

ASSOCIATION ORATION

by

R. RAJAM (MADRAS*)

Fellow Members of the Indian Association of Dermatologists and venerologists.

Let me thank you for the undeserved honour you have bestowed on me to deliver the first oration during the current session of the annual meeting of the Association. If mere chronological age is a criterion for the selection of this honour, then I suppose I am qualified. But I am a spent force and have been put on the shelf for over ten years and more or less out of touch with the rapidly flowing stream of modern medicine including our speciality, and you could not have done worse by choosing a younger man who is an activist in the profession.

An oration, according to the dictionary, is a formal address, harangue or discourse of a ceremonial kind. There is the other cynical definition that oration is the loud mouthed art of carrying conviction without resort to logic or truth. Of course, the latter is the prerogative of the politician.

Venerology was my lawful wife and Dermatology was my occasional mistress. When I was tired of one, I spent the night with the other, as Anton Checkov said about his dual role of a doctor and a dramatist.

Here are some random reflections of a septagenarian who had for over half a century, observed with a certain bewilderment and wonder, the knowledge explosion in the art and science of medicine and had participated in the efflorescence, albeit in a limited narrow field of venerology.

Dr. Barrymore rightly described the accelerating acceleration of knowledge in the art and science of medicine as analogous to the logarithmic phase of a bacterial culture. The concept that medicine is applied biology and medicine is one principal field of application of all the basic science among which the behavioural and social science will come to assume relatively a much more predominant place. The science of epidemiology in its broadest sense is coming into its own and we may by the epidemiological method paralleled with physiological, biochemical and immunological study, identify disease-prone individuals in a community before they become sick. The study will help to understand the concept of variation in immunity and vulnerability to disease. Specialisation and Balkanisation of medical science and practice have become inevitable with the ever-widening frontiers of knowledge and seemed to have reached a point of no return. Increasing specialisation is tending to be more and more disease-oriented, and less and less patient-oriented.

The Newer Concepts in Medicine

The first of the concepts is the stress reaction or the general adaptation syndrome enunciated by Selye way back in 1935. It may be caused by diverse noxious agents as emotional disturbance, infection, haemorrhage, trauma or undue exposure

to heat and cold and hence unspecific. These reactions entail the participation of the pituitary and the adrenal glands, the liver, the kidney, the skin and the haemopoetic tissues. Through the mediation of the neuro hormonal mechanism, chemical metabolic circulatory and psychological changes occur. The adrenal hormone seems to play the key role.

The second concept is genetics which is the youngest of the sciences in biology and its efflorescence into various subspecialities within the past decade is something breath taking. Talking of genetics in relation to medicine, the growing realisation of the importance of the genetic material in the causation of disease coupled with major technical advances, particularly in the fields of biochemical and chromosome genetics has naturally led to a world wide awakening of interest in human genetics. Although still confined mostly to research laboratories the medical profession is beginning to appreciate the clinical significance of these developments. Genetically definable deviations from the theoretical norm multiply so fast and genetic factors in diseases not generally regarded as genetic (such as the influence of blood groups in peptic ulcer) are emerging so frequently that it is ever becoming easier to defend the extreme view that no one is congenitally normal, and no disease is altogether devoid of genetic basis. There are many genetically determined abnormalities which can be recognised in the heterozygotes by biochemical or physical tests.

The third of the new aetiological concepts in disease is derived from the science of immunology; the autoimmune phenomenon. This concept is an example in scientific thought of a theory trying to prove a fact. For many years, immunity and immune response have been considered as teleological mechanism whose purpose was to destroy pathogenic micro-organisms and to neutralise their toxins thus benefiting and curing the disease caused by the pathogens. 'But we seem to have travelled so far from the days when all immunological reactions were supposed to be necessarily beneficial, that immunology is hardly less commodious than psychology in providing an aetiological funk-hole for diseases of which the physical causes are still unknown'. (Medawar). Under normal circumstances, immunological reactions are necessary, not merely for remaining in health but for remaining alive at all. In a normal individual, every cell and every chemical component of every cell in the body is an expression of the genetic nature of the individual. Except in identical twins, each individual is genetically and biochemically different from any other individual and strongly defends his integrity against any entry of foreign material. Clinical examples of the reaction of the body against foreign substance are the various forms of allergy, hyper sensitivity, haemolytic disease of the new born, the rejection of homograft of the skin of one person to repair another's what Medawar describes felicitously as 'a miscarriage of immunological justice'. MacFarland Burnet and co-workers postulated that the thymus is the principal centre of immunological homeostasis and immunologically competent cells were derived from the thymus. They believe that homoestatic failure is the essential feature common to all auto-immune

diseases. According to them, auto-immune disease is ascribed to the appearance of clones of immunologically competent cells which are insensible to the homeostatic control. A wide variety of defects, some of genetic origins, others due to infection may be responsible for the failure and perversion of homeostatic controls.

