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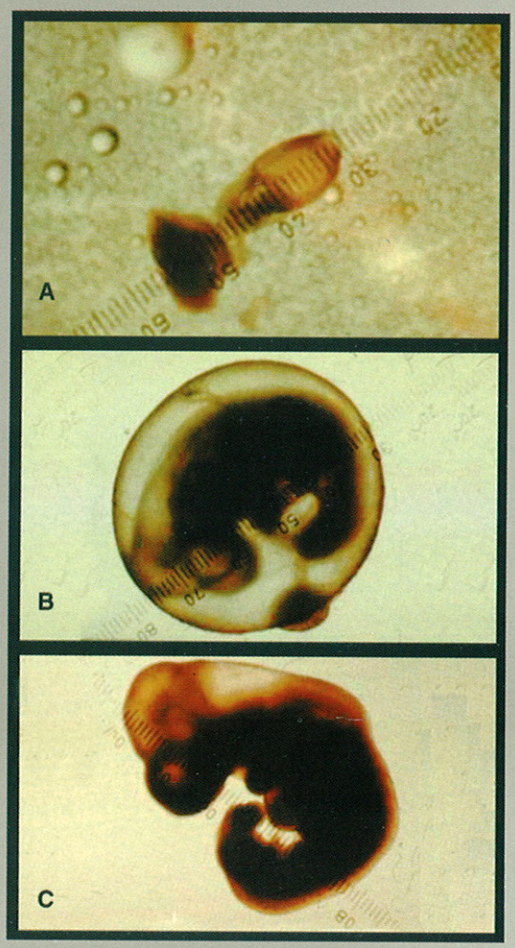

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Cover

A - Egg cylinder conceptus microdissected from decidual mass harvested from a 9.5 day pregnant rat.
B - Cultured embryo in yolk sac with heartbeat and vitelline circulation visible (4.5 mm c-r length).
C - After completion of organogenesis, embryo (5.5 mm c-r length) demonstrating limb bud and tail development.
(Embryo cultured in the department of anatomy and photographed through an Olympus dissecting microscope - Photographs and photomontage by Subramaniam Krishnan)

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Manuscripts: All manuscripts should be submitted in duplicate, typed on one side of A4 size paper and double-spaced with at least 2.5 cm margin. A computer diskette (3.5 in) containing the manuscript in MS Word 6.0 or Word Perfect and a covering letter, stating that the work has not been published or under consideration for publication elsewhere, should be submitted to the Editor. Presentations at meetings do not class as prior publication. The text of the manuscript should be in the following form:

Title page: The title page should contain a concise title of the article. It should identify all the authors, the name(s) of the institution(s) and their full addresses where the work was carried out. The initial and address of the corresponding author should also be indicated.

Abstract and Keywords: The second page should contain an abstract of about 150-200 words. It should state the purpose of the study, a brief description of the procedures employed, main findings and principal conclusions. Three to ten key words should also be listed below the Abstract.

Text: Wherever possible, the text should consist of an introduction, materials and method, results, discussion and references.

References: Number references consecutively in the order in which they are first mentioned in the text. References in the text should be indicated by a figure within parenthesis. The titles of journals in the list should be abbreviated according to the Index Medicus. Authors are responsible for the accuracy of all references. Examples of correct forms of references are given below:

i) ***Journal reference:***
Roberts CW, Alexander J and Bossi L. Studies on a murine model of congenital toxoplasmosis. Parasitol 1992; 104: 19-23.

ii) ***Personal author(s) of book:***
Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice-Hall, 1976.

iii) ***Chapter in book:***
Weinstein L., Swartz MM. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, Eds. Pathologic physiology: mechanisms of disease. Philadelphia: WB Saunders; 1974; 457-472.

Tables: Type each table on a separate sheet and number in arabic numerals. The tables should be as few and as simple as possible, with the title above and any notes or description below. Explain all abbreviations.

Figures: Graphs, drawings and photographs should be submitted as clear, glossy prints measuring 12 cm by 17 cm. Figures should be identified on the back with the title of the article and figure number (in light pencil) and an arrow to indicate the top. Legends to the figures should be submitted on a separate sheet. Explain all abbreviations and symbols used.

Letter of Consent: Submissions must be accompanied by a letter of consent, signed by ***all*** authors, containing the following text:

"The manuscript represents original, exclusive and unpublished material. It is not under consideration for publication elsewhere. Further, it will not be submitted for publication elsewhere, until a decision is conveyed regarding its acceptability for publication in the JUMMEC. If accepted for publication, I agree that it will not be published elsewhere, in whole or in part without the consent of the Journal of University of Malaya Medical Centre. The undersigned author(s) hereby transfer/assign or otherwise convey all copyright ownership of the manuscript entitled *(the title of article)* to the Journal of University of Malaya Medical Centre."

SOME THOUGHTS ON THE CHANGING FACE OF ACADEMIC MEDICINE

These are difficult times for academics in general, and particularly so for those in medical faculties everywhere. Most of us arrived at the medical school for various reasons - narcissistic, altruistic, or perhaps even sheer "somatic destiny". And we strive (or at least try) to bring order to the system we are in, and seek for opportunities to give what we did not receive or better than we did. After all, most of us are surely concerned about our chosen discipline, and anxious that certifiable incompetence does not lead our departments and institutions.

It is convenient to think that our duties are perched on a tripod, the legs of which support the functions of teaching, research and service. Sometimes one wonders if that tripod seems to be toppling, the legs overstretched, and the aspirations it embodies eclipsed by the harsh realities of life.

As academics, our original and abiding purpose has been to be guardians of the knowledge base, and to teach it in theory and practice. The task of physicianship remains an overriding obligation to relieve suffering, to enhance the patient's ability to heal himself, and to allow for the collaborative synergy to drive the healing process. We utilize the best of science, sense and sensitivity, confident in the knowledge that in our formative years we have seen the worst; but that we have learned to hope for the best.

However, these are trying times to be an academic leader. Escalating health care costs, hard economic times, health care cost constraints and the emergence of managed care as an important factor in the health care equation has thrown the entirety of medicine, governance of ourselves and our interfaces with society in disarray.

The essential clash of value systems may be illustrated by the shifting focuses in the way we conduct our daily businesses, as the challenges and concerns of a Medical Center become intertwined with the ideals of a medical school - a business vs. an academic environment; a top-down, flexible and fast response vs. a bottoms up, reiterative, often slow, consensus based style of governance; output as measured in dollars vs. publications; organizational success dictated by budget, the bottom line, and patient and employee satisfaction vs. faculty bibliography and inflow research dollars. These problems are global, and the fate of teaching hospitals in the US and UK are testimony; many of these ravenous monoliths face the tide of mismanaged care and have become fragmented by competitive health care institutions.

It is clear than, that if we are not vigilant, academic medicine could become an increasingly depersonalized, bureaucratized, fragmented and increasingly commercialized practice.

Medical faculties have generally been well tolerated within universities. Thankfully or not, society and government has always had an investment in our profession. Universities have been the seat of quiet reflection, whereas professions combine both reflection and action. That delicate tension between medical knowledge and its practical application indeed provides much of the attraction of a medical career. One vital role of academic leaders and chairs in medicine is to mediate these tensions between the pure sciences and the messy clinical sciences, the practitioners and artisans of medicine and the clinician-investigators, between education and vocational training. For the University, this brings overheads plus risks and abstract business concerns that seek to distract from the "goals of the mind".

These complexities have also inflicted the research leg of the tripod. The modern day researcher has to contend with animal and human ethics committees, local and national research review boards. He has to be mindful of miscalculating statistics, guard against inadvertent plagiarism, trust computer printouts of complex clinical research, and strive for multidisciplinary direction and commercial fruit at the end of the line for a project to be ensured longevity. Marrying these with a truckload of faculty responsibilities and achieving good annula performance reviews is a thrilling challenge, but .. it is a challenge.

The net result of this has been that some of the best teachers, physicians and researchers now actively seek different arrangements than that

available in academe to pursue their essential purpose. Perhaps the independent research institute, or one situated within the university, or sometimes private enterprise companies, some of which our brightest investigators start and in which they invest in, as a far more effective way to achieve their goals of pursuing knowledge gain. The proliferation of multi disciplinary approaches to patient care and research (the neurosciences and biotechnology leap immediately to mind), have resulted in clinicians budding off into groupings of experts in the community, or has resulted in them signing up with for-profit hospitals essentially in the search for more congenial locales to support scientifically tutored medical practice.

So what is to be done ?

It is probably not enough to say that our work in the Faculty is a costly but necessary and cost-effective national resource. It may be timely to bring the full direct and indirect costs of medical education out into the open, to grapple with issues such as how much a research bed costs, or for the need for equipment and the funding for research education. Biomedical research remains an enthralling adventure, and were it not for the sheer excitement and fun that it offers, and the stimulus afforded by students, there would have been far more exits from the system than we've already had. The real monopoly of medical schools is the free flow of undergraduate and postgraduate personnel. We must harness this resource and model the services needed for their education. I have always believed that it is an effort to avoid the anti-innovative thrusts that are ingrained in the system, often involuntarily, developed as a result of sheer convenience from the symbiosis between "the system" and overworked academic and general staff.

The hearts of public policy and academic medicine must meet soon and it is my hope that they find each other in complete collusion. Public policy must find the enormous good that is offered by deliberative, scientifically tutored medicine in the context of the doctor/ patient relationship. I know of no other institution that exemplifies better the complex missions of society than the medical school and its idealistic tripod of goals.

It has been a tremendous privilege for me to be in the extraordinary company of colleagues in academic medicine. And so it can be for our students is we practice what is indeed academic about academic medicine.

PATHMANATHAN R

MAGICAL MOMENTS IN MEDICINE
Part 4: Indian, Chinese & Islamic Medicine

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Most chronicles which document the history of medicine generally eulogise Greek philosophers and healers for the invention of scientific and rational medicine. While it is a fact that Greece has contributed handsomely towards the evolution of medicine as a scientific discipline, it is also true that European scholars, accustomed to trace roots of Western culture back to Greco-Roman times, commonly disregarded the development of medicine, science and philosophy in the East, especially in Arabia, China and India. Magner, in his book has noted that this is particularly distressing, since the medical traditions of these countries are very much alive, unlike the extinct traditions of Egypt and Mesopotamia.

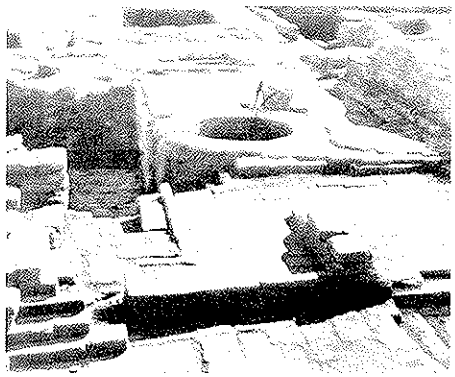
In this episode, we shall attempt to explore three great eastern healing traditions, which among them held a vast amount of medical erudition, contributing significantly towards medical concepts of the present day.

Indian Medicine

Even as it races with China, vying to attain the most populous nation status by the year 2050 (with two babies being born every three seconds), India, with its diversity in race, religion, culture and language, presents a profile of bewildering complexity. Its medical traditions can be traced back to the 15th century BC.

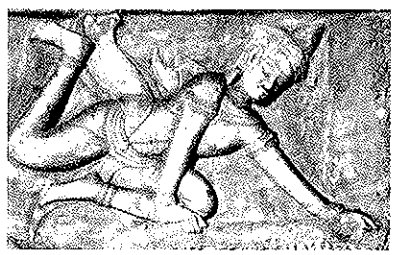
The sands of Sind, (now in Pakistan), kept deep within them, a well guarded secret for centuries. Glorified grave diggers - simply called archaeologists - brought to light the remains of a civilisation going back 5000 to 6000 years and perhaps even further, when two ancient cities called Mohenjodaro and Harappa were excavated in the 1920's. These cities, which were part of the forgotten Indus Valley Civilisation, were well planned and constructed and included houses having adjoining bathrooms, wells and an elaborate public drainage system. (Picture A). Some scholars even believe that ancient Indian civilisation dates back from a period contemporary with the Egyptians and Babylonians.

Three significant periods are described in the development of ancient Indian medicine. The Vedic period started with the Aryan invasion of Punjab around 1500 BC. Aryan culture was amalgamated with the local Hindu style of life and the intricate blend saw the emergence of a new era in culture, art and medicine. Sanskrit itself was one of the dialects of the Indo-European linguistic family, brought to India by the conquering Aryans. Scientific books called Vedas (Sanskrit for knowledge) were composed during this period, the four main Vedas being Rig, Yajur, Sama and Atharva Veda. Atharva Veda is the



Picture A. Paved bathroom and brick well (3300 BC) excavated in the ruins of Mohenjo-daro, indicating the advanced sanitation levels rivaling Mesopotamia and Egypt. *(From Medicine - An Illustrated History)*

earliest Indian document in which many medical references are found, but these are primitive and impregnated with a lot of magic and sorcery. *Ayurveda* (knowledge of long life) is considered an off-shoot or ancillary of the Atharva Veda and dealt particularly with medicine. Its authorship is allegedly attributed to Dhanvantari (Aesculapius' Indian counterpart). Ayurveda, however was not written in his divine capacity. Dhanvantari, (Picture B) a god who supposedly arose from the churning of a sea of milk, was in later life believed to have been moved by the sight of ailing mankind. He is said to have assumed mortal status after being born on earth as a prince, only to later relinquish his position to become a hermit. Withdrawing to the woods he is reported to have eventually prepared the sacred healing book, *Ayurveda*.



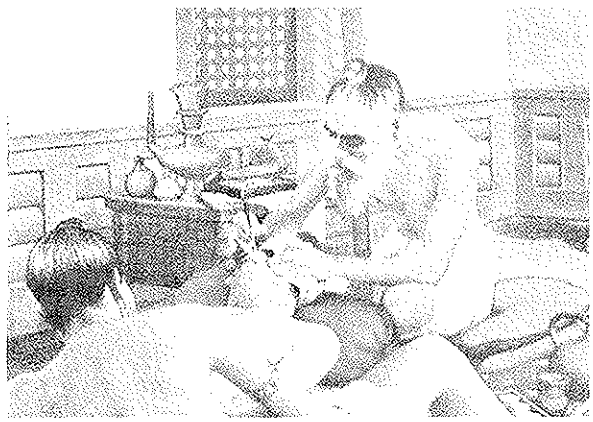
Picture B. Dhanvantari, the patron deity of Indian medicine *(From Medicine - An Illustrated History)*

The second period started around 800 BC and all kinds of learning - be it culture, art or medicine - was totally dominated by a priestly social sect called the Brahmins and the term *vaidya* was applied to all practitioners. The Brahminical period, which represented the peak of development of Indian Medicine, saw the development of great doctors like Charaka, Susruta and Vagbhata - honoured as the "Triad of Ancients". The writings and commentaries of these semi-legendary authors, together with ancient Vedic teachings, helped to enrich the existing knowledge and formed the cornerstone for all the subsequent constructions on the magnificent edifice of Indian *Ayurvedic Medicine*. Ayurveda emphasised on a more "holistic" approach, thus dealing with the body, mind and spirit (or the physical, subtle and causal aspects of the disease).

Ayurveda was delineated into eight specific branches of medicine: internal medicine, diseases of the head, surgery, toxicology, demonic diseases, paediatrics, rejuvenation and aphrodisiacs. There were two main schools of Ayurveda at that time, *Atreya* - the school of physicians and *Dhanvantari* - the school of surgeons. These two schools made Ayurvedic medicine classifiable and scientifically verifiable. Through research and experimental testing, they dispelled the doubts of the more practical and scientific minded, removing the aura of mystery that surrounded the concept of Divine revelation. Consequently, Ayurveda grew into a respected and widely used system of healing in India. People from China, Tibet, Greece, Rome, Egypt, Afghanistan, Persia and numerous other countries came to Indian Ayurvedic schools to learn about this system of medicine and to take it back to their own countries.

Origin of organic life was classified into four groups: *Svedaja* or "sweat-born" (insects), *Andaja* or "egg-born" (birds, snakes and the like), *Jarayusa* or membrane-born (mammals) and *Udbhissa* or "sprout-born (all plants). Chaulmoogra oil was used in the treatment of leprosy and the Indian snakeroot (Rauwolfia serpentina) was used to relieve various disorders, until the early part of this century, when reserpine was extracted for its root when found dramatically effective in the treatment of hypertension and mental disorders. However, like most other civilisations, magic played an important role in ancient Indian medicine. Demons were put down as the cause for several diseases, even in scientific treatises.

Among the whole galaxy of ancient Indian healers, the one illustrious name which traditionally stands out is that of Susruta (Picture C). This distinguished man, who has been cited both by the famous Arabian physician Rhazes, as well as the Chinese Buddhist pilgrim I-tsing, also features in the famous Bower manuscript dated 350 AD. He was an eminent surgeon, and his work, called the *Susruta Samhita* (Susruta's Collection) includes not only surgical procedures but also some principles of medicine, pathology, anatomy, midwifery, biology, ophthalmology and hygiene. The descriptions of human anatomy, however, were comparatively less accurate in details. In fact, the records of that age that we have certainly do not compliment ancient Indian knowledge of human anatomy. Religious laws and beliefs and a taboo on cadaveric dissection could be the reason for this. Forced to comply with religious regulations, Susruta circumvented the problem by proposing an unusual form of anatomical investigation. He suggested that after removal of the excrement from the intestines, the anatomist should cover the body with grass, place it in a cage of fine mesh, and leave it to lie in a shallow pond. A week later, the anatomist could gradually remove successive layers of the skin by gently rubbing with soft brushes.

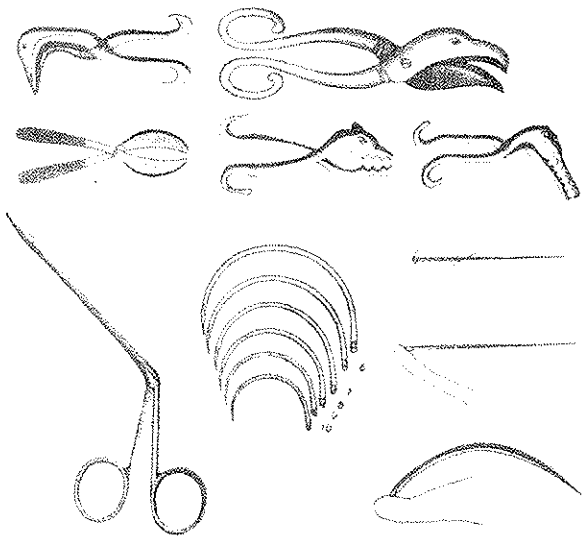


Picture C. Susruta, performing surgery *(From Great Moments in Medicine)*.

Paradoxically, in spite of a weak knowledge of anatomy, he had superior skills in surgery and performed operations ranging from tonsillectomy to amputations. Susruta describes some 125 surgical instruments, including tongs, hooks for nasal polyp removal, rectal specula and even magnets for removal of metallic foreign bodies. The instruments were usually likened to animal parts like the 'lion's jaw' and the 'heron's bill'. (Picture D). Different types of bandages and dressings are described with their indications and contra-indications. Cataract operations were child's play for Susruta and his associates. Obstetric procedures described by Susruta indicates skill in this field not achieved in the West until many centuries later. Operations for haemorrhoids, fistulae and intestinal obstructions are all described in his book. Ancient Indian doctors were familiar with epilepsy, tetanus, hemiplegia, elephantiasis, ulcers and abscesses, osteomyelitis, scrofula, goitre and several venereal diseases. Susruta himself mentions no less than 1120 diseases and 760 herbal drugs.

An interesting mention is made of how wound suturing was done during that time. Various types and sizes of needles (Picture D) and thread were used for closing

simple wounds but when intestines were torn, the edges of the wound were drawn together and the mouth of a large black ant was applied to it. As the ant bit, it was yanked away, but in the process the head and mandible of the decapitated insect held the edges together as a biological clamp. Several such ants were used serially, until the entire wound was closed. Albucasis, the Arab surgeon in his medical treatise written much later, makes a mention about sewing up the colon with a certain species of big-headed ants. This technique of stitching up surgical wounds was used even as late as the 19th century by surgeons during the war between the Greeks and the Turks and might possibly be the forerunner of absorbable catgut.

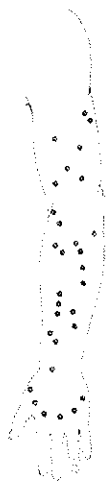


Picture D. Ancient Indian surgical appliances and needles *(From Medicine - An Illustrated History)*

Records lead us to believe that ophthalmic surgeons often 'tricked' their patients into undergoing the operation of cataract removal. While pretending to examine the eye, the operator suddenly and unexpectedly thrust a needle into the cornea and quickly detached the opacified lens. The eyes were then bandaged and the patient advised complete rest for 24 hours. Considering the primitive modes of transportation in ancient days, this was a comfortable period for the surgeon to make a clean getaway, just in case things turned sour.

