UNIVERSITY OF JAFFNA
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INAUGURAL LECTURE

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COMPANION STUDIES IN CLINICAL MEDICINE

Introduction

The lecture by Professor Nadarajah Sreeharan on ''Companion Studies in Clinical Medicine'' is the fourth in the series of Inaugural Lectures established by the University of Jaffna. The lecture is delivered by the newly appointed Professor to the academic community, special invitees and the University Council Members.

Professor Nadarajah Sreeharan in his Inaugural Lecture speaks primarily as a Physician directly involved in the delivery and health care in the Community.

This lecture poses and presents ways and means to answer, the problems encountered in conducting scientific studies within the frame work of clinical Medicine.

Prof. A. Thurairajah
Vice-Chancellor
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1990. 12. 28.

Vice Chancellor, Colleagues, Students, Ladies and Gentlemen. Let me take this opportunity to thank the Vice Chancellor and the Council of the University of Jaffna for granting me the honour of occupying the Foundation Chair in Medicine of this University. I have accepted this post acutely conscious of the responsibility that it carries. It is customary in Inaugural Lectures for the speaker to select topics relevant to his speciality, highlighting areas of personal interest. I have not attempted to deviate from this practice and as a clinician cum scientist I would like to pose the problems encountered and the methods adopted to conduct scientific studies within the framework of clinical medicine.

Role of an academic clinician

The role of an academic clinician also encompasses that of a teacher, a research worker and an administrator. *(Fig. I)*

However, it is his role as a clinician that remains central. A Professor of Medicine is primarily a Physician who is directly involved in the delivery of health care in the community. All his other roles are centred or based on this primary function. His role as a teacher involves the transfer of knowledge and skills necessary for health care to the undergraduate and postgraduate trainees; his research usually involves studies directly or indirectly relevant to his role as a clinician and as an administrator he organises and administers his department and clinical unit towards the above objectives. Maintaining a judicious balance between these varying roles is of prime importance. A clinician in a peripheral non - teaching hospital has limited roles as an administrator, teacher and researcher, However, clinicians in teaching hospitals, particularly those attached to University Units, have significant contributions to make towards teaching, research and administration.

Clinical work load in Teaching Hospitals of the developing world

The main restraint to the academic role of a clinician stems from the clinical work load in teaching hospitals of the developing world (and Jaffna is no exception). The clinical responsibility of academic units is far in excess of what is seen in such units in the developed world and is unacceptable by any standards. A summary of the service function provided for 1983 by the University Medical Unit in the Teaching Hospital illustrates this point - a total of 3809 admissions, 2666 clinic referals and a total clinic attendance of 14052. This is not particular to our unit and is representative of other University as well as non University Units. The reason for this

high clinical load lies in the nature of the position the Jaffna Hospital holds in the context of health care of the community. A glance at the distribution of all the hospitals in the Jaffna District and the major hospitals in the adjoining Districts (viz. Kilinochchi, Vavuniya, Mullaitivu and Mannar) highlights the paucity of specialised centres in the area. The Jaffna Teaching Hospital therefore does not function solely as a referal centre, as is the case in many of the teaching hospitals of the developed world. It caters to a population of around a million and is in fact the primary centre for around 200,000 people living in and around the Jaffna Municipality. Many outside the area too use it as a primary centre by passing in the process several local hospitals.

Solution

What then is the solution? If you ask me if this involves a dramatic change in the system so that the hospital solely functions as a referal centre in the tradition of the western world, you would be surprised that my answer is a firm and emphatic 'No'. This is because, although the system is disadvantageous in one aspect, it does confer certain other distinct advantages- firstly, the pattern of diseases in the hospital represents more closely the disease pattern in the community than in the case of a specialised referal centre. Thus, the clinical training in the teaching hospital becomes more meaningful and community oriented; secondly, this system enables a closer contact between the community and the clinician. One of the main criticisms of academics has been the lack of close communication with members of the community. Academic clinicians in the teaching hospitals of the west function as super grade specialities far removed from the patients under their care. The patients no wonder turn to their general practitioners for that close personal touch. However, clinical medicine is not only a science but also an art – viz. the art of healing. The academic clinician in the developing world is therefore given the rare opportunity of combining both these aspects of clinical medicine. He could, if he so wishes, function as an academic, a specialised clinician and a general practitioner, all rolled into one, maintaining a close association with the community.

It is therefore my view that the teaching hospital should continue to function both as a specialised referal centre as well as a primary centre for a selected group of the community – eg. the population in and around the Municipal limits. An attempt should be made to reduce the work load not by changing the system but by imposing a restriction in the numbers. This could be done by improving and upgrading the peripheral hospitals which would then function as the primary centres for the majority of the people who are then referred to the teaching hospital only when the necessity arises.

'Companion studies'

How then does an academic clinician, given the context of his clinical work load and his combined role of a specialist Physician and a general physician, carry out his other roles, particularly those of a teacher and research worker. This could be effectively done by combining his other roles with that of his primary clinical role (Fig. II).