The science of microscopy has travelled far from light microscopy to phase contrast microscopy to the electron microscopy and recently to fluorescent microscopy. Within the last decade and half, the potentialities of the fluorescent antibody technique have been exploited as a versatile tool in many medical fields. The method is put to use in the specific immunological staining of bacteria and viruses, to locate the antibody in immunologically competent, mesenchymal cells, in charting the distribution of auto antigens in auto immune disease and conversely to detect the presence of antibodies in patients' sera.

Increasing numbers of hormones enzymes, blood group substances and tissues antigens have now been characterised with fluorescent technique.

The value of the antibody technique is its specificity, versatility and speed.

The Therapeutic Scene.

The 'Therapia' Sterilisans Magna dreamt by Ehrlich when he discovered Salvarsan for Syphilis 60 years ago now seems a live reality, in the prevention and cure of most of the bacterial diseases. Now we are living in a Therapeutic Utopia or is it a nightmare? The multiplicity of chemo therapeutic and antibiotic drugs, the transformation of endocrine therapy, particularly the adrenal steroids, the development of drugs in bewildering abundance or the hypotensives, the tranquillisers, the antipruritics, the antihistaminics, the anti fungals, the energisires, the sedatives, the pain killers, the antimetabolites have made it difficult, if not impossible, for the conscientious and critical physician to keep up with the torrent.

The medical profession should be indeed grateful to the efforts of non clinical, often non medical scientists associated with the pharmaceutical industry for the discovery, testing and trial of nearly 60 and odd most valuable drugs used in medicine, with the exception of penicillin and streptomycin.

It is an unfortunate fact which Lord Flatt expressed in his Harveion Oration (1967) that the clinical scientists in their understanding of the disease process, have not been responsible or even been seriously involved in discoveries in Therapeutics which have transformed the medical science. It is also being increasingly recognised that the antibiotic and chemotherapeutic control of bacterial, protozoal and treponemal diseases with a tendency to their indiscriminate use is creating imbalance in the competitive life of the pathogenic and saprophytic micro organism in the human tissues, with the result that viruses at one end of the biological scale and fungi at the other end released from the competitive co-existence of the larger bacteria has assumed new and dangerous pathogenic roles afflicting human population.

Research in Medicine.

John Hunter's advice not to think but try the experiment has been taken too zealously, and there is today an over production of experimentation of the Heath Robinson type, often with insufficient thought preceding the experiment. You are all aware how John Hunter paid with his life by inoculating himself with the pus from a case of gonorrhoea to prove the identity of syphilis and gonorrhoea. Unfortunately, the patient from whom the pus was taken had suffered both from syphilis and gonorrhoea and Hunter developed syphilis and died of angina due to syphilitic aortitis. Why Experiment? Why not think was Lord Robert Platt's provocative question. It was the prepared mind that made important discoveries. All clinical research must be applied research. In our country, there is a strong case for directing our limited resources to the achievement of an objective rather than devoting research potential to the investigation of observed phenomena of academic interest.

Among clinical sciences' great failures is its almost complete neglect of psychological, social and ecological factors in disease. 'Science must be a servant of medicine, not a master of medicine. Clinical science in an effort to prove everything by experiment has shown an unfortunate tendency to follow only the methods of physical sciences to the neglect of discovery by observation and the kind of evolutionary thinking, so necessary to the study of Biology.

Importance of Family in the study of illness :

The modern family functions as a marsupial pouch and the family transmits chromosomes and customs. It shares genes and experiences. In the study of disease in any family, it is essential to recognise how the signs and symptoms of disease in different members may be connected and related. Hence the importance of the family in every detail, physical, psychological and social. All sorts of things run in families; baldness to bigamy, atopy to atherosclerosis, diabetes to dyskeratosis, porphyria to peptic ulcer, from boils to blood pressure, obesity to otosclerosis, cancer to collagen disease, vitiligo to varicose veins, accident proneness to alcoholic addiction and so on in the causation of disease, congenital or acquired, there is a spectrum between complete hereditary determination at one end and complete environmental determination at the other.

I plead guilty to have indulged in some of the random reflections on the philosophy and the newer concepts in medicine. They are relevant to every field of medicine, including our own speciality.

Dermatology, venereology and leprology are the cindrella of the medical specialities in the descending order of their attractiveness, appeal, charisma and monetary rewards among the medical profession and the lay public.

Some of the dyed-in-the-wool Dermatologists look down on the Venereologists, and Leprologists, oblivious of the evolution of Dermatology from Syphilology and many of the famous Dermatologists in Europe and America had graduated from the School of Syphilology.

In the present context of our country's limited resources in money, technical scientific man power and inadequacy of physical facilities, let us not ape the Honeses of the highly developed Western countries, but take advantage of their scientific and technological advances and try to organise our health and medical care with reference to our needs and capacity.

In the National Health programmes, venereal disease and leprosy have received some attention in spite of the unwillingness of the doctors to get professionally involved. Hence it is a wise and pragmatic decision that our Association had opted and sponsored a combined major speciality of three disciplines of Dermatology, Venereology and leprology. Academically from the point of view of under graduate training in teaching hospitals and economy in staffing and laboratory services, the combined discipline of the three sub specialities is an advantage. After all, the drama of these disciplines is primarily and predominantly played on the stage of the human integument.