One aspect of human anatomy which all students were expected to master was the complex system of vital points called '*marmas*' (Picture E). These points, which parallel Chinese acupuncture, were thought to be the sites where major arteries, veins, ligaments and muscles unite and where injuries are likely to be incapacitating or fatal. The classical system had 107 points, each with a special name. From Susruta's book, we learn of the first science of massage, using the *marma* points for reference. Even the Polarity Massage Therapy, popular in America, is said to have been developed from ancient Indian massage techniques.

Charaka represented the Atreya school of physicians. Charaka's work the '*Charaka Samhita*' was the first great treatise of Indian Medicine and had eight volumes. The presentation was in the form of a dialogue between a teacher and his pupil. It discussed physiology, anatomy, aetiology, pathogenesis, symptoms and signs of disease; methodology of diagnosis, treatment and prescription of patients; prevention and longevity. Included were internal and external causes of illness. Charaka states that the first cause of illness is the loss of faith in the Divine. According to him, external causes of health included time of day, seasons, diet and lifestyle. There is a whole section discussing the medicinal aspects of herbs, diet, and reversing of the ageing process. For the skeptical modern person, who wonders if this ancient wisdom can be believed, one only needs to read Charaka's month-by-month description of the development of the foetus in the womb to see that it remarkably corresponds to what we know today from using modern techniques.

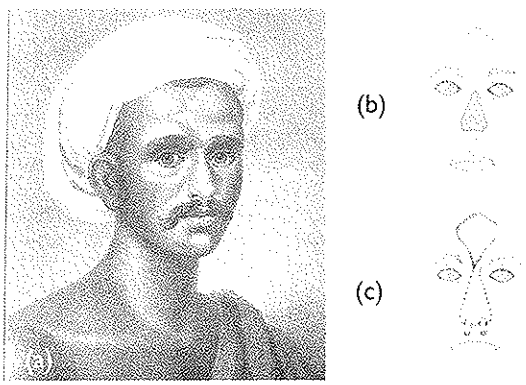


Picture E. Marma points in the arm *(From Medicine - An Illustrated History).*

Vagbhata's book refers both to Charaka and Susruta and is obviously the most recent. Not much is known about the author's biography.

In ancient Indian society, justice was meted out for wrongdoers in the form of physical mutilation and amputation, the severity and degree of punishment depending on the nature of the crime committed. A 'nose-cut' was the penalty for adultery (although one would have expected an amputation of the appendage concerned). This was probably in order to make the countenance gory and unpresentable for future advances towards the opposite sex. This apart, warriors (who were generally not used to fighting with protective headgear) landed at the surgeon's doorstep minus earlobes, noses and lips. Therefore, plastic and reconstructive surgery became the most remarkable aspect of the Indian doctor's achievements (Picture F).

During this period, diagnostic approaches were as much superstitious as they were rational. Omens played an important role. Although severity of disease was often measured by ridiculous parameters like flight of birds and sounds of animals, due attention was also given to the patient, especially his sputum, urine, stool and vomitus. Fever, dubbed as the 'king of all bodily diseases' was observed with great care, the intervals between peak periods giving the key to prognosis. In ancient India, diabetes was called 'the honey urine disease' is said to have been diagnosed by the sweet taste of urine, but it is not known whose gustatory faculty was used for the appraisal. Europe became aware of this procedure of detecting sugar in the urine only after about thousand years. The pulse, an important diagnostic tool, was well studied and classified into an elaborate system. For diseases which the physician thought was caused by improper diet, treatment commenced with a week long fast. Many recovered during this period and needed no other treatment. Some presumably died of starvation and also, needed no further treatment.



Picture F. The first nose jobs: a) Picture of an Indian bullock cart driver, whose nose has been successfully restored after punitive mutilation. When this picture appeared in the October 1794 issue of the *Gentlemen's Magazine* of Calcutta, it reportedly astonished the British sahibs and memsahibs. (*A History of Medicine*) b & c) Ancient Indian Rhinoplasty: A trefoil leaf shaped flap of skin was raised from the forehead, making sure that the end nearest the bridge of the nose remained attached. The flap would be brought down to where the nose should be, twisted skin side out and sewn into place. Two polished wooden tubes or hollow reed were inserted to keep the air passages patent during healing. New earlobes were also fashioned this way. *(From Medicine - An Illustrated History).*

Four types of disease have been described namely traumatic, bodily, mental and natural. A person is said to be healthy if the three *Doshas* (humours) - *vata* (wind), *pitta* (gall) and *kapha* (mucous) - are in perfect balance and in harmony. The basic principles of Indian humoural pathology appears similar to those proposed by Hippocrates, but Ayurveda gets complicated down the line. It states that five elements - earth, water, fire, wind and vacuum - and seven types of tissues constituted the body.

None of the ancient Indian texts on medicine make a mention about anaesthesia. In Susruta's time, suppression of pain was brought about by getting the patient drunk with generous quantities of wine. Inhaling the fumes of burning Indian hemp (cannabis) was also a method used to produce some amount of anaesthesia.

Ancient Indian medical literature reveal that personal and community hygiene were priority areas in their daily life. Tooth brushing twice a day, baths, massage, exercise, proper dietary habits, well-regulated sex life and adequate rest were emphasised. Variolation against smallpox was practised by inoculating people with pus from a small pox skin boil by puncture or scarification and it was from India that the Western world first learned of this method of prevention, which eventually led to the discovery of vaccines in the 19th century.

The third period followed the Muslim conquest in the seventh century AD, which brought Arabic medicine into India.

As has been observed by Keith, "The striking similarity between Greek and Indian medical systems has been long well known. We find in both such things as the doctrine of humours, whose derangement explains disease, the stages of fever and several other lines of thinking which resemble each other. Even the description of a dying patient clutching his bedclothes elaborated in Susruta Samhita is similar to the classical description given by Hippocrates in *Prognostic.* But it must be confessed that it is very difficult to determine how much is due to Greek influence and how much is merely parallel development."

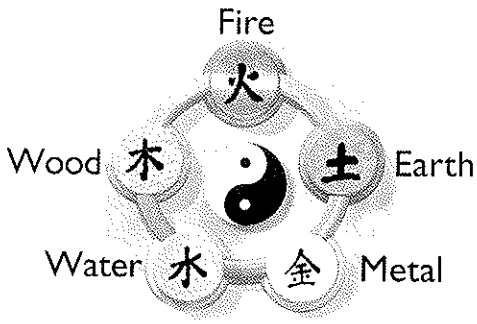
In his foreword to Dr. Julius Jolly's book Indian Medicine, Filliozat observes that 'Indian Medicine has played in Asia the same role as the Greek medicine in the West, for it has spread in the region as far as Japan, as Greek Medicine has done in Europe.' Today, even while India has allowed modern science and medicine to reinforce its medical system, Ayurveda still brings comfort to millions. But its connections with theology and links with religious sentiments have prevented its growth and made it relatively static. However, since Susruta's Samhita and other notable works of Charaka and Vagbhata were all translated into Persian and Arabic, around 800 AD and since Arabic medicine became the basis of European medicine around the 17th century, it can be said that Indian ideas live till this day, having indirectly found their way into modern Western medicine.

Chinese Medicine

Chinese medical traditions are among the oldest in the world and the systems of medicine developed in ancient China have survived till this day in almost its pristine form. In contrast to most other systems of medicine which have either mutated or modified with times, the fine Chinese art of medicine has maintained its identity to a great extent. Although the religion amalgamated a lot of magical and superstitious beliefs, it is said that even as early as 400 BC, Chinese medicine had evolved as a separate entity, efficiently handled by professionals. The doctors were classified according to their achievements and surgeons (not unlike the 'barber surgeons' of the West) were among the lower rungs of the ladder of medical hierarchy. The Chinese called these ulcer physicians 'third-rate graduates' and considered them only marginally better than veterinarians. Clinical successes and failures had to be reported for promotion and grading. Physicians who cured all their patients were ranked first class; the lowest grade was awarded to those who could not cure more than 60% of their patients. Examinations needed to be passed in order to practice. During the period of the Chou dynasty, (1122-255 BC), the government conducted yearly examinations of those who wished to practice and this was several centuries earlier than the first known licensing system of the West. The best candidates were selected for Imperial Service and attached to the Imperial College of Medicine. In the early 14th century, fourteen medical specialities existed in China, with complex subdivisions; doctors for great blood vessels, small blood vessels skin, larynx, mouth etc., Female physicians are mentioned in the Han dynasty documents as early as 206 BC.

Ancient Chinese believed that the universe was self-generated by the interplay of two forces - *Yang* and *Yin* - and not by divine direction. *Yin* was considered the moist, cold, negative, earthly and feminine power. It represented darkness and its literal translation means the 'shady side of the hill'. *Yang* represented the bright, dry, active, warm and positive masculine aspect derived from the heavens. Translated, it means 'sunny side of the hill'. *Tao* (meaning 'the way') was the ultimate principle of the universe which determined *yang* and *yin* in all living creatures. They believed that good health results from a delicate and harmonious balance between these two opposing, yet complementary forces. Anything that altered the balance was considered bad and which resulted in disease. Like the ancient Indians, they also believed in five basic elements (Picture G). Earth, water and fire were common in both countries, but the Chinese believed in wood and metal rather than in wind and vacuum. In fact, the number five was mystical for ancient Chinese who felt there were five elements, five seasons, five tastes, five kinds of drugs, five treatments, five emotions, five colours and five solid organs). According to Lyons, along with Buddhism, some medical concepts Yoga and Ayurveda also found their way to ancient China from India, which were partly incorporated in the gymnastic and breathing exercises in Chinese medical mythology. Chinese ambassadors who travelled far and wide, enriched medical science by bringing back information on drugs and other subjects.

The earliest works of medicine in ancient China are attributed to the Three Celestial Emperors; Fu Hsi, Shen Nung, the Red Emperor and Yu Hsiung, the Yellow or Golden Emperor. These colourful and legendary rulers are revered as the founders of Chinese Civilisation. The *pa kua* which is a symbol composed of *yang* and *yin* lines combined in eight (*pa*) separate triagrams(*kua*) is said to represent all yin-yang conditions(Picture G). Emperor Fu Hsi,(2900 BC) is said to have conceived the *pa kua*. He is also credited with the authorship of *I Ching* or Canon of Changes, considered the most ancient of Chinese books.



Picture G. The *pa kua* symbol, depicting the basic dichotomy in the Universe and the possible combinations of the two.

The compilation of the first Chinese medical herbal, the *Pen-tsao* is attributed to Shen Nung the Red Emperor, (2800 BC) who reports the effects of 365 personally tested drugs. He is also supposed to have drawn the first charts on acupuncture, which is presumably older than these emperors themselves. This "Divine Peasant" is supposed to have taught his people to sow five different types of grain and also to have tested several poisons on himself. He is reported to have, however, lost his life after an unsuccessful experiment.

Yu Hsiung, or *Huang Ti*, the Yellow Emperor, (2600 BC) supposedly gave his people the wheel, the magnet and the calendar, but outshone his predecessors by producing the *Nei Ching* or the Classic of Internal Medicine. This is thought to be the oldest and most comprehensive medical text in existence and combines medical theory with clinical practice. It is said that the wisdom contained within was transmitted orally for centuries before it finally was committed to writing, somewhere around the third century BC. A major

portion of the text is in the form of a dialogue between the Emperor and his Prime Minister, Ch'i Po, discussing various aspects of health, illness, prevention and treatment. The book also corroborates the basic principle of Chinese Medicine that the *yang* and *yin* forces which govern the cosmos and also the human body. For instance, ejaculation in intercourse was believed to reduce a man's *yang*, which upset his natural balance, but at the same time the balance was restored when he was strengthened by the absorption of the *yin* released from the orgasm of the female partner. Likewise, every system of the body was believed to be governed by the yang-yin philosophy. The *Nei Ching* describes 'blood current continuously flowing in a circle without stopping' and it is quite possible that Harvey was beaten to it by the ancient Chinese who seemed to have understood the principles of blood circulation millennia ahead.

The magnum opus of Chinese pharmacology is a 16th century work called *Pen-ts'ao Kang Mu* which is a Compendium of Materia Medica written by Li Shizen, China's purported "prince of pharmacists". It lists 1892 different herbal drugs as well as 11,000 prescriptions, apart from carrying over a thousand illustrations and 900 cross references. It could therefore be observed that in the history of Chinese Medicine, virtually every herb and substance found in nature has been used as a cure for some malady. In addition, Sun Szu-miao led a committee which produced a fifty-volume collection on pathology.

Drug anaesthesia was developed as early as the 2nd century; vertebral fractures were treated using suspension in the 12th century; inoculation for small pox (the 'heavenly blossom' disease) was a widespread practice in China during the 16th century. Doctors collected crusty scabs from small pox pustules and powdered them. The powder was then put into the nostrils; males snorted through the left nostril and females through the right side. These facts prove that the Chinese system of medicine was highly refined and advanced centuries before the same concepts were adopted by Western medicine.

Ephedra is a plant substance uniquely associated with China. It was described as *ma huang* the 'horse tail plant' by the Red Emperor useful in the treatment of respiratory diseases. It's active principle *ephedrine* was extracted and isolated in the late 19th century and has been a useful drug in Western medicine since. *Gin seng*, the 'man shaped root' which is popular right till this day, is almost a miracle herb to many. Ancient Chinese believed that it could delay ageing, increase libido, and calm the agitated and stimulate the fatigued. The gathering and preparation of ginseng was surrounded by a rich body of folklore, ritual and myth. Only wooden knives and earthenware pots were used to prepare ginseng since metal was believed to destroy its virtues. Wild ginseng was also supposed to roam about at night, with a luminous glow, disguised as a bird or a child, luring ginseng hunters to their death. Many research studies are on to find out the constituent structure of this root which has been attributed with such miraculous healing powers. Remedies made from noxious or repulsive ingredients - the "dreck" apothecary - is also part of the Chinese materia medica. Dried salamander, donkey skin, medicinal urines were some of the less appalling constituents; please use your foul imagination for the rest.

Surgery is reported to have generally been outside the domain of China's scholarly medicine, probably due to legal prohibitions on dissection and general reluctance towards mutilation of the body. Nevertheless, forensic medicine was highly sophisticated as evidenced by the *Hsi Yuan Lu*, a codified forensic medicine compilation produced in the 6th century AD. Chinese history provides accounts of surgeons of great skill who performed miraculous operations. But only one surgeon of sufficient prominence has gone down in the history books. Hua T'o, who lived 1800 years ago, is credited with the invention of acupuncture anaesthesia, hydrotherapy, and medical gymnastics. As the story goes, he once successfully treated Kuan Yun, a warlord who was injured by a poisoned arrow. Later, he was called on to treat a nagging headache of Emperor Ts'ao Ts'ao, who, incidentally, hated Kuan's guts. Hua T'o advised trepanation. Just when the procedure was about to begin, the Emperor, in a fit of paranoia , suspected an assassination plot and ordered an on-the-spot execution of the unfortunate surgeon.

In the twentieth century, Chinese medicine was rejuvenated by Chairman Mao who felt that ancient Chinese medicine and pharmacology were great treasure houses that need to be preserved, explored and improved. It was felt that both Western trained doctors as well as traditional healers were needed to take care of the health needs of the rapidly growing population. The "Great Leap Forward" movement launched in 1958 saw the revival of traditional Chinese medicine. Right now, China has a health care system which is considered a model for other developing countries. Principles of medical education and practice have been carefully restructured whereby the physicians and the paramedical staff share diagnostic and therapeutic responsibilities.

Thanks to the foundations laid by the Three Celestial Emperors, the glorious edifice of Chinese Medicine, built over the centuries, has braved the storms of time and has remained largely unshaken. The refurbishment done by Chairman Mao has revitalised the ancient art, which incorporating old knowledge and new ideas will remain for ever as one of the greatest healing traditions ever known to man.

ACUPUNCTURE

The principles

In acupuncture, the skin is pierced by long needles to varying prescribed depths. 365 points have been described along meridians that vertically traverse the body. These are supposed to transmit an active life force called *ch'i* (pronounced 'chee'). This force roughly means a movement, with reference to something that can be understood as energy. The flow of *ch'i* influences one's health and the process of acupuncture is said to obtain and manipulate the *ch'i*, which travels throughout the body via "channels" or meridians. Presumably based on human dissections performed over 2,000 years ago in China, twelve Primary Meridians were described. Two additional meridians were added during the Song Dynasty (c. 1000 AD), making the total number of meridians fourteen.

Picture H. The Chinese character for Acupuncture is made up of characters for Gold and a Needle. On the left, you see the top of the mountain, under which is hidden, between strata of earth, two small nuggets of gold. On the right is a needle with thread passing through it.

The words 'acupuncture point' are derived from the Chinese characters meaning orifice and position (hole position). During the time of the Han Dynasty (c. 202 BC) it was discovered that certain points on the body reacted to the presence of disease. Each of these acupoints is related to a particular organ, but it must be remembered that these do not correspond to the body's nervous system. For instance, a certain spot on the ear lobe may be related to an abdominal organ. The meridians are like rivers flowing through the body to irrigate and nourish the tissues. An obstruction in the movement of these acupuncture energy rivers is like a dam that backs up the flow in one part of the body and restricts it in others. Acupuncture needles remove the obstructions at the dams, and re-establish regular flow. The earliest instruments used for acupuncture purposes were called *bian* which were made out of stone, bone, bamboo, or bone. They have been found to date back to the 17th century BC. Metal needles (iron) were used during the Shang Dynasty rule in the 16th century BC. By the 5th century BC, fine steel needles were being used. During the later centuries, gold, silver, and alloyed metals were used to fashion needles.

Acupuncture is said to work by stimulating the release of endorphins, which are morphine-like peptides in the brain and the natural pain-killers of our body. It is thought that the needles stimulate peripheral nerves, (especially the small myelinated A delta-type III fibres) in the muscles which send messages to the brain to release endorphins. These in turn cause analgesia by blocking the transmission of painful messages. The needles are also supposed to remove blockages allowing *ch'i* energy to flow. Since the needles are very fine, the procedure is virtually painless. However, acupuncture has been found to be effective only in approximately 70 to 80% of humans and animals. It does not work all the time in all people for various reasons. Individuals with high cholecystikinin (CCK) are found to be poor responders to acupuncture analgesia and on the other hand those who respond well have been found to have less CCK.

Moxibustion uses acupuncture principles, points and meridians, but instead of needles, moxa - powdered leaves of the mugwort plant - is placed as a small heap on the patient's skin and burned. This raises a blister and the warmth supposedly increases *yang*. Acutouch is a variant procedure, whereby gentle pressure is applied to acupuncture points to stimulate the related organs. In electrostimulation, electricity of very low voltage is applied to the acupuncture points.

Transcutaneous electrical nerve stimulation (TENS) is a procedure of the West which mimics electrostimulation. The reason why TENS is very much less effective than acupuncture is because it works by using the gate control theory of pain (first proposed by Melzack and Wall) and eventually habituation occurs. Moreover, TENS activates neurones of the skin first and the key A-delta fibres, (which are in the muscle) are not activated. Acupuncture needles activate these small myelinated A-delta fibres which in turn activate selected areas of the brain namely the pituitary, periaqaductal gray neurons in the mid brain and the spinal cord. These three areas are known to be involved in the endorphin mechanism.

The past

Acupuncture was first described by Huang Di "The Yellow Emperor" in China (2696 - 2598 BC) who was the third great emperor of China, but literature records lead us to believe that acupuncture existed even long before that time. Perhaps the clinical application of this science was more carefully studied and documentation initiated during the Yellow emperors reign. The surviving document is the Yellow Emperor's Classic of Inter-

nal Medicine. This Classic text forms the basis for acupuncture and seems to have been the current book of medical care around 2600 BC.

The next significant improvement was in 2006 BC through 202 AD during the reign of the Han Dynasty. Several important books were written at that time. The *Nei Ching*, which was the Yellow Emperor's classic of internal medicine has two parts: *Su-wen* (simple questions) discusses general medicine while *Ling Shu* (spiritual axis) was centers entirely on acupuncture and describes moxibustion as part of acupuncture.

