UNIVERSITY OF NAIROBI

The Dynamic Interplay Between Man, Health and Medicines:

A Historical Perspective

INAUGURAL LECTURE GIVEN BY

CHARLES KARIMI MAITAI, B.Pharm. M.Pharm, PhD
Professor of Pharmacology,
Department of Pharmacology and Pharmacognosy,
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Professor Charles Karimi Maitai

Professor Maitai was born in Tetu Division, Nyeri in 1943. He went to Gathuthi Primary School from 1950 to 1953. He did Common Entrance Examination in 1953 and in 1954 he was admitted to Kagumo Government School which comprised of Teachers Training College, a Secondary School and an Intermediate School. In 1957 he sat for KAPE and proceeded to Form I in the same school the following year. He did Cambridge School Certificate Examination in 1961 and obtained Division I. The following year he was admitted to Kangaru High School where he sat Cambridge Higher School Certificate in 1963. In 1964 he was awarded a Commonwealth Scholarship to study Pharmacy in Otago University, New Zealand. He graduated with B.Pharm degree in 1967 being among the top 3 in the class. From 1967 he studied for a M.Pharm degree and successfully completed it in 1969. After returning from New Zealand in 1969 he worked briefly as a Government

Analyst before joining the University College, Nairobi as a Lecturer in Veterinary Pharmacology in April 1970. He completed his Ph.D in 1973 while working as a Lecturer.

In 1974 he was promoted to Senior Lecturer and appointed founding Chairman in the newly established Department of Pharmacy, Faculty of Medicine. In 1979 he was a Visiting Senior Fullbright Scholar, University of Minnesota, USA. In 1978 he was promoted to Associate Professor and to full Professor in 1983. In the same year he was appointed Associate Dean, Faculty of Medicine, a post he held until 1990.

He has over 55 scientific publications in local and international journals. He served as a Consultant to the United Nations Narcotic Laboratory, Geneva and World Health Organization. He has also served as a member and Chairman of several National Committees in the Ministry of Health, Kenya Bureau of Standards and National Council of Science and Technology. He has undertaken several consultancies in pharmacology and toxicology.

Professor Maitai has served as an External Examiner in Pharmacology in Universities of Dar-es-Salaam, Makerere, Addis Ababa and as an Assessor in Professorial appointments in many universities in East Africa and West Africa.

He is married with 4 children

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THE DYNAMIC INTERPLAY BETWEEN MAN,HEALTH AND MEDICINES: A HISTORICAL PERSPECTIVE

According to Darwins theory of Evolution, put forward in the last century, man is merely the winner of a race codenamed, "Survival of the fittest" in which the winning card was dealt by chance.

The Bible's version of man's origin is that he was created in God's image and all creatures put at his disposal from the very outset.

For the purpose of this presentation, I shall lean more on the evolution theory while not necessarily discrediting the Bible version.

The history of man's long journey from the early primitive gatherer-hunter stage to the dawn of recorded history, approximately 6000BC, is still a puzzle. Even archaeologists who have been piercing together information gleaned from pre-historic excavation sites readily admit that there are glaring unexplained gaps, not to mention contradictory interpretations. Primitive stone implements and cave drawings are subject to different interpretations; yet these are the most important source of information about the pre-historic man. Radioactive carbon dating also give little additional information.

There are 3 important landmarks in the evolution of man.

The first one was the adoption of bipedality in response to thermoregulatory imperatives. This occurred approximately 4,000,000 years ago.

The second one is the harnessing of fire, approximately 1,500,000

years ago. Instead of going to roost early men could sit around the fire at night, narrate stories, plan for the next day and generally promote social interactions.

The third landmark was the adoption of farming which in turn necessitated establishment of settlements approximately 10,000 years ago. The transition from gatherer-hunter to the farmer had a profound effect. It is not by accident that the earliest civilisations developed along the fertile valleys of Nile, Euphrates, Tigris, Indus and Yellow rivers. It is here that the earliest records of writing (Papyrus Ebers and clay tablets) were discovered.

If one was to telescope the entire human history into 24 hours, the last 2000 years (since birth of Christ) would be represented by the last 40 seconds and the twentieth century by the last 2 seconds. Modern medicine era would be represented by one second.

Because of the geographical and language barriers, various communities (Africans, Indians, Chinese, Arabs, Europeans) evolved differently to form diverse civilisations.

The Middle East region is strategically situated and consequently it became the melting pot for all cultures.

PRE-OCCUPATION WITH HEALTH

The primitive man spent a lot of his time agonizing over his health. This morbid pre-occupation with health, or lack of it, is well illustrated in cave wall drawings. It is also well documented in various religious books (Bible, Koran, Vedas, etc) and classical treatises such as "Kama-Sutra" and folk lores. This trend has continued to the present day.

MAN DISCOVERS MEDICINES

At a very early stage of evolution, man discovered, perhaps through survival instincts, that there were curative agents (medicines) for the many diseases that afflicted him. There are 3 possible ways man would have used to discover medicines.

1. During the gatherer-hunter stage, man would have observed that ingestion of certain plant "food" material (roots, seeds, fruits etc) was followed by some profound physiological changes such as sedation, euphoria, hallucination, diarrhoea, vomiting etc. In some cases, the unfortunate happened, he died. He therefore learnt to associate some pharmacological effects with specific plants. For example, the distant relative of to-day's Masai who, in search of food consumed "seketet" (seeds of Myrsine africana) and later observed dead roundworms in the stool must have realised that he had discovered an anthelmintic which he could use when the need arose. Somewhere in Mexico, a native Indian who consumed "god's flesh" i.e the Mexican mushroom, (Psilocybe mexicana) and experienced hallucinations realised he could use the mushrooms before rituals, whenever he wanted to communicate with God.