Thus, teaching and researching become companion roles to the academic clinician. In all the clinical disciplines in our medical school, over 90% of teaching is carried out in this manner. Didactic lecture hall teaching and tutorials account for only a minute proportion of the learning experiences provided for the students. This is advantageous not only to the clinician but also enables the student to receive a practical and clinically oriented training. A similar process should be followed in researching too, so that the scientific studies are conducted by the clinician within the framework rather than outside his clinical role. I have termed such scientific studies as "Companion Studies". The clinician should always be conscious of his primary obligation to the patient. Ethical consideration towards the patient should always be foremost in the mind of the researching clinician. Scientific studies should not in any way compromise his care to the patient. Information obtained from such studies should on the other hand enhance his patient care. Thus, the companionship of scientific studies and clinical medicine is a two way process (Fig. III.)

Data are gathered from the patients, analysed and after analysis the information is issued directly or indirectly to augment and enhance health care not only to the individual patient but to the community at large.

Scientific studies may be broadly classified into three groups:

a) Biomedical research

b) Applied or clinical research

c) Health service or Operational research

Although the first two categories are well recognised, the third has been a recent though important addition. It forms a priority area for the World Health Organisation. It involves researching into health care systems and is of particular relevance to the developing world. The discovery of Insulin, for example, is no doubt a milestone in biomedical research but is of little value to a diabetic in a remote village in Vavuniya whose main problem often involves inadequate supplies of Insulin and insufficient storage facilities. Researching into the ways and means of improving supplies of Insulin to the peripheries and into the storage properties of it would form an appropriate health service research protocol.

I wish to present some of the studies conducted in Jaffna since the inception of the University Medical Unit and also some aspects of research carried out by me elsewhere, highlighting the format of Companion studies.

Documentation and analysis of hospital admissions

One of the prime requisites for satisfactory clinical research is an appropriate system of documentation of medical records. Unfortunately, this is one aspect that is neglected in many hospitals of the developing world inclusive of Jaffna. We have attempted to overcome this deficiency by a system whereby a summary of data from all patients admitted to the Unit are indexed and filed. An example of a "summery sheet" is illustrated (Fig. IV) and forms the basis for many of our clinical studies.

A study of the admissions to our Unit (1) highlighted certain aspects significant to health care planners of the region. It was noted that Geriatric patients formed 17% of all admissions. Geriatrics should eventually be developed as a separate speciality as in the West and provision should be made for the creation of a Department of Geriatric Medicine at some future date. With the change in the social and cultural status of the Northerner, particularly with the emigration of the younger generation for political and economic reasons, care of the elderly in the community would become a major strain on the health service of the region. This should therefore be anticipated and adequately planned for. This study also showed that 26% of admissions were unwarranted and could have been managed outside the teaching hospital – viz. at home, at the local hospital or clinic. The identification and reduction of this component of the admission load should considerably ease the work load of the Unit. About half the admissions were resident within five miles of the hospital. This component will possibly remain unchanged and would form the basis for the primary care function of the hospital that I have postulated. However, 18% of admissions were from over 20 miles away, by - passing several local hospitals where appropriate therapy could have been obtained. This population should be educated to attend the local hospitals and be referred only when the necessity arises. Only 12% of all admissions were referred to the hospital by a medical officer

The clinician sometimes is preoccupied with the concept of 'disease' that the true concept of 'health' becomes obscured. Health is not merely the absence of disease but concerns perfect physical, mental and social well being. It is therefore prudent to identify in a patient not merely the disease pattern that he is afflicted with but other problems related to his physical, mental and social status as well. The clinician thus should not be merely disease oriented but rather problem oriented. We evaluated the extent of

the health problems in patients admitted to our Unit (2). We noticed that most patients had multiple health problems (range 1 - 6; mean 2.56 problems / patient). 95% of the problems identified were active and over 50% of these were also chronic, highlighting the need for efficient follow up care systems (eg. out patient clinics). It is therefore essential for planners to pay particular attention to the organisation of out patient departments and clinics in the health service structure as much as or perhaps even more than the attention given to the inpatient and acute care facilities. This problem oriented approach to medical diagnosis is not only beneficial to patient care but is also of value in medical education. We therefore now use a Problem Oriented Medical Record for student training (Fig. V). The students identify the problems encountered in the patients, institute an appropriate plan of action and assess the progress. Such a format is invaluable in the evaluation of student trainees and forms the basis of a system of 'in course assessment' in our Unit.