One of the oldest existing texts of acupuncture and moxibustion is a book called *Zhen Jiu Jia Y. Jing* (Comprehensive Manual of Acupuncture Moxibustion) written during the Western Jin Dynasty (265-316 AD), During the rule of the Ming Dynasty, *Zhen Jiu Dei Cheng*, (Great Compendium of Acupuncture and Moxibustion) was written, which serves as a basis for most of the modern acupuncture treatment. In 1671, a Jesuit priest called Harviell, brought acupuncture to Europe via France, when he wrote about Chinese acupuncture in his book "*Les secrets de la Medicine des Chinois, Consitant en al Parfaite Connoissance du Pauls*". Wilen Pen Rhijne, a Dutch East Indian Company fleet surgeon in Japan provided further enlightenment for acupuncture treatment through his book "*Dissertatia de Arthritide*" written in 1683.

Less than a century later - in 1758 - Lorenz Heister, became the first surgeon to recommend acupuncture through his article "*Chiraigeies*". By the year 1820, acupuncture was taught in France at some of the best hospitals. With the French leading the way in European acupuncture, the Dutch and Germans followed suit, as acupuncture received a renaissance in the 1820's.

Franklin Bache, the great grandson of Benjamin Franklin, wrote an article, "Case illustrative of remedial effects of acupuncture" demonstrating the beneficial effects of acupuncture. In 1916, Sir William Osler recommended acupuncture treatment for lumbago in his textbook "The Principles and Practice of Medicine". These gave a transient boost for acupuncture in the United States for a period but however, after the 1920's acupuncture was rarely ever used in the United States for the next fifty years.

In 1971, James Reston, a New York Times reporter in President Nixon's entourage to China, developed appendicitis. The Chinese proposed surgery for his appendectomy using acupuncture anaesthesia which was declined. However, his post operative pain after appendectomy is said to have been relieved by acupuncture at the Anti-Imperialist Hospital in Peking, China.

In that same year, Gray Diamond wrote an article in JAMA, named 'Acupuncture anaesthesia, Western medicine and Chinese traditional medicine', in which he wrote about the experiences in China. Yet, people still felt skeptical about acupuncture. However, in 1973, the New York Society of acupuncture for physicians and dentists was formed and it became the first physician and surgeon organisation in the United States dedicated towards acupuncture. In 1973, The AMA council of Scientific affairs declared acupuncture an experimental medical procedure and the FDA directed that acupuncture equipment be labelled as investigative devices as recommended by the AMA. In 1983, The American Osteopathic Association endorsed the use of acupuncture as a part of the practice of medicine. In 1987, The American Academy of Medical acupuncture was formed as the first national physician and surgeon organisation dedicated to the advancement of acupuncture within America. Since then acupuncture has gained scientific status and recognition and according to a study conducted in 1993, an estimated 500 million dollars is spent every year by the United States public on acupuncture treatment.

The present

Currently acupuncture is a highly specialised science, being taught in premier Universities like UCLA. Physicians are taught traditional Chinese medicine, French energetic, five element, neuroanatomic, auricular and hand acupuncture. These acupuncture treatment systems and microsystems are currently said to be used throughout the United States along with other microsystems including Yamamoto New Scalp Acupuncture and Chinese scalp acupuncture.

According to Feely, acupuncture had a very different paradigm/way of thinking than the Western world. While acupuncture emphasised holistic patterns, relationships, cycles, and processes, the western paradigm emphasised linear thinking, and causality. Therefore, the West could not understand how a needle inserted into the hand could cure a toothache, since the logical and scientific mind of the Western scientist could not fit acupuncture principles into the existing physiological paradigms. This was the main reason why acupuncture couldn't really get a foothold in the West for a very long time.

But now, more and more physicians outside China are using acupuncture to treat many painful conditions especially chronic ones. It is estimated that 5,000 practitioners in Germany, 30,000 in France and 60,000 in Japan use acupuncture along with drugs, nerve blocks and other approaches to treat patients with chronic pain. In the United States alone, it is stated that over 1,000 physicians and surgeons actively practice the art of acupuncture and it is likely that acupuncture will continue to grow attracting more and more physicians as scientists prove by research and evidence, the efficacy and superiority of acupuncture.

Islamic Medicine

In ancient Arabia, a bitter religious dispute existed between two equally despicable characters - Cyril, the Patriarch of Alexandria and Nestorius, the Bishop of Constantinople (now Istanbul). The people, caught between the devil and the deep blue sea, had to flee to Persia and settle there in order to escape the eccentricities of these two tyrannical leaders. Chosroes, the Blessed was gracious enough to grant them asylum and the people started acquiring knowledge by exploiting the works of Hippocrates and Galen, which was further augmented by the knowledge and talents of other refugees and visitors, especially from Buddhist India. Chosroes died in 579 A.D.

Arabian medicine, for many scholars and historians, was synonymous with Arabic medicine since Arabic was the language of the Islamic world. But Arabic texts did not necessarily have Arabic authors; Persians, Jews, Christians and Spaniards played a role in developing Arabic medical literature. The term Islamic medicine represents medical systems and ideas prevalent in the Arabian empire. Like Chinese and Indian medicine, Islamic medicine is still very much alive, being a respected system practised by many a traditional healer.

During Prophet Mohammed's time (569-632 A.D.), Islamic doctrines were established and widely accepted, bringing about the unity of the many scattered tribes in Arabia. It is said that many clinical traditions arose with him, but according to the fourteenth century Arab historian Ibn Khaldun, the prophet's mission 'was to make known to us the prescriptions of the Divine Law, not to instruct us in medicine'. He also said that sincere faith may provide a great advantage for those desire to earn Divine healing and blessing. But according to Magner, the Prophet's general approval of traditional Arab medicine is seen in the collection called the "Medicine of the Prophet", which is a compilation of fragments concerning medical information, extracted from the Holy Qur'an and the *Hadith* which was the 'sayings and doings' of the Prophet. The Prophet himself is said to have advised sensible dietary patterns to prevent disease. The cause of stress as a cause of disease was also known since he declares that "excessive worry makes for physical illness in a person". Honey was considered a natural remedy for several illnesses and the Prophet is seen recommending it in the treatment of certain illnesses. Following the Prophet's death, his followers spread his teachings far and wide across Europe and Asia. Within a few decades, the Islamic empire extended from Spain in the West through Syria and Persia right up to the banks of the Indus in the East and became a force to reckon with by 750 AD. The great empire then split into caliphates, Baghdad becoming one of the key centres of civilisation.

It must be remembered that this was the period where a major part of Europe slipped into medieval darkness and we do not really know much about what happened there during this time. But it was also during this time that Hellenisation of Islamic medicine began, when many ancient Greek and Roman manuscripts of medicine were translated into Arabic. In fact, the period between 750 and 900 AD is known as "The Age of Translations". The Arab conquerors, aggressive as they were in war and conquest, were tame and gentle enough to respect the medical traditions of the nations they vanquished. History books tell us that they were particularly impressed by the school of Medicine in Gondishapur, Persia, which had been founded by a group of Christians under Nestorius. When the Arabs took control over Persia in the 7th century, they reportedly collected every available manuscript and parchment of medicine from the Gondishapur medical school as well as the libraries of every province. These were then translated into Arabic, which became the new vehicle for medicine. The Golden Age of Arabic Medicine extended from 850 to 1050 AD by which time most ancient works had been translated and the knowledge absorbed by the practitioners. Modern medicine thus owes the Islamic world a great deal for helping to purvey classic medicine, by preserving, paraphrasing and passing on ancient medical knowledge and traditions.

Contrary to expectations, most Arabic doctors were Persians, Syrians, Spaniards, Jews, Greeks, Christians or Byzantines, writing in Arabic. Arab doctors - skilled as they were - were also very practical in their approach. "Ask for thy reward while the sickness is at its height" was their maxim. Nepotism was not something unknown since a physician called George Bakhtischu, his son and later his grandson continuously headed the medical school in Gondishapur. Caliph Harun al-Raschid was an ardent manuscript collector and paid heavy premiums to obtain them. In fact, it is said that the Greek manuscripts were his 'most coveted booty' when he conquered the Byzantines. After him, Caliph al-Ma'mun had extensive translations done which were later compared, revised, edited and made into standard text books. He paid the scholars the entire manuscript's weight in gold, which led to translators like Hunain ibn Ishaq honestly make a few extra bucks by using heavy paper and large, bold handwriting.

Hospitals or *bimaristans* were established in all major cities. Cairo had the largest and most famous hospital of the Islamic world. Established in 1286 by al-Mansur Qalawun, it was housed in a former palace and served the rich and the poor alike, without discrimination. It is said to have had the capacity to handle 8000 patients and was complete with a pharmacy, library, lecture halls, a chapel for Christians and a mosque for Muslims. Music was provided to cheer up the patients. Hospital deaths created as much sensation as they do now, since a scan-

dal regarding the death of a patient in a Baghdad hospital resulted in the medical licensing system being reviewed. Not unlike the present day CME programme, doctors were tested if they were up to date in their knowledge. As you may have guessed, 160 (out of the 860 who took the exam) failed to make it!

Even as algebra, astronomy and the numeral system (adapted from India) were getting their refined form, the Arabs - with their admirable knowledge of chemistry - discovered a host of new drugs and started establishing the world's first pharmacies. With the establishment and embellishment of great hospitals and academies in Baghdad, Cairo and other cities, great doctors began to emerge. Rhazes - the man revered as the greatest physician of the Islamic world and one of the most scientifically minded physicians of his time - was one of them.

Rhazes, alias Abu Bakr Muhammad ibn Zakariya Al-Razi (841-926 AD), a musician, songster and a philosopher, took up medicine - almost as a hobby - when he was 40 years old. Arriving in Baghdad from Persia, he set up his practice in a very 'sterile' location. He is supposed to have hung several pieces of fresh meat all over town and later selected the site where the meat showed the least amount of putrefaction! He later becoming totally involved with medicine and eventually his reputation gained him the appointment of physician-in-chief at Baghdad. He was, however, admired for his bedside observational skills and interesting lectures. Rhazes made many practical contributions to medicine, such as animal gut sutures, mercuric compound based purgatives, and tepid sponging. His treatise 'The Diseases of Children' has led some historians to regard him as the father of paediatrics. He was the first to identify hay fever and its cause and did pioneering work on kidney stones. He was also the first to observe and record the pupillary light reflex.

Rhazes wrote accurate descriptions of measles and small pox, drawing from his own personal experiences, which is evident by the tribute paid by the World Health Organization (WHO) in its bulletin dated May 1970, which states: "His writings on smallpox and measles show originality and accuracy and his essay on infectious diseases was the first scientific treatise on the subject." He wrote 237 treatises, of which only 36 have survived. These manuscripts are still extant in the museums and libraries of Iran, Paris, Britain, and Rampur (India). His medical encyclopaedia, *Continens Liber,* brought him a lot of fame. He, however, made the mistake of writing it in one thick volume, since he subsequently incurred the wrath of Prince al-Mansur, who, disappointed with Rhazes' alchemy theories which did not work, ordered that Rhazes be beaten on the head with his own book until one of them broke. The quality of ancient Arabic paper must have been exceptionally commendable, since it was Rhazes' head that broke first rendering him blind (*contre coup*?). It is, therefore, quite understandable why books like Gray's Anatomy were not published until the 20th century!

Rhazes was followed by Avicenna, also known as Ibn Sina, in full Abu 'Ali al-Husayn ibn 'Abd Allah ibn Sina. (Picture I). This Persian, born in 980 AD in Kharmaithen (now in Uzbekistan), was a prodigy even as a kid, and deserves mention in any tale of medicine. Since his father's house was a place where learned men often met, Avicenna was able to profit from the company of the outstanding masters of his day, even from his earliest childhood. Being a precocious child with an exceptional memory, he had memorised the Qur'an and much Arabic poetry by the age of ten and went on to master philosophy, history, poetry, mathematics, law and medicine before he was even seventeen. It was not very long before he entered royal portals to cure royalties of their illnesses. However, he did periodically fall out from royal favour, when he had to move on restlessly from court to court. Though an extraordinary physician, he is known to have had a weakness for the cup.

Avicenna's two most famous works were the *Kitab Ash-*

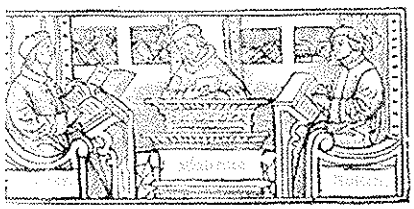
Picture I. Avicenna

shifa (Book of Healing), a vast philosophical and scientific encyclopaedia, and the *al-Qanun* or the Canon of Medicine (with a word count of over a million) - which was a medical bible for several generations right up to the 17th century. It was considered comparable in stature and influence to the works of Hippocrates and Galen, and Avicenna was therefore equated alongside the two earlier doyens (Picture J). Professor Browne, a historian of Arab Medicine considers the work 'systematic, philosophical and reputable' and places Avicenna in the pedestal in par with Aristotle.

In his book, Avicenna describes the contagious nature of tuberculosis, dissemination of diseases by soil and water and advocates the cause for cautery in surgery. He shows amazing knowledge of disease symptoms and pharmacology. However, a great dispute seems to exist whether he was right in classifying love under mental diseases. In *The Inferno,* Dante placed Avicenna side by side with antiquity's two greatest physicians, Hippocrates and Galen (Picture J).

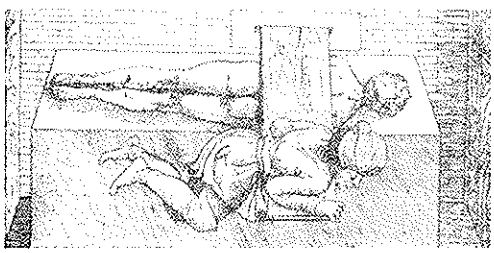
Avicenna is said to have discussed several 'vital' medical problems with his students such as: why hair grows not on the nose; why breasts grow not on the belly; why the stomach lies not behind the mouth and why

calves are not on the front of the legs. Being a gigantic personality himself, he attempted to straighten crooked spines by throwing his weight on a wooden plank placed on the patient's back (Picture K). This apart, Avicenna is described to have used some dramatic grandstand techniques to bring about cures or to demonstrate his point. A woman who complained that she had lost the use of her arms due to a postural defect was proved a fibber when her skirt was abruptly lifted over her head and she hastily pulled it down in a reflex act.



Picture J. Avicenna, Galen & Hippocrates

Brian Inglis, in his book '*A History of Medicine*' narrates an interesting story about Avicenna, who was once called in to treat a young prince who suffered from melancholy and imagined that he was a cow. The hallucinatory prince allegedly went around begging to be slaughtered and made into beef stew. Avicenna, arriving with a knife, examined the 'creature', now bound hand and foot and mooing happily. In his capacity of a 'butcher', he declared the 'cow' too lean and unfit for slaughter. The prince in his eager effort to fatten himself, started eating well, thereby regaining his strength, after which his delusion disappeared. This story summarises, in essence, Avicenna's psychological approach to medical problems and it should be noted that it was the same principle which was rediscovered almost a millennium later, when Freudian psycho-analysts described the technique of entering the fantasy life of a psychotic patient in order to provide a bridge for him to return to reality.



Picture K. Avicenna using his portly physique to straighten a crooked spine. *(From A Picture History of Medicine)*

During the day Avicenna was busy with his duties at court as both physician and administrator. In spite of that, he spent almost every night with his students composing clinical notes and carrying out general philosophical and scientific discussions related to health, patients and medicine. These sessions were often combined with musical performances and gaiety and lasted until late hours of the night.

After several ups and downs in life, Avicenna underwent a period of difficulty that included imprisonment. Even in hiding and in prison he continued to write. Shortly after, he fled to Isfahan, south of Tehran, where he spent the last 14 years of his life in relative peace. Encouraged and esteemed by 'Ala` ad-Dawlah, the ruler, he finished two major works which he had begun earlier and it was here that he wrote most of his nearly 200 treatises. He also composed the first work on Aristotelian philosophy in the Persian language. While accompanying 'Ala` ad-Dawlah to the field of battle during military campaigns, he wrote the masterly summary of his "Book of Healing" called *Kitab an-najat* (Book of Salvation). His last major philosophical opus, *Kitab al-isharat wa at-tanbihat* (Book of Directives and Remarks) was also written during this time. In this work he described the mystic's spiritual journey from the beginnings of faith to the final stage of direct and uninterrupted vision of God. Once criticised by a fellow scholar for lack of mastery in Arabic philology, Avicenna spent three years studying it and produced a vast work called *Lisan al-'arab*. This clearly shows his dedication and thoroughness in academic matters. Avicenna's strenuous academic and administrative activities eventually took its toll and in June 1037, Avicenna died in Hamadan of colic and exhaustion.

The pharmacy was exclusively an Arabian achievement. It developed as an establishment in its own right and complemented the doctor's consulting room thereby relieving the physician the dreary task of compounding his own drugs. By inventing candy coated pills, rose water blended syrups, perfumed mixtures and tantalising tinctures, pharmacists (*saydalani*) made sickness an enjoyable affair. They, however, were shrewd enough to keep their concoctions in unlabeled jars. (Picture L)

Surgery and gynaecology were two areas where significant advances could not be made during this period. Religious taboos which prevented cutting of human flesh - dead or alive - hampered the former, while Islamic modesty (which kept them away from female patients) hindered the latter. Therefore anatomy went into a state of suspended animation and surgery went into a coma, only to be revived by a Spanish born Arab physician known as Albucasis.

Albucasis gave a new lease of life for surgery by reviving cautery methods advocated by his earlier mentors. Branding irons became national instruments to sear wounds, remove cancers, treat abscesses. Flesh cutting was, however, surreptitiously done under the guise of removal of tonsils, polyps and extraction of barbs, but apparently there were no objections.

Arabian doctors had only theoretical knowledge about childbirth since it was mostly only the midwives who were allowed to conduct the deliveries. The doctor, if in attendance, was separated from the patient by a heavy

curtain and prevented from doing any direct examination. An imaginative Albucasis described a position in which the woman in labour lies with her hips at the edge of the table and her legs dangling. This became an instant hit with the midwives who marvelled with admiration at his genius. This position, in modern day obstetric practice, is known as the Welcher's position.

Picture L. A 'smart' pharmacist dispensing medication stored in unlabeled jars.

Avenzoar of Seville (1113-1162AD) was the medical leader of the western caliphate and this man was quite contemptuous about Avicenna and his work *The Canon*, since he is said to have caustically dismissed it as a 'mere waste of paper'. He is attributed to have instituted the concept of a 'nutrient enema' when he injected (per rectum) milk, eggs and gruel into the gut of a patient with throat cancer. The apparatus used - a goat's bladder and a tube. His student Averroes ibn Rushd, the Commentator, was known for his brilliant translation of Aristotle and avid reading skills. The only two instances where Averroes is said to have missed his nocturnal perusals were on his wedding night and when his father died. Moses Maimonides (Musa ibn Maimun), was a Jewish scholar and the court physician of Sultan Saladin. He was a student of Averroes and did many translations of ancient manuscripts into Hebrew and Latin. Avenzoar, Averroes and Maimonides were however less famous physicians of that time, but nevertheless, it was they who carried the torch along before Cordova was captured by Almohades and the Mongols took control of the Eastern part of the empire. Invaluable intellectual treasures were destroyed and scholars and learned men were mercilessly murdered. In the Western part, the Almohades eventually fell before the Christians, but it is said that they absorbed Islamic culture, rather than destroying it, to the benefit of future generations.

As the great sages of Islamic medicine were creating history, contributing to the serious part of this story, we also see some of the quacks providing humour to this narrative. A physician allowed starving vipers to bite his patient suffering from elephantiasis; cure elephantiasis, it did, but nevertheless, induced leprosy, deafness and loss of vision. An unethical physician killed his patient with a poisoned lancet; he was later killed when he unwittingly used the same lancet on himself. Jehangir, son of Moghul emperor Akbar, in his autobiography describes how his aged father had diarrhoea which, with medical treatment, was transformed into dysentery; dysentery was treated resulting in constipation and constipation, thanks to the doctor, turned into diarrhoea once again and finally death. Jehangir rues the day he sought medical attention and declares that "except for God's decree and doctors' mistakes, no one would ever die".

In the nineteenth century, Islamic Medicine came under pressure from doctors practising the Western style of medicine. Claiming that traditional Islamic Medicine had become inert and unproductive, Sultan Mahmud II established a Western style hospital and medical school in Istanbul. French doctors manning the various departments ruled supreme, driving practitioners of traditional medicine underground. Eventually, as a compromise between the two systems, arose a new branch of medicine known as the *Yunani Medicine* or Greco-Islamic Medicine (in Arabic "Yunani" means Greek). The Yunani system was recognised in some countries, but taken up seriously only in India and Pakistan where Yunani medical colleges and hospitals were instituted.