2. Again, during the gatherer-hunter stage and even much later, man observed that when wild animals ate some plants, they exhibited abnormal behaviour. For example, somewhere deep in congo forest, a native observed with amusement, wild boar dig up the roots of Tabernanthe iboga and eat the roots, only to go into a frenzy, jumping around and probably trying to run away from frightening visions. He immediately associated the plant with hallucinations. Yet another person in Abyssinian highlands observed that wild goats which had fed on shoots

of Miraa (Catha edulis) were excessively stimulated. When, out of curiosity he chewed the shoots, he became hilarious. It is generally believed that when wild animals are sick, instinct guides them to appropriate remedy. This subject is covered in a book entitled, "Folk Medicine" by Dr. H.C. Jarvis published in USA in late 1950s. It became a best seller immediately climbing to the top of the non-fiction books in New York.

An article appearing in the British Medical Journal, 19-26 December 1992, Page 1517 under the heading "Can animals teach us medicine" discuss this subject in detail.

3. Apart-from the accidental discoveries referred to in (1) and (2) there is evidence that man actively looked for medicines at the early stage of evolution making use of the Doctrine of Signatures. According to this doctrine, the physical characteristics of the plant (colour, shape etc) was indicative of possible medicinal value. Thus Rauwolfia root (Indian name "Sarpagandha" means snake repellant) was used in Ayuverdic medicine for snake bites because it is shaped like a snake. Chenopodium (Wormseed) was used as anthelmintic. Saffron flowers (yellow) were used for jaundice. Plants with heart-shaped fruits were used for heart diseases. Plants with roots shaped like male organs were used for impotence etc.

Man showed alot of ingenuity by discovering arrow poisons which he could use to immobilise large animals. In S. America, he discovered Curare (Wourali) while in East and Central Africa he discovered Acokanthera species. None of the 3 theories advanced can adequately explain the discovery of arrow poisons since they are not absorbed from stomach when ingested. Could spiritual inspiration or revelation through dreams lead to such discoveries?

Plants with pleasant smell (fragrance) were used to mask perspiration and flavour food.

Apart from medicinal plants, man also used mineral drugs and it is not clear how he discovered their medicinal value. The most commonly used ones were compounds of bismuth, antimony, arsenic and mercury.

Antimonial compounds have been used in medicine since about 4000 BC. To-day they are used in treatment of Leishmaniasis. Arsenical compounds were extensively used as tonic and in anaemia. To-day arsenicals are used in Trypanosomiasis. Bismuth is now being used in combination with antibiotic for peptic ulcers.

Mercury compounds were used in treatment of syphilis until early this century. They are now considered too toxic.

Animal drugs used by early man were few. The most notable was hog testis for impotence. Propolis from beeswax is now widely used in treatment of many disorders such as peptic ulcer, colds, stress, hypertension etc. Mr. H. Lincks an advocate of propolis, uses it extensively in his clinics in Hurlingham and Westlands, here in Nairobi. Cantharidin (Spanish fly) has also been used as an aphrodisiac.

EARLY RECORDS ON HERBAL MEDICINE

The earliest record of medicinal herbs was in China by Emperor Shen Nung in 2800BC. The records were written much later about 206BC - 220AD under the title . It is not clear how the information was preserved before it was recorded. Papyrus Ebers dating from 1,500 BC lists about 700 herbs used in Egypt. The first authentic record on medicinal herbs is attributed to Hippocrates who was born in 460 BC. It contains an

account of 400 medicinal herbs, among them Poppy, Henbane, Castor bean and Peppermint.

The written records of Ayuverda contain over 8000 herbal recipes some dating back to 5000BC.

There are many other records. In communities where no written records are available, the information on medicinal plants was passed from one generation to the other through Folklore.

MEDICINAL PLANTS IN EARLY RECORDS

It may be of interest to note that one of the sources of information on ancient medicinal plants is the Bible. Those mentioned are shown in Table 1.

TABLE 1: MEDICINAL PLANTS MENTIONED IN THE BIBLE

1. Essential oil containing plants	
Frankincense	Myrrh
Cassia bark	Galbanum
Nard	Sandalwood
Cinnamon	Cumin
Ginger grass	Coriander
Rue	Saffron
Nutmeg flower	Mustard
Mint	Dill
2. Others	
Aloe sp	Henna
Salsola sp Jericho	Balsam
Balm of Gilead	Wormwood
Colocynth	Mandrake.

Source, Economic Botany 8 152, 1954

ALOE: Nicodemus brought Myrrh and Aloe to embalm the body of Jesus after removal from the Cross (John 19:19). Widely used by Greeks as a laxative and by Egyptians for embalming.

MYRRH: Together with frankincense and gold comprised the 3 gifts of Magi (Matthew 2:11). Used as a perfume and possibly aphrodiasic (Psalm 45:8, Proverb 7:17, Song of Songs 1:13). In purification of women (Esther 2:12) As an anodyne prior to crucifixion (Mark 15:23).

ESSENTIAL OIL CONTAINING PLANTS

Used to mask perspiration. Also to spice and preserve food. Christopher Columbus, Vasco da Gama etc made their journeys to find alternative route to the "land of spices".

Medicinal plants used by ancient people were those with profound and demonstratable effects such as sedation, hallucinations, diarrhoea etc.

Table 2 show a list of plants with psychotropic effects and which were used by early man.

TABLE 2: MEDICINAL PLANTS WITH CENTRAL NERVOUS SYSTEMS EFFECTS

Cannabis (4000 BC China)
Coca (Inca civilisation 1000 AD)
Opium (Sumerians 4000 BC, Egyptians 1500 BC)
Peyote (Mexican Indians 8000 BC)
Kava (South Pacific, Polynesians)
Cohoba (Acacia niope)
Nutmeg (Myristica fragrance)

Yohembece (West Africa, Nigeria)
Mexican mushroom (Mexican Indians
Morning glory (Mexican Indians)
Caapi or Wild rue
Rauwolfia spp (Ayuverda 5000 BC)
Yage
Henbane, Mandrake (3000BC)
Betel nut
Soma (god-narcotic in Indian mythology)
Miraa (Catha edulis 100BC?)