Venereology :

Way back in 1948, was heard the raucous cry 'Venereology is dead; Long Live Penicillin'. It is a paradox in medical progress that in spite of spectacular discoveries and advances in the aetiology, laboratory diagnosis, epidemiology and therapeutics of venereal diseases, and the birth of vereology as a discipline 50 years ago the effective control of these diseases, is nowhere within sight of the promised hope of a measurable decline of these diseases. During the post-war decade, America and Western Europe, gleefully reported a precipitous decline in the incidence of diseases, particularly syphilis. During the succeeding decade and in the current situation, the premature optimism was shattered with a continuous resurgence of these diseases all over the world. Complex factors, social, economic and psychological are operating and interacting in the acquiring and spread of V. D. Throughout historial times, priests, kings, commissors and parliaments have all tried to put the oldest profession out of business. None succeeded. The resurgence and sky rocketing of venereal diseases all over the world from San Francisco to Shangai, from Calcutta to Copenhagan, is a phenomenon of the sixties.

Paripasu with the population explosion we are witnessing the sex explosion with the rest of the world following the example set by America. There is a super market in Eros in every large city in the world inclding our own. The mid twentieth century slogan runs as follows Teenagers of the world, unite for a sexual Bonaza, you have nothing to lose except your orgasm, and they seem to demand the right to orgasm as one of their fundamental rights. But an orgasm a day does not keep the doctor away. Shame, fear of disease and death and deformity, social odium seem no longer operative against unsocial behaviour.

The speed, simplicity and efficiency of modern treatment is its own undoing and the cause for a high incidence of reinfections. (As a full-fledged speciality its attractiveness has disappeared.)

To the curious and biologically minded clinical scientist, there are still fundamental and fascinating unsolved riddles in these groups of diseases. A virulent *Treponema pallidum* has never been grown on artificial culture medium. An organism morphologically indistinguishable causes yaws in the back woods of central India, Bejel in the middle east, pinta in Mexico and venereal sporadic syphilis among the adults of either sex all over the civilised world. There is clinical evidence to show that the treponemes of syphilis bejel, yaws and pinta present a spectrum of diminishing pathogenicity and natural attenuation. But there is epidemiological and experimental evidence that protection against one disease is afforded by infection with one of the others. Venereal syphilis is a systemic infection affecting skin, mucous membrane, bones, cardio vascular system and central nervous system. Bejel affects predominantly mucus membranes with limited skin and bone lesions, and no involvement of the cardio vascular and central nervous systems. Yaws affects only skin and bone and pinta affects only the skin. Venereal syphilis is the only treponemal infection which is prenatally transmitted to the unborn offspring. So from the point of view of clinical virulence, the treponeme of pinta has the lowest rating, although the immune response is good enough to protect against reinfection with the other treponemes. Immunology is the wonder child of medicine, and it cannot be beyond the competence of immunologists and immuno chemists to evolve a vaccine against syphilis by still further attenuating the treponemes of pinta capable of producing an effective immune response with minimum or no clinical involvement.

From the therapeutic point of view, the treponemes of syphilis continue to be susceptible to the lethal effect of penicillin and with adequate total dosage of 4 to 6 mega units, the early infectious stage of syphilis can be cured. What is cure in a chronic infection like syphilis characterised by periods of activity alternating with periods of clinical quiescence during a period of 20 to 25 years? Cure is of three kinds, clinical, serological and biological. To the clinician, the advent of penicillin and its administration in adequate dosage ensures clinical and serological cure in early infectious syphilis with freedom from relapse, clinical or serological, during the rest of the patient's life. In late syphilis, clinical cure with freedom from relapse is achievable but not serologically. In the classical Oslo follow up study of untreated syphilis it was proved that the vast majority achieved spontaneous cure of the infection.

It was presumed that biological cure took place in course of time in the sense that the last treponemes has been destroyed or rendered innocuous and non virulent by body's immune mechanism. In 1961, the French workers at the Pasteur Institute, Paris, reported persistence of treponemes in lymph nodes in experimental rabbit syphilis treated with adequate penicillin 2 years after infection, and also in human subjects with neurosyphilis and latent syphilis who were treated in the past with massive doses of penicillin. In either case, the recipient rabbits inoculated with part of the lymph nodes from both the rabbit and human subjects, failed to develop any signs and the T. P. I. test was negative, but spiral organism in stained smears from a proportion of the recipient rabbits was found. Another series of disturbing

reports document the presence of treponemes in late seronegative syphilis with prior adequate treatment in the aqueous humour, in the normal spinal fluid and in the liver biopsy, both by Darkfield examination and fluorescent antibody technique. In these later reports, no information was available whether inoculation into rabbits was tried with the production of lesions. There has not, however, been complete acceptance that all of the demonstrated organisms were in fact *treponema pallidum*.