> Well knew he the olde Esculapius
> And Deyscorides and eek Rufus
> Olde Ypocras, Haly and Galeyn,
> Serapion, Razi and Avycen,
> Averrois, Damascien and Constantyn,
> Bernard and Gatesden and Gilbertyn.

The verse quoted above is found in the prologue of The Canterbury Tales, by Geoffrey Chaucer. Rhazes, Avicenna and Averroes feature in this 14th century sonnet simply because Chaucer regarded them among the great medical authorities of that time. When the Roman empire collapsed in the fifth century, Europe lost touch with much of its intellectual heritage. The Latin library was limited to Pliny's Encyclopedia and Boethius's treatises on logic and mathematics and a few other insignificant manuscripts. After collecting ancient manuscripts, Arab physicians translated, augmented and finally codified the classical Greco-Roman heritage that Europe had very nearly lost and laid the foundations of the institutions and the science of modern medicine.

To conclude this narrative, I shall appropriate the words of Arnold and Guillaume to epitomise the grandeur of Islamic medicine which served as a vital link to amalgamate ancient medical traditions with those of modern times:

"Islamic medicine and science reflected the light of the Hellenic sun, when its day had fled, and they shone like a moon, illuminating the darkest night of the European Middle Ages. Some bright stars lent their own light and that moon and stars faded at the new day - the Renaissance. Since they had their share in the direction and introduction of that great movement, it may reasonably be claimed that they are with us yet."

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NON STEROIDAL ANTI-INFLAMMATORY DRUGS AND THE STOMACH – A REVIEW

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Introduction

Non steroidal anti-inflammatory drugs (NSAIDs) are standard prescription drugs in the treatment of rheumatic disease, but it is also well known that they carry a high risk of adverse events, particularly in the gastro-intestinal tract. Studies have indicated that the prevalence of GI symptoms among patients taking these agents is in the region of 30% to 40% (1,2) with symptoms ranging in severity from the occasional heartburn or indigestion to severe dyspepsia. Gastric erosions are seen in one third or more of patients who use NSAIDs (3) and continued NSAIDs therapy produces ulcers in 10-20% of patients with gastric ulcers being more common more than duodenal ulcers. Serious and life threatening gastroduodenal complications such as bleeding and ulcer perforation which is the major concern of all doctors, have been reported to occur in about 1-2 % patients during 3-6 months of NSAID therapy or 4-6% of patients treated for a year (4).

It is estimated that worldwide, more than 30 million people consume NSAIDs daily (5). In United Kingdom, about 1.5 million people aged over 60 years take NSAIDs at any one time. Patients who take NSAIDs have a 4-6 fold increased risk of developing peptic ulcers (6). Every year, about 12,000 ulcer complications and 1,200 deaths occur as a result of NSAID therapy (7). In the United States, more than 75,000 hospitalizations and more than 7,500 death occur annually in the elderly directly related to NSAID use (8). Documented NSAID ingestion in Malaysia appears to be low (9). In a cross-sectional survey of 1060 consecutive patients with dyspepsia undergoing endoscopy at the University Hospital, Kuala Lumpur, the prevalence rate of NSAID ingestion was only 0.6% (63/1060) (9). This figure is likely to be an underestimation as many patients do not report nor recognize ingesting NSAIDs taken in the form of herbal or traditional medications. Nonetheless, compared to Western populations, the prevalence of rheumatic diseases is low in Malaysia and the prescribing habits of medical practitioners may be different and as a result, the amount of NSAIDs prescribed may in fact be low as well. The majority of prescriptions for NSAIDs is probably aspirin prescribed as prophylactic therapy for coronary artery disease.

This review article addresses the following issues: mechanisms in maintaining normal gastroduodenal defenses, types of NSAID and mechanisms of NSAID induced gastroduodenal lesions, risk factors for gastroduodenal ulcer complications with NSAID therapy, interaction with *Helicobacter pylori* infection, treatment and prevention of NSAID gastroduodenal lesions.

Mechanisms Involved in Maintaining Gastroduodenal Mucosal Defenses

There are three mechanisms involved in maintaining mucosal integrity: in the normal stomach:

1. Pre-epithelial: Secretion of mucus and bicarbonate from surface epithelial cells to increase pH at the apical mucosal surface.

2. Epithelial: Epithelial cells account for at least a component of the "gastric barrier" (10). Evidence suggests that the apical surface of the epithelial cells directly resists back diffusion of acid and tight junctions on the epithelial surface can withstand acidification. There is also a process called 'restitution', whereby there is migration of existing epithelial cells along the basement membrane to fill in the defects created by the sloughed off cells. Active extrusion of back diffused H^+ via the Na^+/H^+ antiport or Cl^-/HCO^3 exchangers also takes place.

3. Post-epithelial: Mucosal blood flow is critical for delivery of HCO_3^-, O_2 and nutrients to cells and disposing of back diffused H^+. Lamina propria is also filled with nerves, inflammatory cells and mesenchymal cells that participate in wound healing. The ability of blood vessels to form in granulation tissues may be an important step in the healing process.

Type of NSAIDs and Mechanisms of NSAIDs Induced Gastropathy

NSAIDs are inhibitors of both cyclo-oxygenase (COX) isoenzymes (COX I and COX II) though they vary in degree of inhibition of each enzyme. This results in variable potency in anti-inflammatory, analgesic and antipyretic activity and as well as in their potential of

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causing gastrointestinal complications. NSAIDs produce gastric damage by two independent mechanisms: a) Irritative topical effects b) Systemic effects.

Topical effects

Only aspirin and other salicylic acid subtypes of NSAIDs cause these direct toxic effects. The lipoprotein membrane of the surface of epithelial cells forms a barrier to water-soluble molecules but not to fat-soluble compounds. At pH of 2.5, 91% of salicylic acid is non-ionized but fat soluble and is rapidly absorbed from gastric lumen into gastric mucosal cells, where the aspirin encounters a pH of about 7.0 and ionisation occurs. This results in a high concentration gradient of non-ionized salicylic acid across the mucosal surface. As a consequence, absorption is enhanced, with tendency for aspirin to accumulate within the cells in high concentration (10). It is postulated that aspirin disrupts the lipid-protein layer on the surface of cells causing desquamation by breaking the tight junction between cells (11). Davenport (10) concluded that salicylate opens the gates of the mucosal barrier and lead to acid pouring through the breached defence destroys capillaries and venules. Vasodilatation and increased capillary permeability resulting from release of histamine within the damaged mucosa aggravate the later action.

Systemic effects

All NSAIDs inhibit the activity of cyclo-oxygenase, the enzyme that catalyses the synthesis of cyclic endoperoxides from arachidonic acid to form prostalglandins from precursor membrane fatty acids and thereby reducing the production of prostaglandins. They also have other effects such as the generation of O_2 free radicals and products of lipoxygenase pathway.

COX I is a constitutive enzyme expressed in most tissues, including blood platelets and gastric mucosa and also cell to cell signaling. COX II is induced in inflammatory cells when they are activated and is believed to be the enzyme that produces the prostanoid mediators of inflammation. Hence, clearly anti-inflammatory action is related to COX II inhibition and probably their unwanted effects are due to COX I inhibition. NSAIDs have three major actions; all of which are mainly due to the inhibition of arachidonic acid cyclooxygenase in inflammatory cells (COX II) and the resultant reduction in prostanoid synthesis. They are: anti-inflammatory action: the decrease in vasodilator prostaglandin's (PGE_2 / PGI_2) means less vasodilation and indirectly less edema but accumulation of inflammatory cells is not reduced; analgesic effect: decreased prostaglandins generations means less sensitisation of nocioeptic nerve endings to inflammatory mediators e.g. bradykinins and 5HT. Relief of headache is probably is due to reduced prostaglandins mediated vasodilatation; and antipyretic effect: due to reduced prostaglandins mediator, which is generated in response to the inflammatory pyrogens.

It is now known that several principal physiological mechanisms which are compromised through COX I inhibition are (12): mucosal blood flow, secretion of mucus, secretion of bicarbonate, cytoprotection effect, maintenance of hydrophobic mucosal surface and reduced basal and maximally stimulated gastric acid secretion.

NSAIDs are also found to be associated with reduced epithelial proliferation and diminished angiogenesis (7) which are important in ulcer healing.

Risk Factors for NSAIDs Induced Peptic Ulcer Complications

Who amongst those taking NSAIDs are most prone to develop GI complications?

In a large case control study by Rodriguez and Jick (13) the overall risk of UGIB was 4.7 in NSAIDs users. The study comprised of 1457 cases of UGIB and 10000 control subjects identified from general practitioner's computerised records in UK. Previous UGIB was identified as the single most important predictor of UGIB with a relative risk of 13.5 (10.3-17.7). The risk was higher with higher doses of NSAIDs than with lower doses (7.0 (5.2-9.6) vs 2.6 (1.8-8.3)). Increasing age, male sex, smoking and a history of peptic ulcer were also identified as independent risk factors. Other risk factors such as concurrent use of warfarin (6.4 (2.8-14.6)) and steroid (2.2 (1.4-3.5)) were also identified

Are some NSAIDs more ulcerogenic than others ?

The relative risk varied widely with different agents, with azapropazone and piroxicam having the highest risks and ibuprofen and naproxen the lowest risks. In a review of the literature, ibuprofen followed by diclofenac has consistently been associated with the lowest risk of complications (13,14,15). Henry *et al* (15) in his review suggested that some of the differences between different drugs may be because of differential doses and the advantage of "low risk drugs may be lost once their dose is increased.

Aspirin and Gastroduodenal Complications

Aspirin: How low is low dose?

Aspirin has been increasingly used as an anti-thrombotic agent in the past 25 years, since the discovery of its ability to inhibit platelet function. Its cardiovascular and neurovascular protective role has been confirmed by

several large studies (16) and its use is now widespread for these indications. As with other NSAIDs, the risk of complications with aspirin is dose-related (17,18) and it is therefore reassuring to note that lower doses of aspirin of 75-325mg daily are now recommended for anti-platelet activity (19). However, even with lower doses, patients are still at risk for ulcer complications. Weil *et al.* reported an odds ratio for UGIB of 2.3 (1.2-4.4) with aspirin 75 mg daily, 3.2 (1.7-6.5) with 150 mg daily and 3.9 (2.5-6.3) with 300mg daily (18).

Table 1. Comparison of serious GI complications with different NSAIDs with ibuprofen used as reference for calculating relative risks (adapted with permission from Henry D *et al.*, BMJ 1996 (15))

NSAID	No. studies	Pooled relative risk	95% Confidence interval
Ibuprofen	-	1.0	-
Fenoprofen	2	1.6	1.0-2.5
Aspirin	6	1.6	1.3-2.0
Diclofenac	8	1.8	1.4-2.3
Sulindac	5	2.1	1.6-2.7
Diflunisal	2	2.2	1.2-4.1
Naproxen	10	2.2	1.7-2.9
Indomethacin	11	2.4	1.9-3.1
Tolmetin	2	3.0	1.8-4.9
Piroxicam	10	3.8	2.7-5.2
Ketoprofen	7	4.2	2.7-6.4
Azapropazone	2	9.2	4.0-21.0

Aspirin associated gastrointestinal toxicity: Do different formulations differ?

As aspirin has substantial direct mucosal irritative effect, it would appear reasonable to develop special formulations to bypass the above effect in order to improve its side-effect profile or tolerability without compromising antiplatelet efficacy. For enteric-coated preparation, the tablet is coated with cellulose, silicon or other inactive ingredients that has resistance to disintegration in the stomach; hence, allowing dissolution of the drugs in the more neutral to alkali environment of the duodenum (41). Whereas, in buffered aspirin, buffering agents (Mg oxide, Mg carbonate, calcium carbonate, etc) lower H^+ concentration in the microenvironment of aspirin particles and results in increased gastrointestinal solubility of aspirin and reduced contact time between aspirin particles and the gastric mucosa (20).

To compare the risk of major upper GI bleeding between these formulations with plain aspirin, a large multicentre case-control study was carried out by Judith *et al.* (21). Relative risks of upper gastrointestinal bleed (UGIB) for each type of formulation used regularly were calculated overall, according to dose and site of bleeding, by multiple logistic regression, controlling for age, sex, marital status, education smoking, alcohol and concomitant other NSAID use.

Result showed relative risks of UGIB for plain, enteric-coated and buffered aspirin at average daily doses of 325 mg or less were 2.6, 2.7 and 3.1 respectively. At doses greater than 325 mg, the relative risk was 5.8 for plain and 7.0 for buffered aspirin, and there were insufficient data to evaluate enteric-coated aspirin at this dose level. There were no substantial differences in risk attributable to all three aspirin forms to bleeding site (gastric vs duodenum). A possible explanation is that systemic effects, which are unlikely to differ according to the aspirin preparation used, may overwhelm any differences in local effects on the gastric or duodenal mucosa.

This study did not show any substantial reduction in relative risk for low dose enteric-coated aspirin in UGIB occurrence which is inconsistent with the findings from previous endoscopic studies (20,22) which had reported much less gastric erosion and microbleeding in enteric-coated aspirin users as compared with plain aspirin users. This discrepancy is explained by the fact that mucosal erosion and submucosal haemorrhage detected in the endoscopic studies are actually poor indicators of UGIB (22).

Interaction Between NSAIDs and *H. Pylori*

H. pylori and NSAIDs are the 2 most important etiological factors in gastroduodenal ulceration. It is not entirely clear whether, when present together, they act independently or synergistically in causing ulcers. Both *H. pylori* and NSAID have been shown to interfere with various protective mechanisms in the gastroduodenal mucosa. Several of these pathogenic effects are common to both and include their effects on gastric mucus, mucosal prostaglandins and mucosal blood flow (23). *H. pylori* is known to cause hypergastrinaemia and increased acid secretion in duodenal ulcer patients; NSAIDs are also known to cause an increase in basal and maximally stimulated gastric acid (24).

There are several questions that need to be answered which will help clarify this interaction between NSAID ingestion and *H. pylori*: Are gastroduodenal ulcers more common in patients who ingest NSAIDs and are *H. pylori* infected? Is *H. pylori* more commonly found in NSAID patients with ulcers compared with those without ulcers? Data on this is conflicting. Several cross-sectional studies have shown an increase prevalence of ulcers in NSAID users who were *H. pylori* positive (25,26,27) while other

have not (28,29,30). On the other hand, two studies have reported a higher prevalence of *H. pylori* in patients with ulcers compared to those with a normal gastroduodenal mucosa (31,32).

Two longitudinal follow-up studies have again yielded conflicting results: Kim *et al.* reported no significant increase in the incidence of gastroduodenal ulcers among chronic NSAID users with *H. pylori* infection (33) while Taha *et al.* (34) found that *H. pylori* positive patients with duodenal erosions were more likely to develop ulcers during chronic NSAID treatment.

Can we prevent the development of NSAID ulcers by eradicating H. pylori (when present))?

A recent study form Hong Kong (35) addressed this question and convincingly demonstrated that it was indeed worthwhile to eradicate *H. pylori* before commencing on NSAID therapy. Twelve of 47 patients (26%) develop ulcers in the group that did not receive *H. pylori* eradication therapy compared to 1 of 45 (7%) patients who had received such therapy before commencement of NSAIDs (p=0.01). The implications of this study may be important, as it would support a strategy of testing for *H. pylori* routinely in patients undergoing NSAID treatment.

Is healing of ulcers retarded in H. pylori positive patients?

It seems intuitive to assume that ulcer healing would be impaired in patients who are *H. pylori* positive. On the contrary, in the large ASTRONAUT study (36) comparing the effect of omeprazole vs ranitidine in the treatment of NSAID associated ulcers, consistently higher healing rates were achieved for duodenal and gastric ulcers in those who were *H. pylori* positive.

Does eradication of H. pylori affect ulcer healing and ulcer relapse in NSAID users?

Seppala *et al.* (37) have shown a reduction in gastric ulcer recurrence in patients who had their *H. pylori* eradicated. In another study, Bianchi *et al.* (38), showed a trend towards lower recurrence rate with a dual amoxicillin-omeprazole therapy.

In an on-going study (HELP) (39), no difference was seen between *H. pylori* eradicated and not eradicated patients in terms of ulcer healing and ulcer relapse.

Treatment of NSAID Induced Gastroduodenal Ulcers

Almost all NSAIDs induced ulcers heal after cessation of NSAID therapy. Continued NSAID use delays healing despite standard anti-ulcer treatment. Thus, if the patient can be managed reasonably well without NSAIDs, it should be stopped.

Acid-suppression therapy is the cornerstone of treatment. In general compared to non-NSAID associated ulcers, healing appears to take a longer time when NSAID therapy is continued. Early studies using H_2 antagonists showed gastric and duodenal ulcer healing in 8-12 weeks in 80-90% ulcers despite the continued use of NSAIDs (40). Sucralfate, a surface coating agent was shown to heal duodenal but not gastric ulcers. In a review of the earlier studies (41), duodenal ulcers seem to heal more easily compared to gastric ulcers and large gastric ulcers were found to be slow and difficult to heal with treatment.

The first reported use of proton pump inhibitors in NSAID ulcers was by Walan *et al.* (42) who in a randomized controlled trial comparing the effect of omeprazole vs ranitidine in the healing of gastric ulcers, demonstrated the superiority of more potent acid suppression in the healing of NSAID ulcers (95% vs 53%). More recent studies specifically designed to look at the effect of omeprazole on the healing and maintenance of NSAID induced ulcers have been carried out and preliminary results have again shown the clear superiority of this drug compared to the prostaglandin analogue, misoprostol and ranitidine (43,36). A recent study using high doses of famotidine 40mg twice daily achieved a comparable ulcer healing rate with a longer duration of treatment of 12 weeks (44) again underlining the importance of acid suppression in the healing of NSAID ulcers.

Prevention of NSAID Induced Ulcers and Complications

The most widely studied drug for prophylaxis against NSAID ulcers or maintenance of healing has been the prostaglandin E_1 analogue, misoprostol. In placebo controlled studies, misoprostol was shown to significantly reduce the incidence of gastric and duodenal ulcers in NSAID patients (45,47). In the latter study, Graham *et al.* (47), showed that misoprostol reduced the incidence of endosopically detected gastric ulcers by 75% and duodenal ulcers by 87%. In a more recent large scale practice-based study (MUCOSA), Silverstein *et al.* (48) showed a 40% difference in incidence of serious gastrointestinal complications in patients taking misoprostol compared to placebo. In comparative studies with ranitidine and sucralfate, misoprostol has been shown to be more effective in preventing gastroduodenal lesions (48,49). Side-effects have limited the use of misoprostol; with doses of 200 µg qid, up to 1 % of patients have been reported to have diarrhoea. Lower doses of misoprostol have been used to reduce the side-effects without lowering the efficacy of the drug (50). Abdominal cramps is another frequent complain

of patients and because of the effect on the uterus is contraindicated in pregnant women.

What about H_2 antagonists? In 2 well-conducted placebo-controlled studies (51,52), ranitidine was shown to be effective in preventing duodenal but not gastric ulcers. However, recent study by Hudson N *et al.* (44) demonstrated that with a higher dose of famotidine 40 mg bid the relapse rate of gastroduodenal ulcer could be reduced from 53% to 26% at the end of 6 months. There have been few reports on sucralfate. Several small studies have produced conflicting results (53,54,55).

In recent years, large trials using the proton pump inhibitor, omperazole have been carried out. In the OMNIUM study (43), following healing of ulcers in the acute treatment phase patients were entered into a prophylactic maintenance phase. Omeprazole at a dose of 20 mg daily was again shown to be superior to misoprostol and placebo in the prevention of recurrence of ulcers. Only 32% of placebo treated patient remained in remission after 6 months whereas 64% and 51% sustained remission being achieved by omeprazole and misoprostol (200 µg bid) respectively. Similarly, in the ASTRONAUT study (36), omperazole at a dose of 20 mg daily was shown to be superior to ranitidine in keeping patients in remission. After 6 months of maintenance treatment, 80 % omeprazole treated patients remained in remission as compared with 66 % of those receiving ranitidine.

In 2 further studies, the SCUR (56) and OPPULENT (57) studies, omeprazole was again shown to be superior to placebo in preventing the occurrence of new ulcers. SCUR showed 74% remission rate in omeprazole group as compared to only 48% in the placebo group at the end of 3 months. Consistent findings have also been shown in the OPPULENT study where after 6 months of treatment, 78% of patients ($p<0.01$) remained in remission compared with 53% of those on placebo ($p<0.01$).

Conclusion

NSAIDs are perhaps one of the most widely prescribed drugs in the world today. They are valuable therapeutic agents for a broad range of rheumatic diseases. Aspirin is now widely prescribed for prevention of vaso-occlusive disorders. There are however, major side-effects associated with its use. These are mainly in the upper gastrointestinal tract where serious complications such as bleeding and ulcer perforation can occur. Risk factors include older age group, concomitant serious medical illness, higher dose of and use of multiple NSAIDs.