Caffeine containing plants

Coffee (Coffea arabica), Tea (camelia theca),
Cacao (Theobroma cacao), Mate (Ilex paraguayensis)
Guarana (Panela supana) Kola (Cola nitida)

Other important plants used by ancient people are shown in table 3 below.

TABLE 3: MISCELLANEOUS PLANTS USED IN PRE-HISTORIC TIMES

Ginseng*	Ancient Chinese drug
Ephedra	Ancient Chinese drug
Rhubarb	Laxative drug used in China
Cinchona	Antimalarial, S.American Indians
Ipecacuanha	Emetic " "
Curare	Arrow poison " "
Chenopodium (wormseed)	Indian, Ayuverdic medicine
Male fern	Ancient, anthelmintic
Squill	Papyrus Ebers 1500 BC
Digitalis	Europe, for heart disease
Willow bark	Antimalaria (fever), S. America
Acokanthera	Arrow poison, East Africa
Calabar bean	Trial by ordeal, West Africa
Cascara	Laxative, South America
Aconitum	Anti-rheumatism, China

Hemlock	Poison used by Greeks to kill Criminals and Philosophers. Socrates drank it.
Neem tree	Antimalarial, Ayuverdic medicine

* Ginseng: Ancient Chinese herb - Reference: "The Root of Being" by Stephen Fulder, Hutchison & Co Publisher (1980).

At the beginning of the first millennium, marked by the birth of Christ, use of medicinal plants was common. At that time, the practice of medicine was a mish-mash of religion, magic and empirically acquired ideas and practices. This situation continued through the Middle Ages and to the time of Renaissance in the Fifteenth Century.

Renaissance had very little impact on science generally and medical sciences in particular. At the beginning of the Eighteenth century, most drugs in common use were still of plant origin. A few had been isolated as pure drugs from plants (eg quinine).

On the whole, treatment of diseases was very ineffective. Diseases such as oedema and headache were treated by bloodletting.

Hospitals were institutions of mercy, motivated less by hope of curing diseases and more by brotherly love of God. This attitude was consonant with the prevailing believe that diseases represented a departure from holiness and spiritual health alternatively it was seen as a retribution for sins. This situation remained relatively unchanged throughout Renaissance and up to the end of Nineteenth century.

At the point where Europeans colonised Africa, in the late Nineteenth Century, the practice of medicine in Europe was probably no better than traditional medicine practised by the

indigenous people they colonised. The only exception was surgery.

The period between 1800 and 1900 stand out in the history of science because of important developments in physical and biological sciences which later gave impetus to drug research and development.

Table 4 show important landmarks in biological and chemical sciences during this period.

TABLE 4: IMPORTANT DISCOVERIES IN BIOLOGICAL AND CHEMICAL SCIENCES 1800-1900

1749-1823	Jenner discovered the principle of vaccination. Injection of cowpox virus produced immunity against smallpox
1820	Quinine isolated from Cinchona bark
1827	Salicin glycoside isolated from Willow bark
1835	Nitrous oxide discovered
1846	William Morton, a dentist use ether as anaesthetic.
1847	James Simpson used chloroform as anaesthetic
1862	Chloralhydrate synthesized. First sedative
1827-1912	Lister did pioneer work on antiseptic and introduced phenol to sterilise operating rooms in 1867
1874	Sodium salicylate synthesized
1882	Barbital synthesized
1895	Louis Pasteur established diseases caused by bacteria. Introduced rabies vaccine.
1897	Ronald Ross discovered human plasmodial parasite.
1843-1910	Robert Kock isolated bacteria responsible for anthrax, tuberculosis and cholera between 1876-1882.
1876-1928	Japanese Hideyo Noguch working in USA produced vaccine against Yellow fever. Also did research on treatment of syphilis.

In the field of physical sciences (Chemistry and Physics) there were monumental breakthroughs. This was the era of J.J.

Thompson, Rutherford, Roentegen, Michael Farady, Marie Curie, Dalton, Gay-Lussac, Avogadro and others which any student of chemistry or physics will have come across.

Arising from the work of J.J. Thompson and Rutherford, the atomic theory was crystallised. Developments in chemistry and biological sciences provided impetus for synthesis of new drugs. Nothing much happened for the next 20-30 years. The first breakthrough in the search for new drugs was in 1929 when Benzylpenicillin was discovered. Another significant discovery soon after was sulphapyridine (MB 693) the first safe and effective drug for treatment of bacterial diseases and pneumonia in particular. The discovery of MB 693 was monumental because bacterial infections then, as of now, were leading cause of morbidity and mortality.

Table 5 show some important drugs discovered between 1930 and 1950.

TABLE 5: SOME IMPORTANT DRUGS DISCOVERED DURING THE PERIOD 1930-1950

Penicillin G	Sulphapyridine (MB 693)
Chlortetracycline	Chloramphenicol
Streptomycin	Isoniazid
Pyrazinamide	Dapsone
Polymyxin	Neomycin
Nitrofurantoin	Nystatin
Griseofulvin	Quinacrine
Chloroquine	Chlorguanide
Primaquine	Diethylcarbamazine
Piperazin salts	Cortisone
Warfarin	Diethylstilboesterol
Ergometrine	Nitrogen mustards
Vinca alkaloids	Chlorpromazine
Thiopental	Phenytoin
Physostigmine	Antazoline

Discovery of important drugs after 1950 continued unabated. If the list of drugs discovered up to 1965 was to be compiled, it would include most of the drugs in use to-day.

During the euphoria that accompanied discovery of new drugs, the focus was on efficacy and little attention was given to possible toxic effects, particularly chronic toxicity.