At the serological laboratory of the Institute of Venereology Chacko and Coworkers have demonstrated motile *treponema pallidum* from the aqueous humour of a patient with interstitial keratitis and non motile organisms from the aqueous humour of treated late syphilis in 3 cases. In recent years, a number of laboratory scientists, particularly the Russian workers, have been studying the ultra structure of the treponemes of syphilis with electro microscope and have described in laborious detail and micro photography the morphology of the organism and have been unable to give a definite explanation of the functional significance of the morphological findings. The Russian workers have also carried out an electron microscopic study of the treponemes of yaws and failed to find any distinct structural differences between the two strains of organisms.

It may be worthwhile and interesting to study the ultra structure of the *treponema* in the lymph nodes and body fluids discovered and reported both in treated rabbit syphilis and sero negative late human syphilis, since they failed to produce disease in recipient rabbits to determine any marked morphological difference between the attenuated and virulent organisms.

Syphilis had been a swear word from the time of Shakespeare up to the beginning of the 20th century known as Pox, because of its great prevalence among the high and low and even Osler said "If it comes to syphilis, suspect your grand mother".

In the Mother of Parliaments, during a verbal duel in the 18th century, between a Lord of the Treasury Bench and the famous dissolute democrat John Wilkes, the Lord exclaimed "Wilkes, I am convinced that will you die of pox or on the gallows." Wilkes immediately retorted, "That my Lord, depends on whether I embrace your mistress or your principles". Joking apart, I find in the current antibiotic honey moon, the index of suspicion of syphilis in the differential diagnosis, be it a skin rash or a painful thickening of a bone or an aortitis, or a psychosis, has fallen so low that the average practising physician often misses the luetic aetiology of a clinical condition.

Gonococcal infection.

This ancient parasite of *Homo sapiens* continues to flourish and defy in succession the chemotherapeutic and antibiotic assault that may be stated in a lighter vein that the hardy gonococcus eats penicillin and sulpha for its breakfast. A fourth of the strains of gonococci isolated, showed penicillin resistance or

decreasing sensitivity and these strains prove resistant to other antibiotics as well. Improved methods of treatment have made no impact on the epidemiological problem. Epidemiological control is bedevilled by multiple factors; the very short incubation period, asymptomatic infection in women, repeated infection and absence of immunity. Both for diagnosis and test of cure, we have improved methods of culture of gonococci (Thayer-Martin selective culture, Chacko-Nair new egg enriched selective medium) and delayed fluorescent antibody technique and the latest micro precipitation test devised by Chacko are available. But these highly sophisticated techniques of diagnosis and test of cure are not practicable in the routine day to day examination and treatment and epidemiological survey of the incidence of Gonococcal infection. There has been neglect of fundamental research in Neisserian infection, a subject which medical opinion has too long despised and ignored—an attitude determined by moral reprobation and later by over confidence in antibiotic therapy. It is a matter for genetic research, whether a mutation has occurred in the strains of Neisserian gonorrhoea under the impact of antibiotics, the mutant strain resembling *Mimosa* organism in its resistance to antibiotics. Short of dextrose fermentation test, the two organisms cannot be distinguished clinically, bacteriologically or culturally.

To the frustrated and disappearing venereologist, a few more diseases have been included in the catch basket of V. D.

Post-gonococcal urethritis is a phenomenon of post penicillin treatment of gonorrhoea and is reported in increasing numbers from the V. D. clinics all over the world. Many aetiological factors have been implicated in its causation that one is reminded of Huxley's lines modified to the present context:—

'I am a crowd obeying as many laws as it has numbers, chemically, virtually, fungally, protozoally and bacteriologically impure are all my beings. There is no single cure for what can never have a single cause'.

Herpes proenitalis, trichomoniasis have been increasingly encountered in the practice of venereology that they are now regarded of venereal aetiology. There is a threat of infectious mononucleosis being included in the venereal disease group, because of kissing as a mode of transmission of the virus, which allows intimate oral contact with salivary exchange.

Looking at the world picture, it would appear that the social educational law enforcement measures and individualised treatment with antibiotics have failed to stem the rising tide of these diseases. It is good to remember that at no time in the history of medicine was a communicable disease such as syphilis or gonorrhoea which is dependent on human sexual behaviour and whose aetiological agents have no natural extra human biological existence ever eradicated completely. But control and a measurable decline in the incidence of these diseases can be achieved through organised education, epidemiological and therapeutic measures. But the future hope lies in the advancing science of immunology.

