case Taking Protocol incorporating comprehensive patient history, recording the disease in Subjective, Objective, Assessment and Plan (SOAP)format wherein subjective and objective parameters are recorded in problem oriented medical record format (POMR) examination of etiology ,recording of parameters of Dasavidha Pareeksha, in-depth recording of Samprapthi Ghataka to assess pathogenesis of the disease has been planned.

iv. AYUSH Ph.D. Fellowship Scheme

CCRAS was nominated as Nodal Council by Ministry of AYUSH to initiate AYUSH Ph.D. Fellowship Programme to encourage research in AYUSH Systems and to further enhance Research Opportunities for meritorious AYUSH Scholars. The AYUSH- National Eligibility Test for Ph.D. Programme (a computer based online examination) was successfully conducted and total 45 candidates qualified the AYUSH-NET in Ayurveda, Yoga & Naturopathy, Unani and Homoeopathy Streams. AYUSH-NET Qualifying Certificates have been issued to all qualified candidates for getting registered themselves in CCRAS Institutes or Ayurveda Institutes/ Universities (conducting Ph.D. Programme) of their choice during 2 years validity period.

Two other Advertisements regarding "*Ph.D. Fellowships/ Junior Research Fellowships (JRF) for Non-AYUSH Candidates of Bio-medical Sciences related to Life Sciences in Ayurveda, Yoga& Naturopathy, Unani, Siddha and Homeopathy*" and regarding "*Selection of Universities/ Institutes running Ph.D. Fellowships/ Junior Research Fellowships (JRF) for streams in Ayurveda, Yoga& Naturopathy, Unani, Siddha and Homeopathy*" were published in Employment News and other national newspapers. Two Scholars of Non-AYUSH fields were awarded Scholarship (JRF) after selection by Expert Committee. Selection of Universities for AYUSH Ph.D. Fellowship Programme is under process for which an Expert Committee has been constituted.

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DR. R. D. LELE

HISTORY OF MEDICINE IN INDIA

A book compiled by Prof. Dr. R.D. Lele, MBBS (Osm) D.T.M&H (Eng) MRCP (Edin) FRCP (London) Hon. D.Sc. Hon D.Lit. Emeritus Professor of Medicine (for life) & Ex-Dean, Grant Medical College & Sir J.J. group of hospitals, Mumbai, Emeritus Director of Nuclear Medicine , Jaslok Hospital & Research Centre, Mumbai Ex-Medical Director & Director of Research, Jaslok Hospital & Research Centre, Director of Nuclear Medicine & RIA, Lilavati Hospital & Research Centre, Mumbai (2000-2015) Emeritus Professor of Medicine, National Academy of Medical Sciences. Chairman, Research Advisory Committee, Haffkine Institute of training, Research & testing, Mumbai; President, Arogya Bharati Konkan and Mumbai regions Rotary International, Paul Harris Fellow.

Awards:

- First recipient of Gifted Teacher Award, Association of Physicians of India 1990 Padma Bhushan (1992) Dhanwantari (1998)
- Homi Bhabha Life Time Achievement award (2007)
- API Dr. Parmeshwar Life Time Achievement award (2014) Books by Dr. R. D. Lele

Books by Dr. R. D. Lele

1. Principles and Practice of Nuclear Medicine 1984. Arnold Heinemann
2. Ayurveda & Modern Medicine 1986, Bhartiya Vidya Bhavan, 2nd edition 2001, 3rd edition 2018
3. Computers in Medicine 1988, Tata Mc Graw Hill, 8th reprint 1998
4. Medical profession & the Law 1992 Sajjan Sons 2nd edition 1993
5. Clinical Science & Clinical Research 1993, Sajjan Sons. 2nd edition National book depot.
6. Rural Reconstruction: Challenges & opportunities 1996 Bharatiya Vidya Bhavan
7. Clinical Approach 1997 Oxford University press, 2nd edition 2007 National Book Depot. 3rd ed 2015, 4th ed. 2018
8. Computers in Medicine: progress in medical informatics 2005. Tata Mc Graw Hill
9. Principles and Practice of Nuclear Medicine & correlative Medical Imaging CT/MRI/US 2007 Jaypee Brothers
10. 40 years of Jaslok: Life begins at Forty 2013
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National Centre of Indian Medical Heritage

Central Council for Research in Ayurvedic Sciences

Ministry of AYUSH, Govt. of India, New Delhi

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