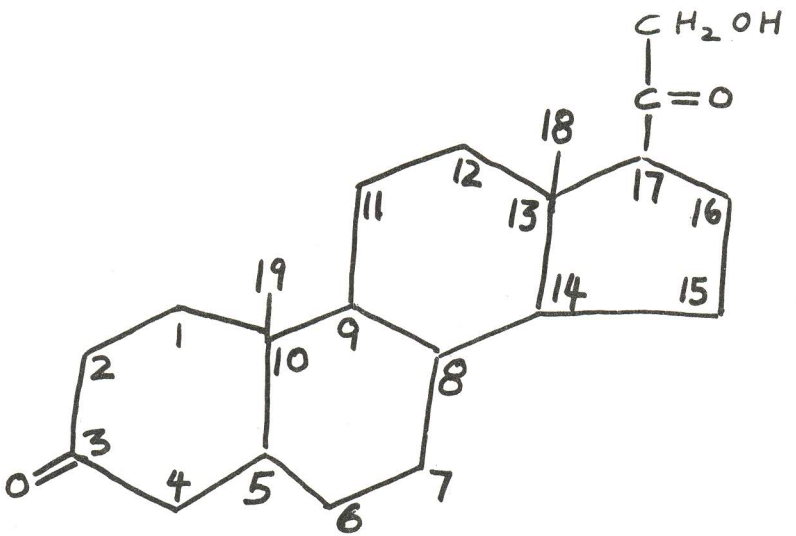
The situation changed dramatically in 1962, when thalidomide, a hypnotic-sedative introduced into clinical use in 1958 was shown to cause extreme limb deformities (phocomelia) in babies born to mothers who had taken the drug during the early stages of pregnancy. This led to drastic legislative measures aimed at curbing hasty introduction of new drugs, without adequate safety data. To-day it is mandatory to give teratogenic and mutagenic data on new drugs before they are registered.

In the early 1960s there was another important development. It was shown that altering the chemical structure of certain drugs introduced during the period 1930-1950 often produced better drugs with respect to efficacy, decreased toxicity and improved pharmacokinetic profiles.

Table 6 show new drugs obtained after structural modification of cortisone. Introduction of double bond between carbon 1 and 2 increases antiinflammatory effects 4 times. Further modification to produce dexamethasone increases the antiinflammatory effect 30 times while the undesirable side effects (sodium retention) is decreased to one-tenth.

TABLE 6: CORTISONE AND DERIVATIVES

Prednisone - (double bond between position 1 and 2
Triamcinolone - (as prednisone + 9a -F + 16a -0H)
Dexamethasone - (as Triamcinolone <u>but</u> 16a -Me instead of 16a -OH)
Betamethasone - (as dexamethasone <u>but</u> 16ß -Me instead of 16a -Me)
Paramethasone - (as dexamethasone <u>but</u> 6a -F instead of 9a -F)
Beclomethasone
Fludrocortisone etc

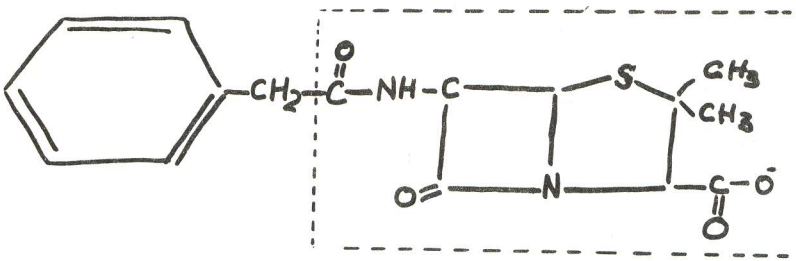


CORTISONE

Table 7 show new drugs obtained after chemical modification of penicillin molecule. Ampicillin and Amoxycillin are broad spectrum penicillins. Methicillin and cloxacillin are penicillinase resistant, etc

TABLE 7: PENICILLIN G AND DERIVATIVES

Ampicillin	Procaine penicillin G
Amoxil	Benzathine penicillin
Pivampicillin	Benthamine penicillin
Talampillin	Penicillin V
Bacampicillin	Mecillinam
Methicillin	Pivmecillinam
Dicloxacillin	Carbenicillin
Flucloxacillin	Carindacillin
Diphenicillin	Carfecillin
Quinacillin	Tircarcillin
Oxacillin	Azlocillin
Cloxacillin	Mezlocillin
Nafcillin	Piperacillin



PENICILLIN G

This trend of modifying chemical structure has continued into the 1990s. What is the significance of this development? Firstly not all derivatives have clear advantage over the parent drug. The claims by manufacturers of these drugs are sometimes difficult to verify. Many of these drugs have been nicknamed "me-too" drugs and often require high powered salesmanship to keep them in the market. A case in point is the Cephalosporin Derivatives shown below.

CEPHALOSPORIN DERIVATIVES (ME TOO DRUGS)

CEPHALOSPORIN C

Cefaclor	Cephapirin
Cefatrizine	Cefroxadine
Cephalexin	Cephaloridine
Cephalothin	Cetazolin
Cephradine	Cefmetazole
Cefonicid	Cefotetan
Cefotiam	Cefoxitin
Cefuroxime	Cefamandole
Cefixime	Cefmenoxime
Cefoperazone	Cefotaxime
Cefpimizole	Cefsulodin
*Ceftazidime	Ceftizoxime
Ceftriaxone	Cefepime
Ceftibuten	Cefprozil

* Appears to be different

Secondly, it has serious implication for Research and Development of new drugs. An application for patent of a novel drug must be comprehensive and even anticipate possible derivatives. When cimetidine (anti-ulcer drug) was launched SmithKline French did not anticipate that slight change in the molecule would give Glaxo another comparatively better drug, Ranitidine.

By 1970, there were effective drugs (certainly not ideal) for nearly all diseases except cancer and viral diseases. However in the case of viral diseases, although there were no curative drugs, they could be prevented by vaccines. Immunotherapy has remained the only option for viral diseases such as Polio, measles, yellow fever, rabies and hepatitis B.

A new phenomenon in the 1980s and 1990s has been the 'recycling of old drugs as is evidence with Vancomycin and Spiramycin discovered in 1954 and 1956 respectively.

WHO ADOPTS A HIGH PROFILE

Any discussion of drug use after 1970 would be totally misplaced unless we shift the theatre of operation and focus on the role of World Health Organisation (WHO).