Dermatology :

Dermatology and I would prefer to call it cutaneous medicine, has come into its own as an important speciality since world war II. The famous London surgeon Russel Howard contemptuously defined dermatology as a name and an ointment. It was facetiously said 'If of the diagnosis you are uncertain, prescribe calamine lotion'. The skin comprises 16% of the body weight and is not simply an organ but an organ system. Dermatology unlike beauty is not merely skin deep. It includes in its scope the whole range of life from the human mind to the filterable virus, a vast external environment and complex physiological biochemical, and immunological transaction within the body. We are indeed indebted to the pioneers of dermatology and syphilology for their minute descriptions of skin lesions, classified, catalogued and given a descriptive name, often jaw breaking. The clinical dermatologists acquired proficiency in diagnosis by visual observation and touch. The skin has the unique distinction of having foisted on it more diseases than any other organ. 500 diseases of the integument and nearly 100 of them are of genetic origin and caused by inborn errors of metabolism. But unfortunately, the descriptive and classificatory phase of dermatology turned out to have no relation to aetiology. Within the last 2 decades, dermatology acquired a new look, thanks to the progress in basic biological sciences whose applications to the physiology, biochemistry, and immunology, immunichemistry of the skin, both in health and disease have unravelled the how of the multiple clinical expression of the cutaneous system, both to the exogenous and endogenous stimuli. But the why of many skin diseases is yet to be investigated. Psoriasis is a classical example in dermatology in which the how of the disease histologically, biochemically and immunologically has been investigated and described in great detail. But why the epidermal cells behave as they do is an unsolved riddle wrapped up in a mystery inside an enigma. The newer highly sophisticated techniques of electronmicroscopy, isotope studies, fluorescent microscopy, auto radiography, immuno electrophoresis, organ culture etc., have been applied in the study of skin and its system.

The understanding of how the lesion of psoriasis came about would be of great significance to the understanding of the skin and its many diseases than the chance finding of its cure. After all dapsone has not helped to understand Dermatitis Herpetiformis nor Chloroquin Lupus Erythematosus (S. Shuster).

There is the hypothesis postulated with special referrence to the aetiology of psoriasis. The lesion of psoriasis is either due to the absence of an inhibitor (Bullough's inhibition of epidermal growth) of a normal growth factor or excessive release or production of an epidermal growth factor. This hypothesis is based on the concept that the primary defect is excessive basal epidermal cell mitotic activity with rapid transepidermal cell migration and resulting in incomplete cell metabolism. The absent granular layer and the abnormal para keratotic horny layer are thereby explained. This concept explains the usefulness of those emperical remedies which are inhibitory of mitosis such as mercury, folic acid antagonists, but fails to explain

the effect of glucocorticosteroids as these have no effect on epithelial mitosis. Recent studies by Lionel Fry and R. M. M. McMuller have shown that the return of a previously absent granular layer is one of the earliest signs of effective therapy preceding any effect on the epidermal cell mitosis. A study to investigate the precise sequence of histological changes which occurred in psoriasis during four different modes of topical therapy by these workers showed that the granular layer reformed rapidly before the mitotic rate fell. The conclusion of the workers that more subtle cellular abnormalities other than increased mitotic activity are responsible for the Psoriatic lesion.

The Eco system of the Human skin and its orifices.

In the current situation when the art and the science of cosmetology, cosmetic surgery have been increasingly sought after by women and men to make the skin beautiful, rejuvenated and socially and sexually seductive, and the man wants to look like a woman and a woman like a man, when the hemline is going up and the neck line is coming down, it may shock the average man or woman to know that the skin supports a large population of micro organisms and that bathing and showering with the use of detergents, soaps and shampoos far from lessening the microbial population actually increases the total by manyfold by bringing out the colonies hidden in the innumerable crevices and niches in the skin. Something may be argued in favour of Louis XIV's reported preferences for mistresses who had not had a bath for 2 years and whose odoriferous potential was fairly high.

Recent studies into cutaneous ecology have revealed that microbes in large numbers that are harmless or even beneficial live and thrive on the skin of most human beings. The acquisition of a cutaneous flora begins very early in life. An infant delivered by caesarian section is completely sterile and has no cutaneous flora. But a baby born by the natural route carries Cocci and Diptheroids from the mother's birth passages and sometimes a colony of Neisseria Gonorrhoea producing conjunctivitis and vaginitis. The colony is augmented soon after birth both directly from adults and indirectly by serial transmission. There is apparently a greater variety of potential pathogens on the skin of infants than there is on the skin of older individuals. The organisms live on the skin and the openings of the ducts of the eccrine glands and hair follicles. The glandular secretions and the by-products of the process that form keratin provide free amino acid as nutrients for the inhabitants of the skin.

Carbohydrates in a readily available state and certain of the vitamins are also in adequate supply. The temperature and water supply are favourable for microbial growth, although for many species the slight acidity of the skin is something of a handicap. ('The microorganisms live as Adam and Eve did, in a paradise where all their needs are supplied'.) There is only one animal consumer the follicle mite *Demodex folliculorum*. This microscopic creature lives, mates and breeds in and round the eye lashes, the hair follicles of the outer nose folds, the chin and a few other restricted areas.

The remaining cutaneous organisms are yeasts, bacteria and perhaps viruses that parasitise bacteria. These organisms can be regarded either as consumers or decomposers of the by-products of keratin synthesis. On the healthy skin, there are several pathogenic species that live in an uneasy balance with the host. A change in the internal or external environment can upset the equilibrium; and the species multiply and penetrate the horny layer. Notable examples are the various kinds of fungi on the skin and candidiasis of cutaneous orifices and herpes simplex virus. A few yeasts live and grow on the greasy areas of the face, folds of the nose and ear but they are usually harmless.