The association with *H. pylori* is an intriguing one. There is persuasive evidence that eradicating the bacteria results in lower incidence of gastroduodenal ulcers. On the other hand, data from on-going studies suggest that NSAID ulcers heal less well when *H. pylori* is eradicated. It seem logical and even intuitive that a second ulcerogenic factor should be eliminated and this has prompted the European Consensus to categorize as "advisable", eradication of *H. pylori* in patients embarking on long term NSAID therapy (58). The controversy is however reflected in the Asian Pacific Consensus statements (59) where, routine screening for *H. pylori* was not recommended prior to initiating NSAID therapy. However, patients with dyspepsia and starting on long term NSAID therapy were advised to seek investigations for their dyspepsia. Dyspepsia has been demonstrated to have high specificity but extremely low sensitivity in predicting the presence of gastroduodenal lesions (60) in patients taking NSAIDs.

Although NSAID ulcers in general heal less well than non-NSAID ulcers, effective treatment can be achieved with acid-suppressing agents, in particular, the proton pump inhibitors. Prevention of gastroduodenal damage by NSAIDs can be achieved with the prostaglandin analogues although recent data shows again the superiority of potent acid suppression with proton pump inhibitors.

What then are the practical recommendations?

NSAIDs should be used judiciously. The lowest doses of NSAID should be used and should be stopped when no longer required. It appears that some NSAIDs are less toxic than others and these should be chosen wherever possible. Newer NSAIDs including selective COX II inhibitors or NO-NSAIDs that incorporate a nitroxybutyl moiety may have lower toxicity. However their predicted lower toxicity has to be proven in wider clinical usage.

How should NSAID associated ulcers be treated?

Stopping NSAIDs helps with healing. Non NSAIDs alternatives such as paracetamol could be substituted for pain relief. Omeprazole at a dose of 20 mg om is recommended for treatment. Where detected *H. pylori*, on the balance of present evidence, should be eradicated.

Should every patient on NSAIDs receive prophylactic therapy?

The consensus at the present time, taking into consideration costs and magnitude of NSAID use is to offer prophylaxis to only the high-risk groups of patients: elderly patients, patients with history of peptic ulcers and /or gastrointestinal bleed and those with concomitant serious medical illness. Recommended prophylaxis treatment includes omeprazole 20 mg om.

Newer proton pump inhibitors (lansoprazole, pantoprazole) are available and are likely to be equally effective but to date there are no published data in support of their efficacy in preventing NSAID complications. Misoprostol is also effective in prophylaxis at a dose of 200 µg qid.

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FLAVONOIDS: DISTRIBUTION, CHEMISTRY AND PHARMACOLOGICAL ROLE IN HEALTH AND DISEASE

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Introduction

Flavonoids: Occurrence and distribution

The flavonoids are one of the most widespread groups of plant substances (1). They are ubiquitous in vascular plants and occur in the root, bark, leaf, fruit, flower, pollen and seeds(1-6). About 2% of the total carbon photosynthesised are converted to Flavonoids which in turn contribute to the myriad bright colours in plant tissues (3,7). These compounds are the largest group of plant phenols and more than 4000 types have been isolated and identified in vascular plants (1).

Role in plants

In plants, apart from contributing to the colour, the flavonoids act in concert with growth hormones and influence the morphogenesis as well as sex determination (8). They are also actively involved in the respiration and photosynthesis processes (1, 3, 4, 8). They are the antioxidants for ascorbate (universal component in plants) (1,8). In addition, these compounds exert allelopathic effects, enzyme inhibition, disease resistance / antifungal properties as well as UV protection especially in epidermal cells (1, 3, 8).

Flavonoids are not synthesised by animals but their presence in some animals such as the scent glands of the Canadian beaver and in the wings and bodies of butterflies are through diet (1). Fruits and vegetables contain flavonoids up to several hundred milligrams (9). The outer skin of onions (*Allium cepa*) contain up to 2.5 - 6.5 mg /100g of the flavonoid quercetin, whilst the celery tubers contain 9 mg /100 g fresh weight of flavone glycosides (9).

Generally in man, the daily dietary intake of flavonoids has been estimated to be 1 - 2 g / day which arise mostly through the intake of coffee, tea, bear, wine, cereals, vegetables, fruits, cocoa and peanuts (9,10).

Basic structure and classification

Polyphenols including the flavonoids were originally described as 'Vitamin P' by Szent Gyorgi *et.al* (11) in 1936. Geissman and Hinneiner (6) first described flavonoids as having the 2-phenylchromone (flavone) structure (Fig. 1) in 1952. Currently, it is widely excepted that the flavonoids are benzo-γ-pyrone (Fig. 2) derivatives, which exist as aglycone (without sugar) or glycoside (with sugar) forms. The benzo-γ-pyrone derivatives can be divided into at least 8 major classes namely; flavanone, flavonol, isoflavone, isoflavonol, flavanol, chalcone, flavone and anthocyanidine (12). Table 1 shows the different classes, representative flavonoids, and the corresponding source .

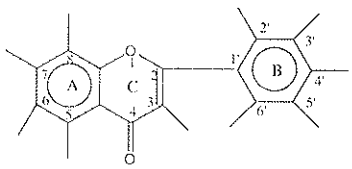

Figure 1. Flavone

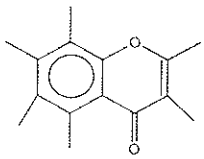

Figure 2. Benzo-γ-pyrone

The hydroxylation pattern, substitution (eg. methoxylation and isoprenylation), degree of polymerization and the types of conjugated groups (eg. glycosylation, sulfation and malonylation) vary within each class of flavonoid (1,12). Naturally occurring flavonoids are often hydroxylated in positions 3,5,7,3', 4' and 5' (Fig. 1). Methyl groups as well as sugar

Table 1. Flavonoid class and distribution (13-18)

Class	Flavonoid	Major Food Source
Anthocyanidine	oenin, cyanidin	cherries and grapes
Flavonol	quercetin, kaempferol	onions, broccoli, apples, tea, leek berries, grapes, red wine
Flavone	luteolin, apigenin	lemon, olive, celery, red pepper, celery, parsley
Flavonone	naringenin, taxifolin	citrus fruits, peel of citrus fruit
Flavanol	condensed tannin, catechin, epicatechin, epigallocatechin	green tea, black tea, red wine
Isoflavone & Isoflavonol	genistein, daidzein	soya beans and legumes
Chalcone	phloretin, butein	(not available)

substituents such as L-rhamnose, D-glucose, gluco-rhamnose, galactose and arabinose can be incorporated into the flavonoid molecule (usually at positions 3 or 7) (Fig. 1) via glycosidic lingkage (1,12).

Metabolism in animals and humans.

The absorption and the metabolism of flavonoids in humans has hardly been studied. Several extensive animal studies show that flavonoids are partly absorbed into the intestine (19-25). Only the aglycones (free flavonoids without a sugar molecule) are readily absorbed through the gut wall. (20). However, most dietary flavonoids are bound to sugars (glycoside form) and the intestinal wall does not contain nor secretes the relevant enzymes for the hydrolysis of the glycosidic bond of the flavonoids (26). Hydrolysis of the flavonoid glycosidic bond only occurs in the colon, aided by the micro-organisms(26). A recent human study has shown that the absorption of orally administered quercetin aglycone was 24%, quercetin glycoside from onions was 52% and pure quercetin rutinoside was 17% (27). The plasma quercetin levels in humans who eat onions regularly have been found to be 200 ng/ml (28). Subsequent to absorption, it is known from animal studies that the compounds are primarily broken down in the liver and the resulting metabolites are excreted as glucuronide conjugates and ring-scission phenolic products into the urine and faeces (19-23). However, the significance of these findings for humans is unclear as there is a great possibility for species variations in secondary metabolism (13).

Biological and pharmacological effects of flavonoids

Pharmacological effects of flavonoids were observed as early as 1936 by Rusynyak and Szent Gyorgi (11). Scorbutic guinea pigs were restored to healthy state when fed with flavonoids whilst, vitamin C alone was not able to do so. The flavonoids which were known as vitamin P then was used in the treatment of capillary fragility (29). Many of these compounds are also found to occur as active components in folk medicines (30). Recent interests in the biological and pharmacological effects and their application in health and disease have increased tremendously. Most of the flavonoids exert their beneficial effects through their ability to scavenge free radicals, inhibit enzymes, chelate ions, mimic hormones and thus competitively bind to the corresponding receptors and various other unknown mode of action (31-45).

The flavonoids are known to affect RNA, DNA, and protein synthesis, anti inflammatory and anti allergic activity, collagen biosynthesis, mutagenicity and carcinogenicity, inhibit key enzymes such as ATPase, aldose reductase, glutathione-S-transferase, iodothyronine deiodinase, NADH oxidase, xanthine oxidase, pp60 kinase, uterine peroxidase hyaluronidase, tyrosine kinase and etc., involved in lipid peroxidation phenomena and various other biological systems (31-45).

The most understood mechanism of flavonoids is their capacity as antioxidants. (43). The so called antioxidant properties of flavonoids may arise as a result of its high propensity to electron transfer, ion chelation and direct scavenging of reactive oxygen species (ROS) or reactive nitrogen species (RNS) (42,43). There is increasing evidence that DNA damage caused by free radicals, ROS and RNS have strong implications in carcinogenesis (42). Various studies showed that flavonoids have anticarcinogenic properties (46). Quercetin, one of the most potent antioxidant flavonoid potentiates the growth inhibitory activity of adriamycin (ADR) in MCF-7 ADR-resistant human breast cancer cells (multidrug resistant breast tumor cell) (47). The flavonoids naringenin and rutin protected the UVB induced template plasmid DNA damage (48).

The isoflavones genistein and daidzein (rich in soya) were able to prevent UVA and UVB or peroxyl-radical induced lipid peroxidation (13). These compounds are also able to compete with the oestrogen receptor in breast tumour cell thus inhibiting the mitogenic actions of oestrogen (13). Genistein inhibits tumour cell proliferation and angiogenesis (13). The flavonoid luteolin has been shown to have radioprotective (gamma ray) effect in mice, believed to be attributed to the hydroxyl radical scavenging potency in a direct or endogenous enzyme mediated mechanism (49). Apigenin is able to inhibit the proliferation of B104 rat neuronal cell, arresting at G2-M phase and induce morphological differentiation.The differentiation process resumed when the apigenin was removed from the culture system (50).

The oxidative damage to LDL is considered to be an important stage in the development of atherosclerosis (13). Numerous drugs and dietary components have been reported to prevent the human LDL oxidative modification (51). The flavonoids in red wine, namely catechin, epicatechin, quercetin, resveratoral, anthocyanins and procyanidines were presumed to be responsible for the protective effects on coronary heart diseases (10, 13). A red wine extract (minus the alcohol) inhibited the oxidation of LDL and also reduced the thrombotic phenomena (10). Genistein in soya has been suggested as an anti atherogenic agent (13). *In vitro* studies have shown that this compound is a potent tyrosine kinase inhibitor(13). Thus it may block the actions of the various growth factors such as fibroblast growth factor and platelet derived growth factor (PDGF) which are implicated in the smooth-muscle cell proliferation that forms part of the atherosclerotic process (13).

Numerous flavonoids have been demonstrated to be effective against the toxic actions of snake bite. Their mode of action appeared to be through the inhibition of hyaluronidase (spreading factor) contained in the venom (36). Several plant extracts have also been claimed to have antivenom properties and flavonoids were found to be the active component (36).

The potent inhibitors of cAMP dependent phosphodiesterase in cell free systems, namely quercetin and fisetin potentiated the beta adrenoreceptor agonist mediated lipolysis in isolated rat adipocytes (38). Some flavonoids were reported to be able to exert anti inflammatory action via the inhibition of the key enzymes, cyclooxygenase and lipoxygenase (52). Ipriflavone has been used in humans in the control of otosclerotic bone remodelling disturbance. In vitro studies have shown that quercetin inhibits bone resorption induced by prostaglandin E2 (PGE2) (53). Numerous reports have demonstrated the anti viral, anti microbial as well as anti fungal effects of plant extracts and flavonoids (54,55).

Conclusions

The natural occurrence of flavonoids in plants, their myriad pharmacological effects and the fact that they are dietary compounds has made it a well sought after avenue for the development of potential new therapeutics. To date, several thousand reports have shown the benefits of flavonoids in health and disease. There are numerous problems that need to be recognised and addressed before these compounds could be used as therapeutics.

The solubility of flavonoids in aqueous solution and the absorption through the gut has to be given due consideration as most flavonoids have poor solublility in aqueous solution. One has to bear in mind that the *in vitro* experiments show the direct effect of flavonoid on the system studied whilst these compounds may be subjected to extensive alterations in the in vivo system. One way to overcome this problem would be to target the flavonoid of interest to the desired location in the body. The ideal vehicle and the method as well as the feasibility of this process need to be studied extensively. The ideal dose which is safe for consumption needs to be established. Several reports have indicated that above a certain concentration, some of the antioxidant flavonoids may become prooxidants (56). In addition the accumulation of the flavonoid metabolites in the body may cause nephropathic damage (57). One has to bear in mind that the protective effects of flavonoids in their natural form (obtained through diet) far outweigh their capacity as therapeutics. The use of flavonoids as dietary supplements has already been practised in many countries including Malaysia. However, the necessity for this is questionable. The best and the most effective way to maintain health and prevent disease is to consume flavonoids and other micronutrients in their natural form. So, eat fresh fruits, vegetables, nuts and grains and lead a disease-free life.

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PROBLEM BASED LEARNING (PBL) IN MEDICAL EDUCATION: WHY, WHAT AND HOW

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Introduction

Why PBL?

Among the oldest of professions are Medicine (the art and science of healing) and Teaching, both of which, in the earliest of times, were accorded the respectability of nobility. Medicine continues to be a highly regarded profession. Many factors contribute in maintaining this notion of nobility, not the least of which is the sentiment attached to the sanctity of human life. It is largely for this reason that, Medicine, historically has remained a profession of a chosen few; from being almost a cult in Hippocratic times to being a profession almost regarded as a cult of the best of students. Two major human factors impinge on the life/professional training of those called to the medical profession. One is the sentiment which humans attach to life for which reason the societal expectations of the doctor is very high. This translates to the doctor being expected to know virtually everything about man, his structure and function, his diseases and the healing of same. A practical manifestation of this societal sentiment is that many a medical school teacher has a mind frame driven by the desire to make the students know virtually every fact that there is on any subject he lectures. This attitude tends to make the medical school curriculum so overwhelming that it creates an inclement learning environment which contributes to the drop out of otherwise brilliant students from medical school (1, 2). The second factor which is closely related to the first is that as time progresses the horizon of knowledge extends even further, thus, compounding the first factor. It is largely for these reasons that inductees to the medical profession can only be drawn from among the best of students. One of the major tasks facing anyone involved in the training of medical doctors, therefore, is working out the best approach to imparting this enormous and increasing body of knowledge to the next generation of doctors, hence the growth and development of new approaches / curricula. It has been said that with time the undergraduate medical curriculum tends to develop a chronic disorder labelled 'curriculopathy' (3). This 'syndrome' arises from the failure of the curriculum to catch up with factors that influence training, such as, increasing body of knowledge, lack of relevance, predominance of basic and biological sciences, faculty attitude to teaching, costs, and the organisation of the delivery of medical education (4). Curriculopathy, thus, hampers the efforts of the medical school at producing knowledgeable and humanistic doctors (5). It is in the search for better ways of imparting medical knowledge that the concept of problem-based learning (PBL) as a focus of training was born. Problem based learning per se is not a new learning technique. It is the adoption of its philosophical notion as the main driving force in a structured medical curriculum that represents a paradigm shift in the field of medical education. Hitherto, the philosophy of medical teaching was teacher centred. In this traditional setting, the teacher was viewed as a reservoir of knowledge from which the medical students should drink. Learning activities centred around the teacher whose main tool for dissemination of knowledge was didactic lectures. As the body of knowledge expanded, didactic lectures became more and more complex in content and required more and more lecture hours. This meant more and more pressure on the teachers and worse still on the student, thus, contributing to 'curriculopathy'. With the prevailing pressure, further aggravated by an ever-increasing public expectation, planners of medical education were left with no choice but to create ideas that can help minimise the obvious shortcomings of the traditional medical curriculum. The PBL concept is, therefore, a child of necessity. Pioneered by the McMaster University in Hamilton, Ontario, Canada as far back as the mid sixties (6), this approach which initially met with resistance (even in McMaster) is gaining popularity (7). It has been adopted by several notable medical schools such as Harvard, Southern Illinois University, University of New Mexico, all in the USA, Sherbrooke in Canada, Xinjiang in China, and Lindkoping in Sweden, etc. It is gradually becoming the standard format for medical training world wide and, therefore, represents a subject that should interest all that are involved in medical education either as teachers or administrators. One other major attribute of a PBL curriculum, is that it represents a practical application of the now established fact that knowledge is much better recalled and applied in the context it was originally learnt. Thus, the philosophy of early exposure of students of PBL curricula to clinical scenarios.

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What is PBL?

What is a PBL curriculum like? As the name indicates, PBL implies learning through facing and solving challenges. This in itself is a well known learning process which over the years has been used by teachers in all fields (including medicine), albeit, to different degrees and without it assuming a special emphasis in the curriculum. In a PBL curriculum, however, PBL assumes a higher value in terms of a well organised systematic application of its principles in medical education; the PBL becomes the driving force and centre of focus of the learning process. In the PBL curriculum, the student and not the teacher is the centre of focus. The teacher's role shifts from that of a giver of knowledge (lecturer) to that of a facilitator, a coach , a guide, a moderator. Knowledge is, therefore, acquired actively by the student who is challenged by problems requiring diverse knowledge base for solutions. In solving the problem the student naturally puts all his genius in seeking the power (knowledge) to solve the problem. Because the process is driven by the student it is a self-directed learning (SDL) process; a term which is sometimes confused with PBL. Possibly the easiest way to appreciate these terms is to understand that in a PBL curriculum the individual student drives his own learning process (SDL) through solving problems and is guided / facilitated by the tutor who ensures that the student's inquisitive mind probes into those areas of the problem that the curriculum requires of him. This active process instils into the student the confidence of being the source of the solution to the problem and many a student has expressed a psychological satisfaction with the learning experience (8,9). Further advantages of the PBL curriculum include the development of communicative skills (10) as the students do most of the talking, and the enhancement of inquisitive rather than rote learning style (11). The cultivation of a positive attitude towards problem solving tends to sustain the interest of graduates of a PBL curriculum in continuing education (12) which enriches their professional lives by, hopefully, making them life-long learners.

How is PBL adopted?

The purpose of this section is two pronged. One is to create an insight, using one or two examples, into how medical schools have transformed from the traditional lecture-based learning (LBL) curriculum (also referred to as the traditional curriculum,TC), to a PBL curriculum. The second is to attempt a brief description of the running of a PBL curriculum. Generally there exists two modes by which medical schools have transformed from the traditional to the PBL curriculum. Apart from the newer medical schools that opt for PBL right from inception, others who have adopted PBL have had to transform. The transformation process for some (e.g. the Sherbrooke School of Medicine, Quebec, Canada) was a complete change from an LBL to a PBL curriculum following years of planning (4), whereas, for others such as Harvard (13) there was an experimental transitional period during which two streams of students were running the LBL and the PBL curricula concurrently. In some cases, for example the Faculty of Medicine of the University of Hong Kong, PBL was gradually introduced, on an experimental basis, to one or two departments (7) and later adopted for the whole faculty. Irrespective of what mode of change is adopted the planning stage preparatory to the full adoption of a PBL appears to be the most crucial for the success of the programme. This is the stage that involves the mobilisation of a teaching staff that is so set in its (LBL) ways that it invariably resists the proposed change. The experience at the Sherbrooke School of Medicine (4,8) is worth a case study for any medical school transiting to a PBL curriculum and we adopt it in discussing this process. The process of transition involves four main strategic steps: 1. Identifying the need for change 2. Selecting a solution 3. Planning the implementation and 4. Adopting the solution.

1. Identification of the need for change: This derives largely from the factors contributing to curriculopathy as earlier described. Chief among these factors is the ever growing medical knowledge base with increasing fragmentation into specialities and sub-specialities and the tendency for each teacher to focus teaching on his own microscientific world, thereby, creating a distorted curriculum that lacks proper integration and, therefore, diminished in its ability to inculcate a desirable holistic attitude in its products. In the particular case of Sherbrooke, the problems included excessive course content, teaching nearly restricted to lecturing, and poor congruence between evaluation techniques and educational objectives (4). Also contributory to the acceptance of the need for a change is the fact that several other curriculum review committees had equally recommended changes because of perceived curriculopathies with similar manifestations as those identified at Sherbrooke. Notable among these committees was the Panel on the General Professional Education of the Physician and College Preparation for Medicine (the GPEP report, 1984) whose report, published by the Association of American Medical Colleges, was unequivocal in its recommendation for a change in curriculum.