From the mid 1970s WHO adopted a high profile and set the agenda which was to guide National, Regional and World Health Policies to the year 2000.

WHO was established in 1948. In the preamble of the WHO charter, health is defined as a complete physical, mental and social wellbeing and not merely the absence of disease or infirmity. Health as defined by WHO charter is truly a UTOPIAN STATE which most of us can only dream of.

From 1948 to early 1970s WHO had been discussing the various strategies of achieving health. A series of resolutions were adopted without putting a timeframe to them. By 1970, thousands of pages of technical papers on Third world problems had been written and filed away in cubic metres of reports. Countless resolutions urging national governments to act on WHO recommendations were adopted by the World Health Assembly.

The Middle East War in 1973 led to a dramatic rise in oil prices and nearly crippled the economies of many third world countries. Many of them looked up to WHO for assistance.

From 1974, WHO made a concerted effort to synthesize the different resolutions into a focused and coherent ideology. The following are important landmarks in this process.

1977. The World Health Assembly (WHA) unanimously decided that the main social target of Governments and of International Organisations in the coming decades should be the attainment by all citizens of the World by the year 2000 of a level of health that will permit them to lead a socially and economically productive life.(Resolution WHA 30.43).

1978. The Alma-Ata international conference attended by delegates from 134 governments and representatives of 67 organisations accepted Primary Health Care (PHC) approach as the key to attaining the target set by WHA above.

PHC was described as essential health care based on practical, scientifically sound and socially acceptable methods and techniques made universally accessible to all individuals and families in the community with their own full involvement. The most important components of PHC include health education, disease prevention, disease control, safe water, basic sanitary measures, maternal and child health, immunization against 6 major communicable diseases (Tetanus, diphtheria, whooping cough, TB and measles), and supply of Essential drugs. A subsidiary component of PHC particularly in African Region is the evaluation and possible use of traditional methods of treatment (traditional birth attendants, herbal medicine).

1978. WHO Action programme on Essential Drugs (ED) was initiated. WHO came up with ED lists (200 drugs) and invited national governments to prepare national ED lists using WHO ED list as a guideline.

I was in the national committee which prepared the first ED list here in Kenya in 1980. It was not easy and as part of a compromise, we agreed that any drug not included in the national ED list could still be ordered provided there was adequate justification. The national ED list has been revised recently (1993). Regrettably this loophole for ordering drugs outside ED list has been abused and at times makes nonsense of the ED list.

1979. WHA at its 32nd session endorsed decision of the Alma-Ata conference.

1981. WHA at its 34th session adopted the Global strategy for Health for all by the year 2000 and invited member states to formulate and implement strategies for health to achieve the stated goal.

Since 1978, National health policies were geared towards implementing the Alma-Ata declaration which in the 1980s was elevated to the status of a creed. Much of the planning was done at the WHO Regional Offices. It is not possible to discuss fully the success of PHC strategy as envisaged by the Alma-Ata declaration. Those wishing to get more details should read the 7th Report on the World Health situation (1986) which covers the period 1978-1984, and also the 8th Report on World Health Situation (1993) which covers the period 1985-1990. Here in Kenya some components of the PHC have received greater attention because they are easier to implement or because specific donors were attracted to them. Maternal and Child Health (MCH) and Expanded Programme on Immuni-

sation (EPI) have been well funded. The essential Drug Programme has also attracted funding from DANIDA, NETHERLANDS and BRITAIN through ODA.

What are the contentious issue regarding drugs here in Kenya? I shall focus on a few.

TRADITIONAL MEDICINE

In any discussion relating to use of drugs in health care delivery, it would be a serious omission if we fail to appreciate the role of traditional medicine.

Traditional medicine is one form of alternative medicine. The term "alternative medicine" is an ill-defined phrase which refer to systems of treatment other than the orthodox or allopathic medicine. It includes acupuncture, homeopathy and herbal medicine among others.

What is traditional medicine?

Traditional African medicine is defined as the totality of all knowledge and practices, whether applicable or not, used in diagnosing, preventing or eliminating a physical, mental or social disequilibrium and which rely exclusively on past experience and observations handed down from generation to generation verbally or in writing (AFRICAN TRADITION MEDICINE -AFRO TECHNICAL REPORT SERIES NO. 1, WHO Regional Office for Africa, 1976).

Attitude towards traditional medicine is usually polarised varying from contemptuous dismissal to romantic glorification. Rarely does one come across people with balanced views. This is what makes traditional medicine contentious.

What kind of people opt for Traditional medicine?
These fall into 3 broad categories.

1. In many countries of Africa about 60% of the population do not have ready access to modern medicine and rely almost wholly on traditional medicine. To them it is not an alternative to any other system.
2. Many people in urban and rural areas who have ready access to modern medicine seek treatment from traditional medical practitioners depending on the type of ailment. The reasons are varied.
3. Some people who are disillusioned with Western (Orthodox medicine go to traditional medical practitioners as a form of protest. In this category are people suffering from chronic diseases such as asthma, peptic ulcer, diabetes and epilepsy. They are bitter and frustrated after paying so much money to specialists who appear to have no answer to their problems. To them, anything which offer a glimmer of hope must be tried.

What is the scientific rationale for traditional medicine practice?

It is not possible to answer this question unless we narrow it to herbal medicine (see definition of traditional medicine). The scientific rationale for use of traditional medicine has been established with respect to many herbs. Work is still continuing in many research institutions and it will take many years of painstaking research to investigate the documented claims of many other herbs. A list of my publications on medicinal plants is appended to this lecture. I have supervised several Masters and Doctorate postgraduate students working on medicinal herbs. Needless to say I have carried out research in other areas of pharmacology and toxicology.