The dominant members of the cutaneous community are bacteria; Gram positive and Gram negative. On the healthy skin the Gram positive bacteria predominate, the aerobic cocci and the anaerobic diptheroids. Almost all the cocci are harmless except the ubiquitous staphylococcus aureus which has received a well deserved notoriety not only as the cause of acute furuncle but also by its facile capacity to acquire resistance to antibiotics has become a veritable hospital plague causing wound infection in surgical wards of hospitals. It is on record that at the Institute of Venereology, Madras eight patients, children and young adults treated with penicillin for congenital and acquired early syphilis developed serious skin and bone infections during the post surveillance period from which Dr. Chacko cultured coagulase positive staphylococcus aureus which was found completely resistant to penicillin and other antibiotics.

In the adult, the chief domicile of this organism is the nostrils and the perineum. In many infants it is found in the umbilicus and abdominal skin. The diptheroids are divided into three ecological groups. One is the corne bacteriamacnees which is anaerobic and lives in the depths of the hair follicle. The other diptheroids are aerobics. On the skin of most people the Gram negative strains of bacteria are also found. One group the Mimeo which includes potential pathogens appears to be common in the feet of children and adult males and in the latter, are also found in the urethra.

As viruses are parasites on living cells and as there are no living cells on the horny layer of the skin, they cannot inhabit the healthy skin. But viruses which parasitise bacteria particularly staphylococcus aureus are present in the skin in significant numbers.

The density of the microbic colony, particularly bacteria, varies from person to person. Some people have high bacterial counts and others a low one. These differences are maintained over considerable time intervals. Besides, there is also a regional variation of density in the different areas of the skin. Examples are the sparsely inhabited desert of the fore-arm, the more heavily populated tropical forest of the axilla and the cool dark woods of the scalp. The denser bacterial populations are found on the face, the neck, the axilla and the groin. The microbial community on the sole of the foot and between the toe is large and diverse. The

workers at the University of Pennsylvania have perfected sampling techniques of estimating the density of the bacterial population. The axilla, the most densely populated area has a mean population of 2.41 million bacteria per square centimetre of epidermis. In contrast, the counts taken from the skin of the back averaged only 314 bacteria per square centimetre.

It was thought that once the characteristic adult cutaneous community was established, there will be no further exchange of inhabitants between individuals. But the story of the staphylococcus aureus cross infection from the surgeon to the patient, from the nurse to the infant, from one patient to another patient, has belied the unconfirmed concept of a stable constant colony in each individual.

‘ Scatter ye microbes as ye may
On Epidermal tissues lying
Nor think that shower baths will stay
Staph aureus from flying.’

Micro organisms depart from the host by air and contact carried by microscopic rafts of skin shed from the body, according to Davies and Noble of St. John's Hospital for diseases of the skin. The new comer is most successful where there is an ecological niche that is not exploited by an indigenous inhabitant. Although pathogenic organisms constantly alight on the skin, they find it a most unfavourable environment and in the absence of injury have great difficulty in colonising it. A certain homeostasis is clearly evident in the skin. Invaders from outside, whether pathogens, or nonpathogenes, fail to establish themselves for three reasons:—

- (1) The acid mantle, (2) the constant shedding of the surface skin layer and
- (3) from an ecological point of view the interesting defence mechanism resulting from the metabolic activities of the resident flora.

It is a well known fact that unsaturated fatty acids are an important component of sebum collected from the skin, and they inhibit the growth of several bacterial and fungal cutaneous pathogens. These substances have been shown to be a metabolic product of the Gram positive members of the cutaneous community which break down by means of specific enzymes the more complex lipids in freshly secreted sebum. These Gram positive species not only protect the skin from invasion by potential pathogens but also exert an inhibiting action on the population growth of Gram negative organisms and the axillary odour is a gift from the metabolic products of the Gram positive species.

Somewhat surprisingly it was found by no means easy in man to produce Tinea of the scalp, body or feet, or to produce Moluscum contagiosum, herpes simplex or furuncles experimentally. The use of cytotoxic drugs, systemic corticosteroids and broad spectrum antibiotics are responsible for an increase in serious often fatal infection with Gram negative organisms, and other little known bacteria reported from bacteriological departments, increased incidence of candidiasis of the cutaneous orifices, infection caused by Mycoplasma and forms of bacteria are called the ‘Jokers’

in the microbiology pack. Recurrent boils, recurrent aphthous ulcers of the mouth, recurrent herpes progenitalis still continue to be enigmas to the practising physician.