2. Selecting a solution: The solution to be selected can only be based on what is known and is judged capable of solving the identified problems and, thus, achieve the set objectives of the curriculum. In Sherbrooke, the set objectives include training doctors who are adequately motivated towards self-directed learning, have a holistic perception of Medicine, are caring, and can relate adequately with the community

through a proper grasp of communicative skills and understanding of the human environment they operate in. These are laudable objectives which any modern day medical school would adopt without much argument. The rest of this paper for practical purposes shall be based on these objectives. The PBL as described above tends to be the natural choice to achieve these objectives as it possesses the ingredients for the realisation of these goals such as its student-directed learning / teaching principles which includes training in communicative skills. Having identified the PBL as the solution, the remaining task is to develop, adopt and implement this solution.

The process of developing the framework of a curriculum should involve a carefully selected committee of faculty with demonstrable interest in medical education and preferably with formal or informal training in the principles of education and pedagogy. At the head of this committee should be a faculty who possesses these qualifications or in the alternative an expert consultant hired for that purpose. Guided by the institutional philosophy and the stated goals of PBL, the committee would come up with a curriculum framework expectedly focused on patients (i.e. community-oriented and humanistic learning) and on students (i.e. a learning process favouring autonomy). An integrated organ/system-based multidisciplinary teaching approach which fits well into the practicalities of a PBL curriculum may also be recommended. The task of this committee expectedly includes looking at existing curriculum and the curricula of other innovative schools and coming up with proposals which are then reconciled and adopted by consensus.

3. Planning the implementation: Once the framework of the PBL curriculum has been identified, planning for its implementation becomes the next task. This, among others, involves:

(i) The promotion of the acceptance of the new curriculum by a large proportion of teachers. A major determinant of the success or failure of any curriculum change is the extent to which the teachers are involved in the planning and execution of the change (14, 15). At Sherbrooke, an eighty-four page planning document linking the history and the educational philosophy of the institution with the process and content of change was widely distributed in the institution. This document formed the basis for a series of departmental meetings during which the vice-Dean for education and the undergraduate program Director were involved in debates with other faculty. Such debates stimulate faculty interest and secure their co-operation once they are convinced. It is a necessary step. (ii) Defining the content of the curriculum more precisely through the establishment of multidisciplinary working groups. The Sherbrooke example is very illustrative. A working group was set up for each of the seven four-week organ/system units for the first year of the new curriculum. The group identified and defined problems of clinical relevance or problems that illustrate basic concepts and mechanisms. The same approach was used in defining the course contents of the other pre-clinical years. A different task-force planned the student learning evaluation system for the entire pre-clinical years. (iii) Educating the teachers. The success of a curriculum change depends on educated teachers. In the Sherbrooke example, several workshops and training sessions were conducted to achieve various goals aimed at improving the teachers. Among the workshops were 1. Introduction to pedagogy in medical education, 2. Basic training programme in medical pedagogy which allows participants to acquire the scientific basis of medical education, master the skills in teaching, and to develop attitudes that place the students at the centre of the educational process (4), and 3. PBL tutor training which aims at introducing participants to PBL methodology, construction of problems and the techniques for small group discussions. Some of these are conducted yearly as refresher courses.

4. Adopting the solution: Once the training of faculty has been achieved a lot of the mobilisation work would have been done through the participation of faculty in these training sessions. With a good number of faculty now willing to give the new curriculum a try, the stage for its adoption has been reached and it could then be presented to the faculty board and subsequently to the university council for adoption. This is followed by implementation which means the admission of the first cohort of students into the new training programme. As the whole process goes on, the tendency is for more and more faculty to become interested and turn into advocates of the new curriculum (8). The initial inertia of faculty to the new curriculum must be anticipated by the planners and should, thus, not constitute a demoralising influence.

The running of a PBL curriculum: The way a PBL curriculum is run is not likely to differ significantly from one medical faculty to the other for as long as the core guiding philosophy remains a student-propelled learning through problem solving. With this philosophy as a constant guide, differences in the running process shall only manifest in the timing and emphasis placed on the different subject matters to be covered within the curriculum. For example, a medical faculty that places greater emphasis on the research orientation of its products may allocate more hours to practical experimentation and tutorials on research methods while one with a greater emphasis on community orientation may expose its students to community practice right from the first pre-clinical year. In all these however, the basic learning format is PBL.

As in all educational settings, the first task in a PBL course

is to draw up the contents of the various courses. This comes after the main structure of the curriculum has been designed. The main structure of the curriculum essentially defines the integrative relationships between the various disciplines that make input to the medical school training. The structure will determine the levels at which particular courses are taught and how the lecture/tutorial hours are staggered to enable a proper integration which in the case of a PBL curriculum is an essential feature. A major determinant of the structure is the philosophy that drives the individual medical school training programme. The philosophy is also reflected in the specific contents of the curriculum and the different courses within the training programme. This principle is very crucial to the success of any training programme, because at the end of the day it determines whether or not the products of the training meet with the originally set goals defined by the programme's philosophy. It also tends to ensure consistency in the quality of the products of the training programme. In the case of a PBL curriculum, extra care must be taken to draw up the contents of the various courses with attention paid to such issues as overloading of the curriculum (1), construction of clinical problems and the proper integration of the various courses. Care must also be shown in determining which areas of the course content are best delivered by didactic lectures and which by tutorial sessions. The achievement of these principles may be a little more difficult for the pre-clinical subjects where clinically qualified expertise is a desideratum.

Teaching methodology: Fundamental to a PBL curriculum is the drastic reduction in the number of hours allocated for didactic lectures in favour of small-group (5 - 8 students) PBL tutorials which take the SDL format. For example, in the Sherbrooke programme, lecture hours were reduced to approximately 130 hours from the LBL curriculum level of 1,645 hours in two and half years while small group PBL tutorial was allocated 5,364 hours in the same period (8). PBL tutorials are basically forums for students to generate/ discuss among themselves the solutions/answers to pre-constructed problems and also problems / issues / questions emanating from the main problem. The role of the faculty is as earlier stated: a guide, tutor, facilitator or moderator. Very important to the principles of PBL is the issue of the tutor's role. It has been asserted that the tutor may in fact know very little about the topic of discussion since this will discourage active participation of the tutor; a very important goal of a PBL tutorial. A Harvard University study group on this subject concluded that ignorance on the part of the tutor about subject content is more of a benefit than a liability as content experts tend to take over the discussions to the detriment of a PBL tutorial. This finding was the basis for the use of content non-experts by Dalhousie University for their first PBL students (16). This practice was later abandoned in favour of tutors with content expertise, thus, falling in line with the respected advice of Barrows (17) that both content expertise and facilitation skills are important for the effective tutor, but forced to make a choice, one should go for the tutor with good facilitation skills. A golden rule is that tutors do not write on the board because the tendency is to fall into a lecture session (18). Problems for a tutorial session are derived from the series of problems constructed for the course curriculum by the expert working groups. As the problem is discussed it ramifies into other problems, thus, enriching the learning process in both depth and width. The problems could be theoretical, real patient case or simulated as in the Paediatric PBL at the Monash University in Australia (19).

Evaluation: Evaluation of the curriculum, including the evaluation of tutors' and students' performances, is an essential component of a well administered educational training programme. This is even more so for an innovative curriculum. Tutor evaluation can take several formats, including feedback obtained from student-targeted questionnaires and / or peer reviews. It must be stressed that such peers should be those adept in the techniques of PBL and preferably with demonstrable understanding of the principles of education and pedagogy. The staff training which the school ought to have instituted in the planning stages would provide it with an abundance of this level of manpower. Apart from these internal modalities of tutor assessment, external assessors could be invited from other institutions with similarly innovative curriculum. Approval of the curriculum by such external assessors could be a booster to the morale of tutors who are still grappling with the inertia of adopting a new curriculum (4). One of the basic contributing factors to curriculopathy is the mismatch between student evaluation processes/content and the goals of the curriculum. It has been observed that ability to match examination with the teaching format is an important factor in mobilising student interest in the PBL curriculum which is a learning approach completely different from what the students are used to (20). For example, examination questions should be problem based since the teaching style is PBL based, otherwise students who ordinarily are motivated towards passing their examinations will see no good reason for approaching learning through the PBL/SDL technique, and this can affect their enthusiasm with possible negative influences on the tutors and consequently on the new curriculum. As with the tutors, student evaluation can be both internal and external. At Sherbrooke, the internal evaluation process involves internally organised exams while the external evaluation includes internally organised exams with external examiners and also an evaluation of the students' performance in national board examinations.

Conclusion

Any medical curriculum is doomed to atrophy. This derives largely from the exponential growth in medical knowledge resulting from increasing technological capabilities which turn, overnight, the sacrosanct medical attitudes of yesterday into the taboos of today. The equally increasing public awareness of medical science fuelled by the ever-expanding influence and sophistication of information technology has created a public that is ever so demanding, inquisitive and critical of the doctor's performance. These, coupled with an equally expanding and not-so-clement legal environment has placed a burden of responsibility on medical educators to fashion out a curriculum that can start to grapple with these modern realities. Because of its inherent capabilities, particularly its capacity to promote self-directed learning and its problem-oriented and, therefore, humanistic bend, the PBL curriculum has become the favourite of innovative medical schools. One after the other, medical schools from around the globe are adopting the PBL as the way to the future. A proper transition from a TC to a PBL curriculum requires a proper administrative structure dedicated to that purpose. A crop of professional educators and /or faculty that is well informed on educational principles, pedagogy and the workings of the PBL is a sine qua non of a successful transition. A critical factor in this process is the management of the initially high anxiety levels of the faculty teaching staff. In this connection, perhaps, the Chinese proverb which says that 'when the wind of change is blowing, some people build fences while some build windmills' could be very instructive. With the realities on the ground, it is safe to say that no medical school with its eyes on the future can afford to be blind to the workings of the PBL. It is a paradigm whose time has come.

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HIGH POTASSIUM-INDUCED EPILEPTIFORM BURSTING IN RAT HIPPOCAMPAL SLICES

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ABSTRACT: Hippocampal slices from adult Wistar rats were used to assess the presence and frequency of epileptiform bursting (EB) induced by high potassium levels in the bathing medium. In vitro hippocampal slices were stabilized initially in 3.5 mM K^+ artificial cerebrospinal fluid for one hour. All slices were checked for evoked responses in region CA1. The bath K^+ was then increased to 8.0 mM. Spontaneous epileptiform bursting was checked and recorded from regions CA1 and CA3. A branching logic design was used to define bursting, non-bursting and non-responsive slices. At the end of the 6-7 h experiment, all slices were checked, again, for evoked responses in CA1. Of 76 slices, 70 were responsive at the beginning and 68 at the end. Exposure to 8.0 mM K^+ produced EB in both regions CA1 (38/68) and CA3 (35/68). Average time to first EB in CA3 was 23 min. Bursting frequencies in CA1 and CA3 were highly correlated (r^2=0.95, df=62). These results suggest that EB in region CA1 is as reliable as that in CA3. Consequently, in screening large numbers of slices for EB, recording from CA1 is sufficient. *(JUMMEC 1997 2(2): 95-98)*

KEYWORDS: Electrophysiology, hippocampal slices, *in vitro*, potassium, rat, seizures

Introduction

High potassium levels (above 6 mM) in artificial cerebrospinal fluid (ACSF) are known to induce spontaneous epileptiform bursting (EB) in rat hippocampal slices in vitro (1,2). The mechanism by which these bursts are generated is not fully understood (2); however, it may be caused by a rise in the intracellular chloride level and/or alterations in the potassium pump mechanism (1).

An extensive study by Korn *et al.* (1) of spontaneous EB in the rat hippocampal slice indicated that bursts seemed to originate from region CA3. This same study showed that bursts were most intense and frequent at the boundary between CA3b-CA3c, but were relatively small and infrequent in region CA1.

The purpose of this study was to assess the presence and frequency of spontaneous EB activity in the rat hippocampal slice, induced by raising the potassium level in the bathing medium to 8.0 mM.

Materials and Methods

Adult male Wistar rats, 250-480 gm, were decapitated and their brains were rapidly removed and rinsed with ACSF. The hippocampi were isolated and immediately cut perpendicularly to their long axis with a McIlwain tissue chopper into 0.4 mm thick slices (Figure 1). Only slices from the middle third of each hippocampus were used in this study. Slices were placed in oxygenated ACSF for 2-5 min, then transferred to an interface chamber (3). Slices were mounted on a nylon mesh and superfused with oxygenated (95% O_2/5% CO_2) ACSF at a rate of 0.4 ml/min. The composition of the ACSF (in mM) was: NaCl 130, KCl 3.5, NaH_2PO_4 1.25, $NaHCO_3$ 24, $CaCl_2$ 1.5, MgSO4 1.5 and glucose 10 (1). Temperature in the chamber was maintained at 34 ± 0.5°C. A humidified gas mixture of 95% O_2 and 5% CO_2 was circulated over the slices in the chamber.

Slices were bathed in the low potassium (3.5 mM) ACSF for one hour to stabilize, after which their viability was checked electrophysiologically, as described by Shields *et al.* (4). A bipolar tungsten electrode was placed in the Schaffer collateral pathway (stratum radiatum) for orthodromic stimulation of the CA1 region pyramidal neurons. A glass recording electrode, filled with ACSF, that had an impedance of 2-5 megohms was placed in the cell body layer (stratum pyramidale) for recording of postsynaptic population field potentials. All recordings of evoked potential responses were made using stimuli 0.1 msec in duration and a voltage level equal to twice threshold. A "Grass S44" stimulator with a "SIU7"

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isolation unit was used for stimulation. Records were taken using a high-impedance headstage, an x100 AC amplifier, and a "Gould - Model 1425" digital oscilloscope. Single or averaged responses were transferred to an XT-type personal computer via serial link, stored on disk, and later plotted for analysis.

After initial stabilization, all slices were checked for evoked responses in region CA1. Those not showing responses of 1 mV or greater in amplitude were discarded. The active slices were also checked in the same manner at the end of each experiment, approximately 7 h from time of placement in the chamber.

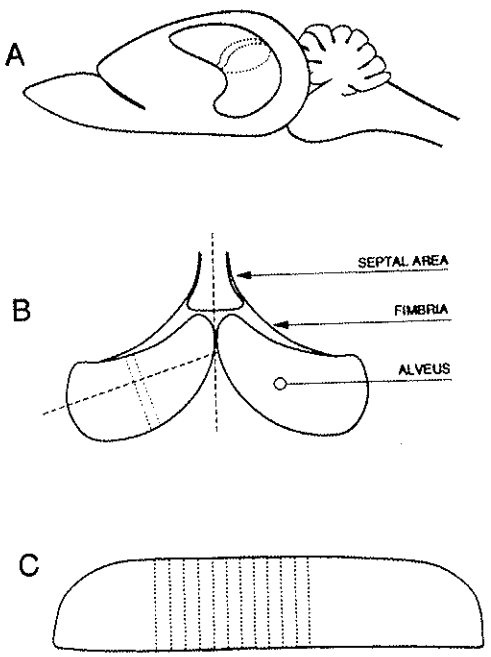

Figure 1. A schematic presentation of the preparation of the rat hippocampal slices: (A) position of hippocampus in the brain. (B) angle of cutting. (C) only the middle third of hippocampus was used in preparation of slices.

In preliminary experiments using 8.5 mM K^+ ACSF, EB rarely lasted long enough for an adequate survey of all slices. For this reason we reduced the K^+ level in the ACSF to 8.0 mM. In this medium EB was sustained for 3-5 h. The high potassium ACSF was introduced 165 min from the time slices were placed in the chamber. This period was used for slice viability checking. Immediately after the change to high potassium ACSF, slices were checked in sequence for the presence of spontaneous EB in region CA3. A branching logic plan was used to check each slice for: (a) presence or absence of spontaneous bursting in region CA3; (b) presence or absence of spontaneous bursting in region CA1; (c) burst frequency in CA3; and (d) burst frequency in region CA1. Due to equipment limitations it was not possible to measure burst frequency simultaneously in both regions CA1 and CA3. Burst frequency was measured only if the bursts were of sufficient amplitude to reliably trigger the "Gould" digital oscilloscope. Bursts of smaller amplitude were noted, and selected bursts captured for analysis, but adequate frequency measurements could not be made.

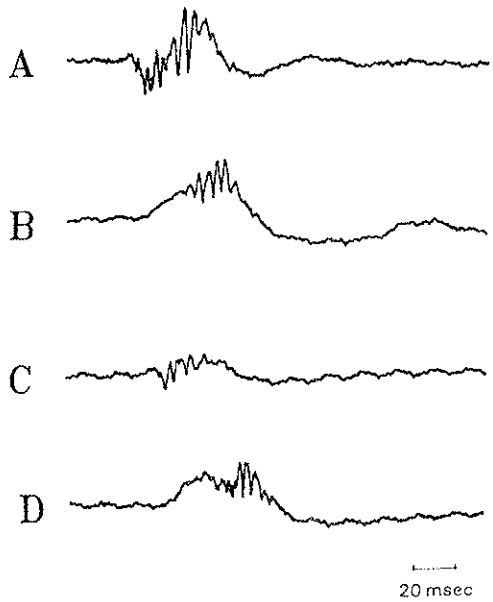

Figure 2. Records of spontaneous epileptiform bursts in CA1 (A and C) and CA3 (B and D) regions of two rat hippocampal slices in 8 mM K+ ACSF. Records A and B were from one slice, C and D from another slice. In A and B, the burst in CA1 is larger than the burst in CA3. In C and D the burst in CA3 is larger than in CA1. Within any one slice, the relative sizes of bursts in CA1 and CA3 tended to be similar.

Results

Of the 76 total slices used, 70 were found viable at the beginning of the experiment. At the end of the experiment, 68 slices were still active; showing evoked responses greater than 1 mV in amplitude in region CA1. The data presented here were taken from only the 68 slices that remained viable throughout the experiment. Almost all population responses showed single spikes when slices were bathed in the 3.5 mM K^+ ACSF. Multi-spike responses were consistently obtained at the end of the experiment as slices were then bathed in the 8.0 mM K^+ ACSF.

Sequential checking for spontaneous activity in regions CA1 and CA3 during the initial viability testing revealed no detectable bursting under low K^+ ACSF bathing conditions. The average time for the first epileptiform burst to appear in region CA3 after changing to 8.0 mM K^+ ACSF was 23 min from the time the high K^+ ACSF reached the chamber. Bursting during the first

15 minutes after the appearance of the first burst was weak, irregular and infrequent. We, therefore, decided to allow slices to stabilize their bursting patterns by waiting for about 25 min after the first burst appeared before assessing and recording burst activity.

Burst amplitude, even after stabilization, was quite variable. Within the same slice, bursts from CA1 could be larger or smaller than bursts from CA3 (Figure 2). As our primary goal was to survey a substantial number of slices, we did not explore these amplitude variations in detail.

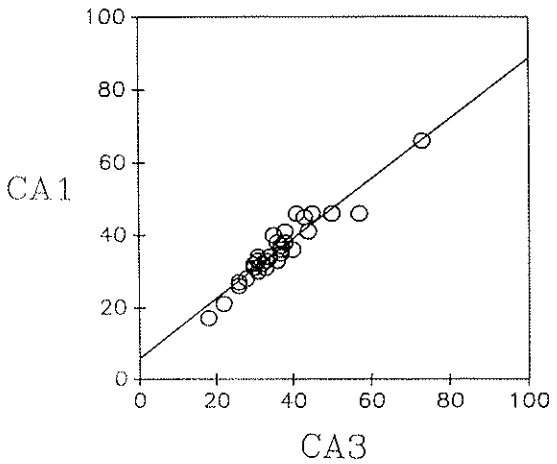

Figure 3. Correlation between spontaneous burst frequencies in CA1 and CA3 regions of the same hippocampal slice

As shown in Table 1, only 68 % of the slices surveyed showed EP activity. Even though the number of slices that had EP activity in region CA1 was identical to the number that had EP activity in region CA3 (46/68), they were not necessarily the same slices. Only 31 slices had bursts large enough for adequate rate measurement in both regions CA1 and CA3.