In the meantime botanists and sociologists have been documenting use of medicinal herbs based on the folklore of various communities. Several books and journal articles have been written. Information based on folklore must be verified through scientific investigation. Specific claims regarding use of herbal medicine are easy to investigate. Unfortunately, for many herbs, the claims regarding their usefulness are vague. A case in point is the category of plants loosely referred to as, "harmony drugs" the typical example being the chinese herb, "Ginseng". A good account of ginseng appear in a book by Stephen Fulder, entitled, "The Root of Being". Another example is Rasayamas (rejuvenating substances) in Ayuverda.

Research on herbal medicine has failed to confirm the usefulness of some herbs. In other cases, commonly used plants have been found to be toxic.

The much publicised view that herbal medicine is non-toxic *per se* is not supported by facts. There have been publicised incidents where people have collapsed after drinking herbal decoction. Many more go unreported. Any medicine will be toxic if given in excess. In the case of chronic toxicity, the deleterious effects will be manifested weeks or months later making it difficult to establish a cause-effect relationship. An example is the pyrrolizidine alkaloid containing plants (Senecio, Heliotropium, Crotalaria) sometimes used in herbal medicine.

The practice of herbal medicine uses several plants concurrently and there is a possibility that they may potentiate or neutralise each other. This is an aspect which is overlooked when scientists investigate each medicinal herb separately.

The importance of traditional medicine is not an issue as important drugs have been isolated from medicinal plants used by ancient people. Examples of such drugs include Morphine from Opium, Ephedrine from Ma huang, Emetine

from Ipecacuanha, Digoxin from Digitalis, Reserpine from Rauwolfia, Physostigmine from the Calabar bean, Vincristine and Vinblastine form Madagascar periwinkle, Artemisinin from Qing Haosu, etc.

Traditional Medicine and Culture

Traditional medicine is deeply rooted in people's culture. In Africa, the colonial powers had downgraded traditional medicine to the level of a nuisance cultural practice. After independence many African Governments set out to rectify this anomaly through legislation. Often the legislative measures were unbalanced thus creating further confusion. This certainly happened in Tanzania and Zimbabwe. Many countries are still trying to reconcile conflicting interests. For example although Witchcraft is illegal, medicinal plants to "Ward off the evil eye" are tolerated. Generally it is considered bad manners to subject claims by traditional medical practitioners to vigorous probing. Many African governments have adopted an ambivalent stance and often the official pronouncements are tailored to suit the audience and the occasion.

What qualification do we expect of traditional medicine practitioners

From the definition of traditional african medicine given earlier, it is difficult to establish common criteria by which to judge the practitioners. This difficulty is compounded by the chronic in-fighting among the members.

It is estimated that over 60% of those practising traditional medicine are not genuine and are only motivated by economic gains. Certainly, few of those selling "MITI NI DAWA" can claim to be genuine practitioners.

Although the practice is exempted from the requirements of

Medical and Dental Practitioners Act, there is a rider. This exemption only applies to people practising in their "own community".

The current practice where herbalists practise in urban areas is not consistent with this spirit. If a herbalist cause death or is judged incompetent in the rural area he will be forced to close his practice. In the urban areas he just relocates to another area.

Why has there been resurgence of interest in alternative medicine in general and traditional medicine in particular?

Earlier I referred to a class of people, mostly in the West who are disillusioned with modern medicine. This category of people is increasing. The occasional indulgence of Royalty and prominent people (Nobel Laurates) in alternative medicine has helped to erase the stigma associated with alternative medicine. The feeling of betrayal in people suffering from such diseases as asthma, diabetes, cancer, epilepsy and diseases associated with sexual functions has been another contributory factor. Affected people fail to understand why the same human intellect that has landed man on the moon has no answer to their problems. Traditional medicine then becomes a convenient safety valve for their frustrations even if it only offers slim hope.

An important feature of traditional medicine is that the sick is treated in familiar surroundings with supportive relatives and friends around. This is particularly useful in diseases of adaptations (asthma, peptic ulcer, hypertension, mental depression etc). It is not often realised that the much publicised "health care team" concept is infact retrogressive.

In the Middle Ages (treatment was comparable to present traditional medicine) treatment was highly personalised, home care being the rule rather than exception. This approach made

up for lack of medicine. Could it be the case too with the present alternative medicine? No wonder the practitioners of traditional medicine are able to claim a high cure rate and there are many grateful people to back up these claims.

DRUGS AND HIV INFECTION

While I was preparing for this lecture, a colleague told me that the lecture would be incomplete if I did not "mention HIV infection". Having satisfied that minimum requirement I shall go further and explore the subject.

When late in the 1970s WHO set the World Health agenda up to the year 2000, AIDS pandemic was not a factor. Nor did the Alma-Ata conference take into account the impact AIDS would have on the Primary Health Care parameters.

The situation changed considerably from the mid 1980s as the full implication of the pandemic continued to unfold. To-day up to 40% of hospital beds in many countries are occupied by HIV-infected patients. Resources, initially meant for PHC have been re-directed to care for HIV patients. Diseases such as TB which had been brought under control are back due to fulminating or pathogenic infections.

A lot has been written on AIDS but as any clinician will tell you, the amount of literature on a disease condition is usually inversely proportional to what is known.

To understand the use of drugs in AIDS patients we should briefly look at the disease and specifically the life cycle of the HIV.

To maintain persistent infections and clinical "latency" the virus has evolved an elaborate regulatory network to establish a steady level of **low virus expression**. Three genes tat, rev and

nef are involved in this regulation. HIV has evolved yet another strategy for persistent infection, i.e a genetic "drift" mechanism to evade host immune control. Fig 1 on page 33

RADICAL THERAPY

The most vulnerable points in the life cycle of the virus are marked as A, B, C, D, and E. I shall not discuss how HIV is spread as that is common knowledge now. Similarly, I shall not discuss the diagnosis of HIV infection through laboratory tests (ELISA and WESTERN BLOT). I shall briefly discuss the clinical findings to enable me bring out some points pertinent to drug use.

Clinical finding

Acute infection

In early stage of infection some patients have transient signs compatible with acute mononucleosis syndrome or aseptic meningitis. Symptoms subside without treatment.