Talking of recurrent boils on the skin, I had opportunities to record six families in whom the recurrent boils affected only the male members of the families. It has recently been reported that it is familial, an inborn error of metabolism inherited as a sex linked recessive occurring only in males and due to defective phagocytosis of the polymorphonuclear leucocytes caused by absence of oxidase and defective degranulation of the polymorphs. It may be worth-while of a research minded dermatologist with a flair for numbers and a training in the science of microbiology and biochemistry to undertake a time consuming study of the cutaneous ecology of the different strata of our society, of the power and pelf mad politician, the fat akinetic industrial magnate, the cosmetically covered filmstar, the unwashed slum dweller, the oil and carbon soaked factory worker, the religious leader who takes a bath every time he sneezes, urinates or defecates, or sights a widow, the pre-pubescent girls and the post menopausal women and the octogenarian who refuses to die.

The skin is the primary and predominant tissue involved in emotional inter communication and elemental sensory satisfaction. The integument along with the orifices has an erogenous capacity with a vast potential for fulfilment and deprivation. In the new born, the infant's very first postnatal sensory experience is usually contact with the warm soft body of the mother. Deprivation of all tactile relationship appears to result in prolonged emotional apathy and withdrawal. Most of the earliest feelings of love, security and satisfaction, pleasure and relaxation are transmitted via the skin. The tactile and kinaesthetic pathways are the first to be myelinated. In later years, the eye and the ear take over part of the sensory inflow. Even in adults love remains a skin game, holding hands, caressing, petting, kissing and all the reported elaborations thereof are ectodermal or mucocutaneous activities. 'Mothering is vital, but mothers may be unnecessary. The importance of post partum stimulation is evident in other mammalian species; when some animals are not licked by their parents soon after birth, they do not survive. In emotionally disturbed patients, holding his hands or a pat on the back provide emotional support to calm him. The buttock's pat is another singular custom to convey solace or encouragement. Skin contacts have a quality of genuineness. The hands clasp, the lip kiss, cheek kiss, the nose rubbing, the Muslim habit of embrace have all a quality of genuineness and mutual trust. The lie detector is an application of the principle that the skin can only tell the truth. Man has no awareness of his internal organs, the skin structures form the major part of the image of himself.

In a lighter vein, but true, here is what Tennyson wrote about the skin :

'Man is the hunter; woman is his game. The sleek and shiny creatures of the chase. We hunt them for the beauty of their skins.

Leprosy :

A western medical scientist said ' If only leprosy affected the affluent classes of the West, as cancer and heart disease, it would not have been neglected, as it had

been by the medical scientists and research workers. Unfortunately, the disease has affected millions of people in the tropical and subtropical regions of the world labouring under the synergistic effects of poverty, malnutrition, social rejection, and concomitant other infectious diseases. Our country has the unique distinction of having the largest number of people afflicted with the disease.

Leprosy continues to be an epidemiological and microbiological puzzle. Doctors including dermatologists in general are not professionally involved and interested and dedicated to the study of the multifaceted problems of the disease. Although mycobacteria leprae was one of the first to be linked specifically to a human disease, before even mycobacteria of tuberculosis, the study of the pathogenesis has been till recently severely restricted because the organisms cannot be cultivated or the disease transmitted to experimental animals.

Here are a number of problems posed on the several aspects of the disease :-

- (1) Why leprosy continues to be a dominantly rural disease ?
- (2) The relation of cutaneous pigmentation to susceptibility and resistance to the disease.
- (3) Source of contagion and mode of transmission, person to person, or insect or mammalian vectors not proved.
- (4) The high attack rate in children and the high rate of spontaneous cure in them, each other contradict.
- (5) The immunology of leprosy is conundrum. Hyper gamma globulinaemia in lepromatous leprosy with plenty of bacilli in the tissues and negative lepromin reaction. Normal gama globulinaemia in tuberculoid cases with fewer bacilli and positive lepromin reaction.
- (6) The unique predilection of mycobacteria leprae for nervous tissue with differing tissue reaction in lepromatous leprosy and the tuberculoid type.
- (7) On the preventive side, the relative merit, feasibility and desirability of chemoprophylaxis versus BCG vaccination has to be reviewed and considered.
- (8) On the therapeutic side, the only drug which has been widely used is dapson. It requires 4 to 8 years or longer for clinical arrest in lepromatous leprosy and two to four years in the tuberculoid type. There is no assurance of the destruction of the last viable bacilli and freedom from relapse. The most optimistic reports of dapson treatment have come from countries where.
 - (a) The lepromatous tuberculoid ratio is low,
 - (b) when the incidence of prolonged and severe reactive episodes is low,
 - (c) when the rate of spontaneous regression is high,
 - (d) when the occurrence of eye complication is infrequent. These observations have a positive correlation to the deeply pigmented peoples of the developing countries.
- (9) Dapsone treatment of the disease has been bedevilled by a most disturbing reaction. Erythema nodosum leprosum (E. N. L.) usually occurring in lepromatous leprosy and characterised by severe local and constitutional signs and symptoms of hyper sensitivity of the Arthus type.