Data on frequency of EB in CA1 and CA3 are summarized in Table 2. The mean bursting frequencies in regions CA1 and CA3 were the same for those slices from which counts and records of bursts were made. The range of burst frequencies observed was substantial: from 20 to over 70/min. Nevertheless, burst frequencies recorded from CA1 and CA3 regions of the same slice were highly correlated (r^2=0.95), as shown in Figure 3.

Discussion

Korn *et al.* (1) reported that the average number of bursts/min resulting from raising the potassium level from 3.5 mM to 8.5 mM was 58±3 (standard deviation of the mean) in region CA3 (n=64). Dingledine and Korn (5) reported a rate of bursting of 1/sec (60/min) under similar experimental conditions. Traynelis and Dingledine (6) reported a rate of 47.5±0.8 (N=490), also with 8.5 mM K^+. Our results show a lower count/min in both regions CA1 and CA3 (Table 2), at least in part because we used an 8.0 mM rather than 8.5 mM potassium medium. Rutecki *et al.* (2) recorded increases in intensity and frequency of spontaneous bursting as the level of potassium in the ACSF was increased from 5.0 mM to 10.0 mM; from this data a change from 8.5 mM to 8.0 mM K^+ would be expected to reduce the burst frequency by about 6/min.

Table 1. Distribution of epileptiform bursting activity in regions CA1 and CA3 of the rat hippocampus

Region	CA1	CA3
Total No. of active slices	68	68
No. of slices with bursting activity*	46	46
% of total slices	68	68
No. of slices with counted bursts**	38	35
% of total slices	56	51
% of bursting slices	83	76
No. of slices with counted bursts in both CA1 + CA3	31	31
% of total slices	46	46
% of bursting slices	67	67

* Whether with counted bursts or not.

** Bursts that were large enough for accurate counting.

Table 2. Frequency of epileptiform bursts in regions CA1 and CA3 of the rat hippocampus

Region	CA1	CA3
No. of slices with counted bursts	38	35
Av. No. of bursts/min	33 ± 1.5 (n = 38)	35 ± 1.7 (n = 35)
No. of slices with counted bursts in both CA1 + CA3	31	31
Av. No. of bursts/min	36 ± 1.6 (n = 31)	36 ± 1.8 (n = 31)

Our results differ from those reported by Korn *et al.* (1), regarding the presence and frequency of spontaneous bursting activity in region CA1. Our finding of a level of EB in region CA1 equal to that present in CA3 may be attributable to the fact that our hippocampal slices were cut perpendicularly to the longitudinal axis; as well as our use of slices only from the middle third of each hippocampus. Anderson *et al.* (7) showed that the Schaffer collaterals and the

mossy fibers in the hippocampus are oriented in a direction nearly transverse to the longitudinal axis of the hippocampal formation. Our method of slicing the hippocampus and our choice of slices may have improved the chances for the connections between regions CA1 and CA3 to remain intact, in at least 46% of the slices used. We do not have an explanation for the fact that nearly 1/3 of the slices we tested showed no detectable spontaneous bursting activity. We did not observe the prolonged electrographic discharges in CA1 described by Traynelis and Dingledine (6). The findings presented in this study facilitate the detection of measurable spontaneous bursting activity in hippocampal slices. Because of the high correlation between activity levels in region CA1 and region CA3, checking for EB activity in region CA1 may be sufficient; i.e., if EB is present in region CA1 then it can be assumed to also be present in region CA3.

It is appropriate to note that the technique and equipment used in this study allow for diverse utilization, for several purposes, involving the biological properties of different tissues.

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THE IMPACT OF THE HAZE ON CHILDREN WITH CHRONIC ASTHMA

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ABSTRACT: To determine the impact of the haze on asthma symptomatology in children with chronic asthma on inhaled prophylaxis. The study was prospective and collected information on asthma symptoms from children attending the asthma clinic. A comparison of peak expiratory flow rate (PEFR) measurements before and during the haze was performed for children above 7 years. A total of 97 children were included into the study. Forty (41%) children complained of increased respiratory symptoms during the haze. The most common complaint was an increase in nocturnal cough (55%) followed by nasal symptoms (40%), daytime cough (40%) , nocturnal wheeze (25%) and daytime wheeze (18%). About half of the children who had increased symptomatology during the haze had to limit outdoor activities. In the 43 children in whom PEFR studies were available, 29 (67%) of them had a fall in the PEFR. However, children with no increase in asthma symptomatology showed a similar fall in PEFR measurement when compared to children with increased asthma symptomatology. The haze appeared to be detrimental to the well being of some children with chronic asthma despite being on inhaled prophylaxis. *(JUMMEC 1997 2(2): 99-102)*

KEYWORDS: Haze, cough, wheeze, peak expiratory flow rate

Introduction

Air pollution secondary to widespread forest fires resulting in a haze is peculiar to parts of the world where deforestation for land cultivation is achieved by open burning of the land. Many parts of Malaysia were shrouded with a thick haze for the most part of August to October in 1997. The haze then was attributed to uncontrolled forest fires that raged in parts of Sumatra and south Borneo. The severity of the haze was locally monitored by Alam Sekitar Malaysia Sendirian Berhad (ASMA) using the Air Pollutants Index (API). The API was a uniform measurement that took into account 5 different air pollutants namely carbon monoxide (CO), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), suspended particulate matter less than 10 microns (PM 10) and ozone (1). An API level above 100 was considered unhealthy and a potential health threat.The haze became a major environmental disaster and health threat when the API in parts of Sarawak reached unacceptably hazardous levels and prompted the state government to declare a state of emergency causing closure of schools, businesses and public services.

The most worrying effect of the haze was, of course, the impact it had on the health of the nation's population, both young and old who were continuously exposed to the unhealthy air. Children and the elderly who already have chronic respiratory problems appeared to be exceptionally vulnerable to the effects of the haze. There was a significant correlation between the daily number of children and adults seeking treatment for acute asthma at the emergency unit of University Hospital Kuala Lumpur with the API index in the Klang Valley during this period (personal communication Lim Kim Hatt, Department of Medicine, UHKL).

This study looks at the asthma symptomatology during the haze in a group of children with chronic asthma whose illness severity warrants inhaled prophylaxis treatment and who attend regular follow up at the paediatric asthma clinic of University Hospital Kuala Lumpur.

Materials and methods

The study was prospective in nature. Children who fulfilled the following criteria:

1) aged 1 - 12 years
2) diagnosed to have chronic asthma of moderate severity

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3) receiving inhaled prophylaxis as regular treatment (either steroids - beclomethasone/budesonide or mast cell stabiliser - sodium cromoglycate)
4) reside in the Klang Valley

were included into the study. The children and parents were interviewed individually using a standard questionnaire concerning asthma symptomatology during the period from August to October 1997 when the haze surrounding the Klang Valley had API values above the unhealthy levels. The asthma symptomatology enquired during the interview included daytime and nocturnal cough, daytime and nocturnal wheeze, nasal symptoms i.e. nasal stuffiness, running nose and sneezing attacks and exercise induced cough and wheeze. Patients were also asked if the presence of the haze influenced a change in their life style namely the use of a facial mask when going outdoors or limiting their outdoor activities. PEFR measurements were obtained for children above 7 years during the clinic visit and were compared to the PEFR measurement done at the last paediatric asthma clinic visit for 1997 before the month of June.

Data collected was analysed using a statistical programme SPSS Version 6.13 for Windows 95. The Students t test was used to compare quantitative data and the Fisher's exact test was used to compare dichotomous variables.

Results

A total of 97 children were included into the study. The mean age of the children was 7.1 ± 3.5 years with a median age of 7.1 years. There was a marked male preponderance with a male:female ratio of 1.85:1. Malays (50%) constituted the majority of children and this was followed by Chinese (28%) and Indians (22%).

Forty (41%) children complained of increased asthma symptomatology during the haze. The most common troublesome asthma symptoms were nocturnal cough (55%) followed by daytime cough (40%), nasal symptoms (40%), daytime wheeze (18%), exercise induced cough (15%) and exercise induced wheeze (15%). Six children required a course of systemic corticosteroids and four children needed in - patient care for acute asthma during

Table I. Clinical characteristics of children with/without increased asthma symptomatology during the haze

Clinical parameter	Children with increased asthma symptomatology (n = 40)	Children with no increased asthma symptomatology (n = 57)	*p* value
Mean age ± SD (years)	7.4 ± 3.2	7.2 ± 3.6	0.71
Children above 5 years	27 (68%)	36 (63%)	0.65
Mean age ± SD at time of asthma diagnosis (years)	2.8 ± 2.0	2.8 ± 2.1	0.91
Sex (Male : Female)	2 : 1	1.6 : 1	0.66
Race			
Malay	40%	56%	
Chinese	38%	21%	0.34
Indian	22%	23%	
Inhaled steroids for prophylaxis	77%	91%	0.06
Change in lifestyle	48%	23%	0.015*

*significant p value

Table 2. Fall in PEFR measurements for children above 7 years with/without increased asthma symptomology during the haze

PEFR	Children with increased asthma symptomatology (n = 22)	Children with no increased asthma symptomatology (n = 21)	*p* value
Number who have PEFR fall	17 (77%)	12 (57%)	0.16
Mean PEFR fall	17.8 ± 9.2%	17.6 ± 8.3%	0.90
PEFR fall more than 15%	13 (59%)	7 (33%)	0.26

this period.

There was no difference between the clinical characteristics of children who complained of increased asthma symptomatology and that of those who did not (Table 1). As expected, children who had increased asthma symptomatology were more likely to adjust their lifestyle to reduce exposure to the haze by limiting outdoor activities and using a facial mask. Children who used inhaled steroids for prophylaxis instead of inhaled mast cell stabiliser were less likely to have increased asthma symptomatology but this failed to reach statistical significance.

PEFR measurements suitable for comparison were available for 43 of the 49 children above 7 years of age. Six children were excluded from the analysis because a PEFR measurement before the haze was not available. Twenty nine (67%) children had a decline in PEFR measurements during the haze with a mean fall of 17.7 ± 8.8 % and a range of 3 to 33%. Only 20 (47%) children had a PEFR fall of more than 15%. Although a higher number of children with increased asthma symptomatology had a decline in their PEFR measurements when compared to children who had no increased in asthma symptomatology, this difference did not reach statistical significance (Table 2).

Discussion

There is little doubt that the quality of air that children breathe has a direct effect on their airway mucosa and lung. Rapid urbanisation resulting in the deterioration of air quality due to increased levels of air pollutants is now increasingly recognised as a potential health problem in Malaysia. The air quality is more likely to be important for children with chronic respiratory problems namely chronic asthma, bronchopulmonary dysplasia and cystic fibrosis. The study of the impact of air quality and pollution on the health of children with chronic respiratory illness is complicated as there are a number of types of air pollution and the influence of common confounding factors like exposure to cigarette smoke, indoor pollution from heat sources used for cooking and plant pollen derived airborne allergens cannot be easily excluded. Air pollutants which may affect the respiratory health of children include concentration of nitrogen dioxide (NO_2), sulphur dioxide (SO_2), ozone and suspended fine particulate pollutant less than 10 microns [PM 10] (2). Large amounts of suspended particulate matter in the air resulting in a thick haze appears to be quite unique to this part of the world and other developing nations where widespread open land burning is used by farmers for forest clearing. A thick haze secondary to forest fires that shrouded South East Asia occurred in 1994 and was associated with an increase in the emergency room attendance by children with acute asthma (3).

Children with chronic asthma of moderate severity are vulnerable to changes in the environment as unfavourable conditions like the haze can precipitate troublesome asthma symptoms. We studied a group of patients whose asthmatic symptoms were usually controlled with inhaled prophylaxis and despite on-going prophylactic treatment, 41% of them complained of increased asthma symptomatology during the haze. This is not a surprising finding as numerous studies have shown that poor quality air has a definite adverse effect on children with chronic asthma causing an increase in asthma symptomatology (4, 5, 6), hospitalisation rate (7,8) and emergency room attendance for acute asthma (9, 10). It has been shown that a transient deterioration in the pulmonary function occurs in children with increasing levels of air pollutants and that children with bronchial asthma are most at risk to the detrimental effect of these unfavourable environmental changes (11,12,13). More than three quarters of children aged 7 years and above with increased asthma symptomatology had a decline in their PEFR measurements. Fifty nine percent of them had a 15% or more reduction of their usual PEFR measurement. Interestingly, 57% of children aged 7 years and above with no increased asthma symptomatology also showed a decline in their PEFR measurements during the haze. This suggests that despite being symptom free, the poor air quality during this time did have a detrimental effect in this group of children. Although we expect that children who have a decline in their PEFR measurements to also complain of increased asthma symptomatology, a deterioration in the pulmonary function of these children especially a fall in the PEFR measurement does not always mirror an increase in asthmatic symptoms (14).

Children with moderately severe chronic asthma who attend our paediatric asthma clinic usually first receive inhaled mast cell stabiliser for prophylaxis followed by inhaled steroids if response to the former is not satisfactory. It was interesting to find that there was a trend for children who receive inhaled steroids instead of inhaled mast cell stabiliser to be less likely to experience increased asthma symptomatology although it did not reach statistical significance. This observation may suggest that the group of children on inhaled mast cell stabiliser with increased asthma symptomatology could benefit from a change to inhaled steroids for prophylaxis. The effect of the haze on children with chronic asthma also caused changes in lifestyle with limitation of outdoor activities and the use of an uncomfortable facial mask. These steps taken voluntarily by the child or imposed upon them by their parents are futile attempts at decreasing exposure to the haze.

The long term effects of the haze on the young child is just as important as the acute effects of the haze on the health of children. There is now increasing circumstantial

evidence to implicate air pollution in the pathogenesis of reactive airway disease in genetically predisposed children (15, 16, 17). Children who are continually exposed to poor quality air also show chronically depressed lung function studies that may be clinically important (18). These observations therefore suggest that the haze experienced in the Klang Valley in 1997 may have had a detrimental effect on the health of normal children that could manifest later in life.

The haze that plagued most parts of the country in late 1997 provides an insight into the tremendous impact the environment has on the health of children especially those with chronic respiratory disorders like asthma. The long term consequences of breathing polluted air in children whose lungs are growing cannot be ignored. Perhaps, the most important lesson learnt from the haze in 1997 is that keeping the environment healthy is just as, if not more important as keeping children healthy.

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THE USE OF BRONCHODILATORS AND CORTICOSTEROIDS IN RESPIRATORY SYNCYTIAL VIRUS LOWER RESPIRATORY TRACT INFECTION

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ABSTRACT: We reviewed the treatment practices namely the use of nebulised bronchodilators and oral steroids in 185 children admitted between 1st January 1993 and 31st December 1995 with the diagnosis of RSV chest infection. 135 (73%) of them received nebulised bronchodilators. Nebulised bronchodilators were more likely to be prescribed for patients who were younger (7.85 ± 5.1 vs 11.8 ± 7.4 months, p = 0.001), had a family history of bronchial asthma (36% vs 16% p = 0.008), a higher respiratory rate (151 ± 15 vs 146 ± 13 per minute, p = 0.0001) and Respiratory Distress Assessment Instrument Score (RDAI) score (4.5 ± 2.4 vs 3.0 ± 2.4, p = 0.001). Patients who were clinically assessed to have more severe respiratory distress at admission were also more likely to receive nebulised bronchodilators (p = 0.03). Gender, race and the presence of an underlying illness did not influence the decision to administer nebulised bronchodilators. There was, however, no difference in the duration of hospital stay between the patients who received nebulised bronchodilators and those who did not. (7.1 ± 4.9 vs 6.6 ± 6.2 days, p = 0.53). Only one patient received oral steroid treatment. Nebulised bronchodilators were generally administered to patients who were younger, those with a family history of bronchial asthma and who were clinically in more severe respiratory distress. *(JUMMEC 1997 2(2): 103-106)*

KEYWORDS: Nebulised bronchodilators, Respiratory syncytial virus

Introduction

Respiratory syncytial virus (RSV) is by far the commonest virus responsible for lower respiratory tract infection in the young paediatric age group. In Malaysia, RSV has been isolated in 20% of children diagnosed with lower respiratory tract infection (1). Nonetheless, there is no available treatment that appears to be effective in the management of RSV chest infection and treatment approach is essentially supportive. An effective treatment is understandably more important for patients with RSV chest infection who are at risk of severe disease and respiratory failure. This group of patients are essentially young infants who are less than 6 weeks old or previously premature or have an underlying illness such as congenital heart disease, bronchopulmonary dysplasia or immunodeficiency (2).

Adequate hydration, oxygenation, minimal handling and treatment of any complications such as respiratory failure are the cornerstones of caring for patients with RSV chest infection (3, 4). The use of nebulised bronchodilators in the treatment of this group of patients remains controversial. However, there is still a trend among clinicians to administer nebulised bronchodilators despite the apparent lack of benefit from this mode of treatment as reported in the literature (5).

The objective of this study is to determine the treatment practices of clinicians namely in prescribing nebulised bronchodilators and oral steroids for children admitted with RSV chest infection.

Material and Methods

This study is a retrospective review of children who were admitted to the Department of Paediatrics, University Hospital Kuala Lumpur from 1st January 1993 to 31st December 1995 with the diagnosis of RSV chest infection. They were included into the study if they fulfilled the following criteria: 1) aged two years or less; 2) had a respiratory illness with cough, running nose, breathlessness, wheeze and tachypnoea, crepitations or rhonchi; and 3) RSV was isolated in nasopharyngeal secretions.

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We reviewed all the case notes of these patients with special emphasis on the treatment prescribed for them. The clinical condition of the patients at admission was also evaluated with the use of a modified Respiratory Distress Assessment Instrument Score (RDAI Score) as illustrated in Table I (6,7). The sum total of all 4 clinical parameters based on the patient's clinical condition would equal the RDAI score. The severity of respiratory distress of these patients was then categorised into mild (RDAI score 0 - 4), moderate (RDAI score 5- 8) and severe (RDAI score 9 - 12).

Data collected was then entered and analysed using SPSSWin Version 6.13 statistical programme. The student's t test was used to compare quantitative data and differences between proportions were compared using the Chi Square test. A p value of less than 0.05 was considered statistically significant.

Results

The treatment profile of 185 patients were studied. 135 (73%) of them received nebulised bronchodilator therapy. Nebulised ipratropium bromide was used in 70 % of these patients while 11 % and 19% of them received nebulised salbutamol or a combination of both, respectively.

Clinicians were more likely to prescribe nebulised bronchodilators to patients who were younger and in those who had a family history of bronchial asthma (Table 2). There was, however no difference in the use of bronchodilators when considering the gender, ethnicity or the presence of an underlying illness in this group of patients. Patients who received nebulised bronchodilators also had higher heart rates, respiratory rates and RDAI scores. Patients clinically assessed to have moderate and severe respiratory distress at admission as defined by the RDAI score were also more likely to receive nebulised bronchodilators. The mean duration of hospital stay was, however, similar in patients who received nebulised bronchodilators and those who did not (7.1 $\pm$ 4.9 days vs 6.6 $\pm$ 4.2 days, p value 0.53). Only one patient received oral steroids during his hospital stay.

Discussion

Respiratory illnesses constitute one of the commonest childhood diseases that require hospital admission. Although RSV is recognised as an important aetiological agent of lower respiratory tract infection in young children, there is no well established treatment that is considered effective for this condition. The majority of these infections are mild and self limiting. RSV chest infection in patients at risk of severe disease constitute the group of patients in whom an effective treatment is needed. Although the mortality of this illness remains low, 20 -30% of these 'high risk' patients will develop respiratory failure (2) and require paediatric intensive care which at present is a rather limited and expensive facility. The cornerstone in the treatment of RSV chest infection remains supportive with maintenance of adequate oxygenation, fluid intake and monitoring for respiratory failure.