Asymptomatic infection

After HIV infection, there are no symptoms in some people but ANTIBODIES for HIV can be detected during laboratory screening.

HIV virion avoids antibodies and continue to multiply

Generalised lymphadenopathy - Common in HIV patients
AIDS Related Complex (ARC)

Is a severe life threatening condition. Usually the cause of symptoms is not obvious. Typical symptoms include the following:

Persistent fever for over 1 month, Fatigue, Involuntary weight loss greater than 10% baseline, Persistent diarrhoea for more than one month, Multidermal herpes zooster, Neurological complications (amnesia, hyperreflexia, impaired concentration etc)

Opportunistic infections

Protozoans: PC, Toxaplasma, cryptosporidium.
Bacterial: Mycobacterium, salmonella, klebsiella, E.coli
Fungal Candida, Histoplasma, Cryptococci
Viral Cytomeglovirus, Varicella Zooster, H. simplex I & II.

Drugs are used for treatment of opportunistic infections and in radical therapy directed at the HIV.
As the immune system become progressively impaired opportunistic infections and pathogenic infections become evident.
Treatments for these infections follow the standard regimen:
TB - streptomycin + Thiacetazone + Isoniazid + Rifampicin
PCP - Cotrimoxazole, Pentamidine aerosol
Toxaplasmosis - Sulphadiazine + pyrimethamine
Herpes Simplex I & II - Acyclovir
Cytomegalovirus - Ganciclovir
Candida albican - Fluconazole, Nystatin
Cryptococcal meningitis - Fluconazole

Radical therapy

This aims at eliminating the virus or stopping replication.
From the life cycle of the HIV, the vulnerable points are:
A. Attachment to the receptor (CD_4+fusin) of host cell - no drug.
B. Reverse transcriptase - Dideoxyinosine, Dideoxycytidine, Zidovudine and Lamivudine (3TC) .

C. Replication - Zidovudine + other nucleoside analogues.
D. Viral protein coat - Protease inhibitors eg Saquinavir, Ritonavir, Indinavir and Nelfinavir.
E. Release of virus - No drug.

Infection with HIV can be compatible with long survival with or without medical intervention (latent period 2 - 20 yrs before AIDs is expressed). The actual contribution of chemotherapy is therefore not certain. For now multidrug therapy is recommended. Drug toxicity is a major problem.

PHARMACOTHERAPY FAILURE

Pharmacotherapy means use of drugs to treat disease conditions. There are several reasons why treatment with drugs might fail. Each case need to be considered separately as often there are multiple reasons.

The following are some of the important causes.

1. If an irreversible damage has occurred, treatment is usually palliative or directed at stabilising the physiological functions through replacement therapy which has to continue for life. Examples include juvenile diabetes, osteoarthritis, and some degenerative diseases. If patients are not advised, the treatment may create a false hope of cure. When certain drugs are administered over a long period the receptor sensitivity may decrease leading to therapeutic failure unless the dosage is adjusted.

2 Pharmacotherapy failure might result from misdiagnosis. Cryptococcal meningitis may be mistaken for bacterial meningitis. In toxaplasmosis, patients present with neurological symptoms (eg seizures) and since the condition is rare, the chances of wrong diagnosis are high. Occasionally, upper respiratory tract infections which

are of viral origin are mistaken for bacterial infections. In an ideal situation, tentative clinical diagnosis should be confirmed by laboratory tests.

3 Another possible explanation is failure to address the underlying cause, concurrently with treatment. An asthmatic may be allergic to some material in his/her environment eg animal hair, dust mite, toilet soap, cosmetic etc. Drugs are useful during asthmatic attacks or when used prophylactically. When steroids are used over a long time, the histamine receptors in the smooth muscle of the bronchiole become hypersensitive, necessitating an adjustment in dosage regimen. There are some disturbing statistics which indicate that mortality rate is higher among asthmatics treated with steroids than control groups. Another example is the stress-related disorders such as general anxiety, peptic ulcers, anorexia etc. Needless to say treatment of obesity with anoretic drugs is meaningless without dietary management. Similarly treatment of persistent cough with expectorants and antitussives is meaningless unless the underlying cause is investigated.

4. Medical literature give general guidelines on dosage and frequency of administration of drugs and these apply to the majority of patients. Occasionally an individual may exhibit idiosyncracy. For some disease conditions, treatment has to be individualised because a slight fluctuation outside the lower and upper therapeutic range has serious implication. Examples include use of warfarin in thromboembolic conditions, and digoxin in congestive cardiac failure. In our situation where patient follow-up is poor, individualised treatment is only possible in hospitalised patients.

5. There are many instances where patients seek treatment when the disease condition is too advanced. This may be due to economic reasons or failure to appreciate the seriousness of the condition. There are effective drugs for treatment of pneumonia, Tuberculosis and malaria, yet the mortality rate is high.

6. Many cases of pharmacotherapy failure result from poor patient compliance. This is particularly prevalent in chronic diseases eg diabetes, asthma, etc. In other cases the side effects discourage patients from taking drugs. Iron salts used in iron-deficiency anaemia cause nausea. Similarly, nitrofurantoin used in urinary tract infections also cause nausea. Many patients do not complete the prescribed course of treatment.

7. When antimicrobial agents are used in treatment of infections, pharmacotherapy failure is usually attributed to microbial resistance. Bacterial resistance is particularly widespread, with some showing multidrug resistance. Ideally, before prescribing, a clinician should establish: the susceptibility of the particular pathogenic microorganism to various antibiotics. In practice, this is rarely possible. To circumvent this problem, clinicians have tended to over use the broadspectrum agents (ampicillin, amoxil, co-trimoxazole). Overuse of broadspectrum antibiotics have resulted in many bacteria developing resistance to them. How do bacteria develop resistance to antibiotics? Bacteria mutation (single step or multiple step) produce resistant strains capable of the following:
   a. They have enzymes that destroy the drug making it inert eg penicillinase (several classes and subclasses).
   b. They modify the drug molecule so that it can no longer fit in the receptor site e.g Aminoglycoside

modifying enzymes (AMES) and Chloramphenicol acetyltransferase (CAT).

c. There are enzymes that modify target site (receptor) so that the drug can no longer fit. This help to explain bacteria resistance to erythromycin.

d. Some bacteria mutants have altered cell membrane structure to decrease uptake of antibiotics.