According to Turk, the defence mechanisms against Myco bacteria are mainly associated with cell mediated and not circulating anti body mediated response. In lepromatous leprosy the cell mediated responses are too poor to eliminate the bacilli. But circulating anti body production is not impaired. The E. N. L. reaction is the result of immune complexes caused by the interaction of Mycobacterial antigens with the circulating anti body with complement fixation. It is a moot point whether such an impairment cell mediated immune response is due to the lepromatous leprosy or whether the impairment predates and predisposes to the lepromatous form. In this connection, a genetic factor is postulated. An antigen named the Australian antigen is found in the sera of Australian Aborigines, Pacific Islands, Filipinese, and South East Asian population but is rare in Europe and America. It was reported that this antigen is more common in patients with lepromatous leprosy than in patients with the tuberculoid form or in non-leprosy controls and higher in males.

Now there seems to be a break through in the unpromising therapeutic horizon with the advent of the new Riminophenazine compound G. 30.320 (B 663) synthesised by Barry of Dublin. The drug has received extensive trials and seems to be the most promising agent. It is both antileprotic and anti-inflammatory and the recommended dosage is 100-400 mgm. daily by mouth. The one drawback of the drug is the tendency for the substance to be deposited in the skin particularly in lesions where it turns the skin red and makes it hypermelanotic. Apropos of this peculiar hyper melanotic effect on the skin, it may be worthwhile to try the drug for vitiligo.

Experimental Leprosy.

1960 is a landmark in the otherwise bleak history of futile attempts over the years to cultivate mycobacteria leprae in vitro. During the past decade, important advances have been made in the field of experimental leprosy. Quantitative techniques using Myco Lepramurium provided the first model for developing an indirect method for distinguishing dead from living bacilli based on morphological differences observed by Electron microscopy and stained smears with Ziehl Neelson. But the most important advance is the successful but limited and localised growth of Myco bacteria Leprae in the foot pads of mice and rats and later the more substantial and generalised multiplication of the organism in immunologically deficient mice (Thymectomised and irradiated) and in the immunologically deficient animals the infection eventually resulted in a disease replicating that of lepromatous leprosy in man including the involvement of peripheral nerves.

The experimental infection has provided new information of great importance concerning the properties of mycobacteria leprae.

(1) During the logarithmic phase of multiplication in the foot pad of mouse, a generation time of 13-25 days has been observed. The organisms start multiplying only after a lag period of 90 to 120 days.

(2) The mouse foot pad technique has been used to screen anti leprosy drugs, and their minimal inhibitory concentration. Assuming that it is permissible to extrapolate the findings in the mouse foot pad infection from mouse to mouse, they

suggest that a daily dose of 1 mg. of dapsone would be effective in man which will also reduce the incidence of reaction.

(3) Drug resistant strains can also be investigated through mouse foot pad infection.

(4) The foot pad infection technique provides an experimental model for investigating the prophylactic effects of various vaccines. Thus, recently, Shepherd and Ribí from Atlanta have shown that vaccination with the cell wall of BCG incorporated in an oily base is as protective as living BCG weight for weight against infection with *Mycobacterium leprae* in the foot pad of mice.

(5) The enhanced infection in thymectomised and irradiated mice provides a more rapid method for screening drugs against the organism.

(6) The problem of relapse even after years of therapy with dapsone conjectured to be due to inaccessibility or invulnerability of *Mycobacterium leprae* within Schwann cells or arrectores pili muscles may be investigated in generalised infection of mouse by drugs labelled with radio-active isotopes and it may be possible to determine both the distribution of the drugs and of degenerate and normal bacilli at an intracellular level.

(7) The route of infection and the source of infection, whether man, insect or mammal may be investigated with the mouse, foot pad infection, since this technique could provide for the first time a reliable method of identifying as *Mycobacterium leprae* any non cultivable acid fast bacilli isolated from potential vectors. Since both mouse and rats are susceptible to the human *leprae* bacillus, it is possible that wild mice and rats in leprosy endemic areas could be infected with *Mycobacterium leprae* and thus be a source of human infection.

Leprosy is a challenge to the biologists and medical scientists of the world particularly of countries like ours where the disease is endemic affecting millions of human beings. Continuing, devoted, painstaking research, both on the organismal and therapeutic fronts should be carried more vigorously. Side by side, the man and his environment have to be studied with great scientific precision. Norway is a signal example of a country in which leprosy which was once common with predominant Lepromatous tupe has disappeared without drug therapy or segregation.

It is an unedifying commentary on the medical profession in our country that while voluntary agencies, Christian and Japanese Missions have been devotedly working in the field and laboratory for the study and control of this disease, doctors in sufficient numbers are not coming forward to implement the National Leprosy Programme. Dermatologists in teaching and non teaching hospitals should take an abiding interest not merely on the therapeutic side but on the epidemiological and immunological aspects of the disease. Ladies and gentlemen, I may tell you that in this my rambling address, I have merely made up a bunch of other men's flowers and have provided nothing of my own but the string to bind them.

References

1. Marples Mary. J; (1965) The ecology of the Human Skin Springfield. Ill. Thomas.
2. Rees; R. J. W; New prospects for the study of leprosy in the laboratory Bull W.H.O. 40 : 788.
3. Cohen, Sydney; Skin-Brain barrier, Arch. Derm. 83 : 738.