There appears to be a tendency to prescribe nebulised bronchodilators in our study population as almost three quarters of them received either nebulised ipratropium bromide or salbutamol or both. The degree of respiratory distress on admission namely a higher RDAI score and respiratory rate is most likely to have prompted the clinician to prescribe bronchodilators for this group of patients. The use of nebulised bronchodilators in RSV chest infection remains a controversial management issue with the apparent benefit from its use being questionable. Numerous

Table I . Modified Respiratory Distress Assessment Instrument Score (RDAI Score)

Clinical Parameter	Score 0	Score 1	Score 2	Score 3
Respiratory rate	Less than 40 per minute	40 - 60 per minute	61 - 70 per minute	More than 70 per minute
Use of accessory muscles	None	One accessory muscle used	Two accessory muscles used	Three or more accessory muscles used
Colour/Cyanosis	Pink in room air/no cyanosis	Cyanosed when crying	Pink with oxygen supplement or cyanosed on room air	Cyanosed with oxygen or cardiorespiratory arrest
Auscultation finding	Normal	Decreased air entry No rhonchi	Decreased air entry Rhonchi heard	Silent chest

studies have shown an apparent lack of benefit from the use of bronchodilators in RSV bronchiolitis (7, 8, 9) and a more worrying consequence is that its use may be associated with a detrimental effect on the patient (10, 11). Despite its misgivings as reported in the literature, clinicians still favour the administration of nebulised bronchodilators to this group of patients (5, 12), not unlike in our study population. A meta analysis carried out on clinical trials that studied the efficacy of nebulised bronchodilators in bronchiolitis showed that its use was significantly associated with a favourable effect on the patients' clinical condition but did not influence hospitalisation or improve oxygen saturation in these patients (13). In our study population, ipratropium bromide was more commonly used than salbutamol as the nebulised bronchodilator of choice. Perhaps this preference may be due to the fact that salbutamol has been reported to be ineffective in very young patients (14) and ipratropium bromide has an advantage due to its effect on bronchial secretion and mucosal oedema. Nonetheless, studies have shown that ipratropium bromide is not more effective than salbutamol whether given individually or in combination for the desired bronchodilator effect in these patients (15, 16). Instead, nebulised adrenaline has been shown to have a more effective bronchodilator property when compared to salbutamol and a placebo (17). However, adrenaline is not widely prescribed for bronchiolitis and none of our patients received nebulised adrenaline. It would appear that there is no clear indication for the use of nebulised bronchodilators for RSV chest infection. It is, however, recognised that there may be a subset of patients with RSV chest infection whose respiratory distress will respond to nebulised bronchodilators (18, 19) and therefore, a trial of nebulised bronchodilators for these patients is an acceptable clinical option. The nebulised bronchodilators may be continued if there is a favourable clinical response as determined by the clinician.

Airway inflammation causing bronchiole narrowing and air trapping plays an important role in RSV chest infection. These changes share many clinical and pathophysiological similarities to childhood asthma suggesting that the effective therapeutic approaches used for the treatment of bronchial asthma may be effective in treating RSV chest infection. Interestingly, this unproven assumption has prompted clinicians to prescribe corticosteroids, a conventional asthma treatment, for RSV bronchiolitis (12, 20). Clinicians treating our study population did not routinely prescribe corticosteroids as only one patient, a 14 month old Chinese boy who was initially diagnosed to have acute asthma for his first wheezing episode received prednisolone. There is no role for corticosteroids in the treatment of RSV bronchiolitis even in patients with a family history of atopy or asthma (21, 22).

There are many other modalities of treatment for RSV chest infection in addition to nebulised bronchodilators and corticosteroids. Ribavarin is the only approved anti-viral agent for RSV infection. Although it was initially shown to improve the clinical status, shorten viral shedding and reduce the need for ventilation and oxygen supplementation, a re-evaluation of the efficacy of Ribavarin in RSV infection did not show significant benefit with its use and it is therefore no longer routinely recommended (23). Other modalities of treatment that

Table 2. Patient characteristics and clinical features

	Group who received nebulised bronchodilators	Group who did not receive nebulised bronchodilators	p value
Mean age (months)	7.8 ± 5.1	11.8 ± 7.4	0.001
Sex (M : F)	76 : 59	35 : 15	0.120
Race (M:I:C: Ind)*	82:21:26:6	22:15:12:1	0.090
Family history of asthma	36%	16%	0.008
Underlying illness	26%	26%	1.000
Heart rate (per minute)	151 ± 15	146 ± 13	0.050
Respiratory rate (per minute)	58 ± 12	50 ± 11	0.001
TWBC (10^9/L)	13.2 ± 5.3	12.0 ± 4.8	0.230
RDAI score	4.5 ± 2.4	3.0 ± 2.4	0.001
Respiratory distress			
Mild	65%	35%	
Moderate	89%	11%	0.030
Severe	80%	20%	

* M:I:C: Ind = Malay : Chinese : Indian : Indonesian

has been evaluated in RSV infection include Vitamin A supplementation (24) and Interferon alpha 2A (25).

In conclusion, the majority of patients in our study population received nebulised bronchodilators especially if they were young infants with clinically more severe respiratory distress and a family history of bronchial asthma. Although there is a tendency for our clinicians to prescribe nebulised bronchodilators for these patients, its use is not clearly supported by the literature.

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THE PATIENT'S CHARTER – VALIDATING ACTUAL SERVICES PROVIDED TO THE OUTPATIENT

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ABSTRACT : The Patient's Charter tells about the rights and standard of service a patient can expect. However, little information is available to gauge the reality of the charter in real practice. This survey was performed to determine the validity of the charter to the services provided and to identify areas of improvement if the charter is to be revised. A questionnaire-based survey was used to seek information from 196 patients who attended the Outpatient Department in Banting District Hospital over a period of four days. The overall waiting time for registration, to be seen by a doctor and for medication were 17.4 ± 2.0 minutes, 25.3 ± 2.6 minutes and 15.8 ± 1.3 minutes respectively. The overall waiting time for the whole consultation was 61.4 ± 4.9 minutes. Only 30.8% respondents knew about the Patient's Charter. The Patient's Charter appears to be valid for the actual services provided. There have to be measures to increase the awareness of the charter to the public perhaps via pamphlets and to provide a multi-linguistic charter. *(JUMMEC 1997 2(2): 107-110)*

KEY WORDS: Patient's Charter, Outpatient Department, waiting time

Introduction

There have been many studies done on the relationship between consultation time, list size and workload to gauge the different aspects of quality care to the patient (1,2). Heaney (3) reported that reducing waiting times is a key issue in the provision of quality services for patients. Much has been said about a standard charter for the patient and how the charter may bring new and positive changes in the care provided (4). However, little work has been carried out pertaining to various aspects of the patient's charter for example to gauge the effectiveness of the patient's charter or its' reliability in providing the medical care to the patients.

Therefore, this survey aims to examine the Patient's Charter, to test its reliability and to identify changes if required. The Health Division of the Ministry of Health has taken over the Outpatient Department administration of the Banting District Hospital since 1 June 1997. To monitor and to further improve the health service at the local level, the opinions and perceptions of the patient, the consumer, are necessary to marry the charter with the actual care provided (5). The health administration needs to know what the consumer thinks of the current care delivered, and whether it is satisfactory or not satisfactory. The consumer is encouraged to complain if things have gone wrong and to suggest how things could be done better. Thus, the present study aims to examine the Patient's Charter, to test its reliability and to identify changes if required.

Materials and Methods

This survey was carried out at the Banting District Hospital, Selangor from 23rd to 26th September 1997. It was done as part of our district health posting in the final year programme. Located about 70 km from the University Hospital, Petaling Jaya, the hospital began its operation 22 years ago, catering for the increasing population in the Kuala Langat District. The hospital consists of eight buildings with 151 beds. The bed turnover was 31 patients per day up for the first six month in 1997. The hospital served about 53 289 outpatients for the first six month in 1997. There are 165 staffs with nine doctors.

Each department of this hospital has its own Patient's Charter, displayed via a large wooden banner in Bahasa Malaysia. The charter (Table 1) explains what a patient should expect from the health service and the standards the service intends to deliver. The charter speaks of the Government's interest to improve quality of health care at all levels, to make changes when these standards are below par and by improving quality, to improve value for money.

The instrument for this study was a self-developed questionnaire based on the Patient's Charter in the

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Outpatient Department. This was to assess several aspects of satisfaction with services cited in the charter. The departments that were assessed in this survey are the outpatient, radiography, laboratory, and pharmacy. The questionnaire was pilot-tested prior to the actual survey. 196 patients were interviewed (with a failure rate of 2%), both in the morning and the afternoon sessions over a period of four days survey. All patients who were waiting at the pharmacy department were approached for the interview. The first 50 patients from an estimated 200 patients per day were interviewed. Patients were excluded if they came exclusively for the medication without any consultation or if they came directly from the emergency unit. Statistical analyses performed in this survey include mean, a student t-test, interval confidence and paired t-test.

Table 1. The Patient's Charter (English Translation)

Banting District Hospital

The Outpatient Department

You will be registered in not more than 30 minutes.
You will be seen by a doctor in not more than an hour.
All emergency cases will be tended to immediately.

The X-ray Department

Every X-ray will be taken in not more than 30 minutes during the office hour.
Every X-ray film processed is of quality.

The Laboratory Department

Every patient will be notified about the time taken to process a certain test.
Every patient will be given an appointment to collect the test result if the test result is unattainable on the same day.
Every laboratory test is of quality.

The Pharmacy Department

Every drug given is of quality and safe, with labels.
There will be a clear and concise explanation on the drug given.
The drug will be given in not more than 20 minutes, and counseling will be offered if necessary.

Results

Demography

A total of 196 patients were included into the analysis. The overall male to female ratio was 1:0.9. 102 (52.0%) were male and 94 (48.0%) were female. In terms of ethnicity, there were 133 (67.9%) Malay, 13 (6.6%) Chinese, 49 (25.0%) Indian, and one other. The mean age was 38.4 years with a standard deviation of 15.75 years.

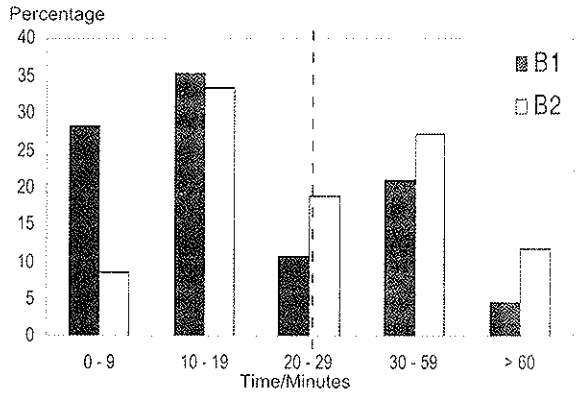

Figure 1. Waiting time before registration and before seen by the doctor (after the registration)

B1 – Time taken for the patient to be registered
B2 – Time taken for the patient to be seen by the doctor
Waiting time as chartered (30 minutes)

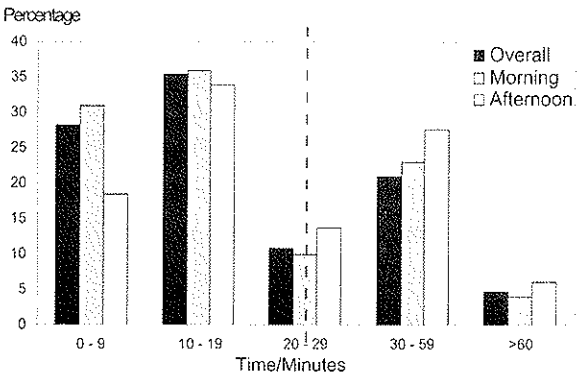

Figure 2. Waiting time – overall, morning session and afternoon session before registration

– – – Waiting time as chartered (30 minutes)

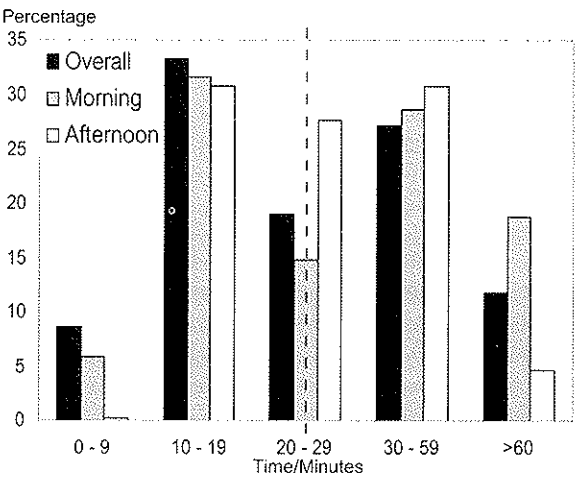

Figure 3. Waiting time – overall, morning session and afternoon session before seen by the doctor

– – – Waiting time as chartered (30 minutes)

More than 80% of the patients had some formal education. 110 (56.0%) had experienced secondary school and 55 (28.2%) had completed primary school only. 10 (5.1%) had tertiary education. There were 21 (10.7%) patients who did not receive any formal education.

The Outpatient Department

The overall mean waiting time before registration was 17.4 ± 2.0 minutes compared to the time chartered at 30 minutes, ranging from three minutes to 90 minutes. In the morning session, the mean waiting time before registration was 17.6 ± 2.7 minutes compared to 19.7 ± 4.2 minutes in the afternoon session. However, there was no significant difference between the two sessions (t = -0.899, d.f. =166, ns).

The overall waiting time before a patient was seen by the doctor (after the registration process) was 25.3 ± 2.6 minutes, ranging from five minutes to 90 minutes. The morning session had a longer mean waiting time of 29.7 ± 4.0 minutes compared to the afternoon session 21.8 ± 3.9 minutes. However, there was a statistical significant difference between the two sessions (t = -2.5887, d.f. = 166, p<0.01)

The Radiography Department

The overall mean time taken before an X-ray is taken was 21.8 ± 11.3 minutes, ranging from five minutes to 60 minutes. The overall mean time taken to process the X-ray was similar at 21.7 ± 9.2 minutes, ranging from five minutes to 60 minutes (Figure 4).

The Laboratory Department

43% of 35 patients were not told about the time taken to process a certain test. Similarly, only 54% of patients were given an appointment if the test result was unobtainable on the same day.

The Pharmacy Department

The overall mean waiting time at the pharmacy department before receiving the medication was 15.8 ± 1.3 minutes ranging from five minutes to 30 minutes (Figure 5). There was a slight difference between the mean waiting time in the morning session 17.2 ± 1.8 minutes and in the afternoon session 15.0 ± 2.1 minutes respectively. However, there was no significant difference between both sessions (t = -1.496; d.f. = 166; ns).

196 (100%) patients were given medication with clear labels and were explained by the pharmacist on how to take the medication except for one patient who mentioned that no instruction was given to him.

Overall Time taken for the whole consultation

The overall time taken for the whole consultation was 61.4 ± 4.9 minutes ranging from 15 minutes to 230 minutes. There was a statistically significant difference between the overall time taken in the morning session and the afternoon session (t = -2.196; d.f. = 166; p<0.05). The overall time taken in the morning session was 69.3 ± 7.2 minutes and in the afternoon was 57.0 ± 7.7 minutes.

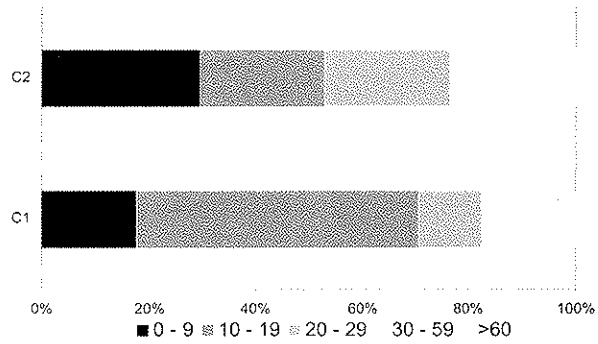

Figure 4. Waiting time to take X-ray and for the X-ray to be processed
C1 – Time (minutes) lapsed before X-ray is taken
C2 – Time (minutes) taken for the X-ray to be processed
(n = 17)

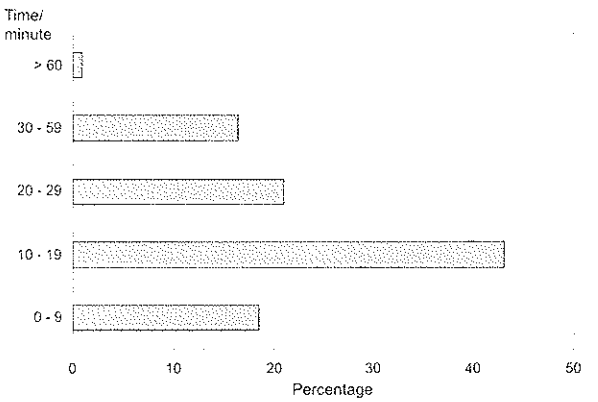

Figure 5. Waiting time before receiving the medication

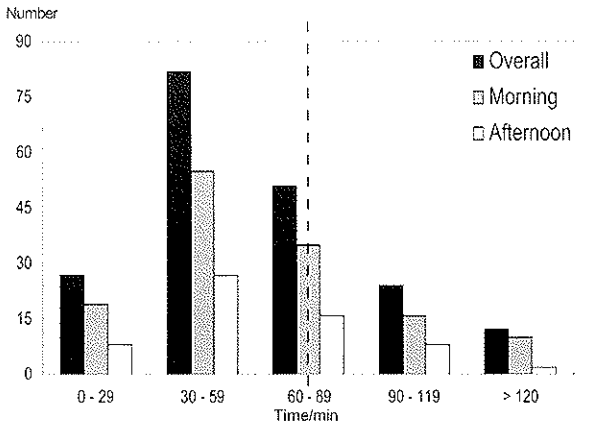

Figure 6. Overall time taken for the whole consultation
– – – – Waiting time as chartered (60 minutes)

The knowledge of the Patient's Charter

Patient's knowledge of the charter was assessed based on whether they have read and understood the contents of the charter. The results showed that 60 (30.8%) respondents read and knew the charter. The remainder did not read or did not bother about the charter after reading it.

Discussion

The Patient's Charter consists of 'rights', which all patients will receive all the time, and 'expectation', which are standards of service which can be delivered to them (6,7,8). In the same manner, patients need to be made aware about the charter. Only few patients (30.8%) knew about the charter. A survey done by Martin Lees reported 54.5% of patients were still ignorant of the charter's existence (9). Thus, there is a large number of patients who are still ignorant of the Patient's Charter whether at the local setting or oversea. Where patients failed to exercise their rights and to acknowledge the weaknesses in the health service, the health service will fail to progress to meet the ever-changing demands of the patient. Thus a vicious cycle will continue and both parties will not benefit from each other.

The charter appears to be valid from the study. The time chartered was statistically significantly lower than the actual time for each department. The waiting time at the registration department was 17.4 ± 2.0 minutes, compared to the time chartered at 30 minutes. Similarly, the actual time taken before being seen by the doctor was 25.3 ± 2.6 minutes compared to the time chartered at 30 minutes. The actual waiting time at the pharmacy department was 15.8 ± 1.3 minutes compared to the time chartered at 20 minutes. The result may suggest the studied departments were indeed efficient in delivering their services. However, one must remember that there is a group of patients who waited more than the time chartered at respective department. Perhaps this could be due to other confounding factors for example staff on leave, insufficient staff, malfunction of the machine, and staff experience which were not taken into account in this study.

The overall mean waiting time before a patient was seen by the doctor taken in the morning and afternoon session was found to be significantly different ($p<0.01$). The overall mean consultation time, by omitting the radiography and laboratory department, was about one and a half-hour on the charter. The actual time taken was 61.4 ± 4.9 minutes. The overall time taken in the morning and afternoon session was found to be significantly different also ($p<0.05$). This may be due to the different volume of patients seen, where more patients were seen in the morning. Studies have shown that a reduction in the waiting times paralleled with an increase in the quality of services and patient's satisfaction (3,13).

This study is not without any limitations. The study did not include the patients/staff ratio and also did not take into account the diseases presented, which both may affect the overall time taken for the whole consultation.

The Patient's Charter is valid within the actual services provided. However, there must be measures to promote the charter and to increase its awareness to the public. The following recommendations are suggested: 1) to revise the charter every year by gaining feedback from the patients for example via suggestion box (10,11); 2) patients should be made aware of the charter for example via pamphlets; 3) to incorporate annual patient satisfaction survey as a means of exploring patients' demand (12).

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Volume 2❖Number 2 December 1997

CONTENTS

Editorial

Some Thoughts On The Changing Face Of Academic Medicine 1
Pathmanathan R

History of Medicine

Magical Moments In Medicine: Part 4: Indian, Chinese & Islamic Medicine 63
J P Judson

Reviews

Non Steroidal Anti-Inflammatory Drugs And The Stomach – A Review 77
Low TS and Goh K L

Flavonoids: Distribution, Chemistry And Pharmacological Role In Health And Disease 85
Kuppusamy UR

Problem Based Learning (PBL) in Medical Education: Why, What And How 89
Achike F I and Kwan CY

Original Articles

High Potassium-induced Epileptiform Bursting In Rat Hippocampal Slices 95
El-Sabban F, Reid KH and Edmonds HL Jr.

The Impact Of The Haze On Children With Chronic Asthma 99
Chan P, De Bruyne JA, Chan TL and Goh A

The Use Of Bronchodilators And Corticosteroids In Respiratory Syncytial Virus Lower Respiratory Tract Infection 103
Chan P and Goh A

The Patient's Charter - Validating Actual Services Provided To The Outpatient 107
Chin MK, Yew L L, Abdul Hakam, Rahmat Z, Sharipah Aini, Johar A and Kassim N