Details regarding bacteria resistance to antibiotics would fit very well in the best science fiction books and often stretch our imaginations to the limits.

8. In a few cases pharmacotherapy failure may be attributed to inappropriate drug formulation. Diazepam injections have been problematic when used in treatment of status epilepticus or in tetanus. The brand product, Valium injection is to be preferred in life-saving situations, as this has proved dependable consistently.

9. The body may have an inherent reflex compensatory mechanism which is activated when a drug is used to treat certain disorders. Use of systemic antacids (sodium bicarbonate) to neutralise acid in the stomach is followed by oversecretion of the same acid a few hours later. Similarly nasal decongestation only give temporary relief followed by severe congestion later. This is normally referred to as "rebound phenomenon".

10. Concomitant administration of several drugs may lead to drug interaction. The interaction may be at the absorption level (stomach), during distribution, metabolism, elimination and even at the site of action. This topoic is discussed in details in Pharmacology textbooks.

GRAVITATION AWAY FROM PROFESSIONALISM

In his book "The Doctors Dilemma", the English writer George Bernard Shaw wrote, "All professions are conspiracies against the laity".

There are several ways the health professionals can conspire against the laity. If a doctor orders laboratory tests to assist a certain laboratory knowing well that such results will not alter the course of treatment he is effecting a conspiracy. Similarly if a pharmacist dispenses expired drugs or dispenses generic product and charges the price of a brand product he is conspiring against the laity. I shall not comment on other professions, certainly not law. Whenever a professional judgement is clouded by monetary considerations or expected political favours, professional ethics are likely to be down graded.

The hall mark of any profession is its ability to regulate the conduct of its errant members through in-built regulatory measures over and above the statutory laws which apply to all citizens. It should have mechanisms to ostracise and if need be weed out those who tarnish its name. In Kenya the response of many professional bodies in dealing with errant members is at best lukewarm. The consequence of professional bodies' inability to regulate the conduct of their members has serious repercussions. It gives opportunity to others, outside the profession to create confusion.

In the past medical and pharmacy professions here in Kenya have been blamed and vilified for drug shortages. The two bodies should have come up, jointly or separately with facts and figures to disabuse these allegations.

A professional is a creation of the society from which he/she springs and therefore reflects the fears, hope and aspiration of that society.

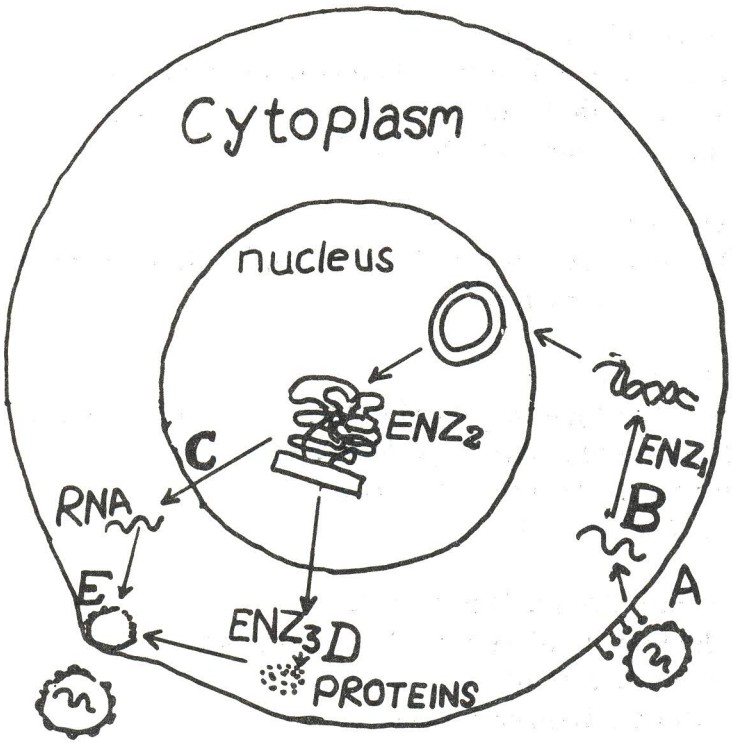
In a society where the rat race for material gain has become a national creed and the rallying clarion of "harambee" is punctuated by a sadistic murmur of "eat or be eaten", it is not surprising that the professionals have been swept by the current, albeit, unknowingly.

Is it reasonable to expect our doctors and pharmacists working in public hospitals to live in servants quarters? Their time-honoured title is a constant reminder of unfulfilled expectations. No wonder the professional ethics have been devalued.

I have been tempted to comment on this subject because lack of professionalism impacts adversely on the use of drugs. Any drug is as good as the prescriber, with few exceptions.

Fig 1 on page 33 shows the life cycle of HIV a retrovirus. The hallmark of retrovirus is their capacity to maintain **persistent infection** without great detriment to the host. **HIV is different.** It is highly cytopathic, pathogenic virus, the active replication of which impact adversely on immune system of the host.

FIG1. LIFE CYCLE OF HIV



ENZ$_1$ REVERSE TRANSCRIPTASE
ENZ$_2$ INTEGRASE
ENZ$_3$ PROTEASE

APPENDIX 1

PUBLICATIONS ON MEDICINAL AND POISONOUS PLANTS BY C.K. MAITAI

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Toxicity of Catha edulis in rats
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Relative potencies of 2 phenylalkylamines found in the abused plant Catha edulis (khat) Life Science 27 2143-2147

18. Guantai A.N. and Maitai C.K.
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21. Maitai C.K. and Manohar D.
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