An analysis of the pattern of diseases in the community is essential as it should form the basis for the curriculum of any discipline. Unfortunately, the curricula of many of the medical schools of the developing countries are carbon copies of the curricula from the schools of the western world (3). But the pattern does not quite fit. The problems encountered by the physicians of the developing world are in many respects different from those seen in the developed nations. The admissions to our Unit over an eight month period (4) are summarised in Tables 1 & 2. 1822 health problems were identified in 1177 patients. The largest number of disorders (15.5%) were encountered in the cardiovascular system. Thus, a substantial morbidity and mortality from cardiovascular diseases is not confined to the west alone but appears to be a universal problem. Infective agents were responsible for around 25% of all disorders seen in the Unit. The common individual diseases encountered were Anaemia (17%), Bronchial asthma (7.7%), Ischaemic heart disease (6.9%), Cardiac failure (6.8%), Pneumonias (5.9%), Hepatic Amoebiasis (5.9%), Viral fevers (5.3%), Dysenteries (4.6%), Hypertension (4.4%) and Enteric fevers (3.1%). It is significant that infections via the gastrointestinal tract accounted for almost 20% of patients admitted to the Unit. This further higlights the importance of preventive measures in health care. Paying particular attention amongst other measures to water supply, food and sanitation would result in a marked improvement in the health status of the community. On account of the high prevalence of infective disorders in the community, facilities for the diagnosis and treatment of these diseases should be improved. The Faculty should develop and provide expertice in the Laboratory diagnosis of infective diseases and an institute akin to the Medical Research Institute in Colombo should be established in the near future.

This study also showed that mental disorders and poisonings each accounted for one in twelve of all admissions.

What is a place of single case studies in the context of scientific research? It is, I believe, apt to postulate that since clinical medicine is in itself a science of its own accord, the analysis of every case is in reality a miniature scientific study. It is on the basis of this day to day scientific approach that senior clinicians built and accumulated their vast 'experience'. But it is a tragedy that due to the lack of documentation, many of such 'experiences' have been lost to generations of succeeding clinicians. Thus, documentation of the case reports should form an essential aspect of clinical research. Such case reports may highlight features that may be of value both in the diagnosis as well as in the treatment of diseases. For example, we have recently identified possibly the first case of Cerebral Mucormycosis in Sri Lanka (5). Its existence has been known for many years in other parts of the world and I am quite certain may have gone undiagnosed and unnoticed in Sri Lanka. Reporting of the case should instruct clinicians to be aware of this highly fatal condition. Our patient was a young girl who presented with diabetic ketoacidosis and features of a cavernous sinus thrombosis (Fig. VIII).

The clue to the diagonsis of mucormycosis arose from the presence of a blood stained nasal discharge and examination by the ENT surgeon revealed the characteristic ulceration of the nasal mucosa caused by the fungus. The diagnosis was confirmed histologically (Fig IX) and on postmortem examination. The disease is caused by a fungus which is normally a saprophyte and under conditions of depressed immunity, particularly diabetic ketoacidosis, invades the cavernous sinus through the nasal mucosa and causes diffuse cerebrovascular disease.

The above case illustrated an aspect of diagnosis whereas the following case report highlights an aspect of therapy Titled "Successful management of cardiac tamponade in two cases of leukaemia" (6) it described the management of two leukaemic patients who presented with cardiac tamponade, a near fatal complication, and were resuscitated by vigorous therapy including pericardial aspiration. We proposed that in view of the variable and occasionally satisfactory prognosis of some varieties of leukaemia particularly of the chronic monocytic type, even near fatal complications should be vigorously treated

Having identified the basic pattern of admissions and disorders in the Unit and the necessity of reporting individual cases whenever the opportunity arises, the need then remains for the identification and indepth study of some of the common problems encountered, particularly those of relevance to the community. I wish to illustrate with three such examples.

(a) **Antibiotic resistance of bacteria** (10)

We have seen that infective diseases form a substantial proporsion of diseases encountered in a medical unit. In most instances, specific therapy with appropriate antibiotics still remains the only opportunity to eradicate the infective agent from the patient and eventually to prevent its spread in the community. It was therefore with alarm that one noticed the prevalence of antibiotic resistance of bacteria in the community, necessitating the evaluation of its extent (7)

Two groups of patients were studied:

(a) Pathogenic bacteria from patients (n = 40) with urinary tract infections

(b) Commensal bacteria from the intestinal tract of patients (n = 84) presenting with unrelated disorders.

The organisms isolated were gram – ve bacteria belonging to the group Enterobacteriaceae. The antibiotic resistance of these organisms were determined in vitro (Table 3). It is seen that the bacteria were resistant in high proportions to some of the antibiotics and less so to some of the others. I have classified the antibiotics into two groups (group I & II) on the basis of this pattern.

What is more ominous than just the high prevalence of resistance is the fact that many of these antibiotic resistance traits could be transferred to other sensitive bacteria leading to a rapid spread of antibiotic resistance in the population. Such transfer could occur not only within the body but also outside it. eg in the hospital environment and in the contaminated well water of the peninsula. The extent of this transmissibility was analysed both in vivo and in vitro (8). The in vitro study revealed that of the 134 strains of bacteria isolated, 32 strains (24%) exhibited transmissible antibiotic resistant traits, particularly to the common antibiotics such as Ampicillin, Chloramphenicol, Tetracycline and Sulphonamides. In the in vivo study, 18 of the 36 patients studied (50%) showed evidence of transmissible traits - a high proposion indeed!

What is the cause for this high prevalence of antibiotic resistance? I believe it is no doubt due to the abuse and overusage of antibiotics in the community. Here, both the medical profession and the public should largely share the blame. It is sad but true that far too many patients are receiving antibiotics both within and outside hospitals. A Study on the antibiotic prescribing habits in Jaffna Hospital(9) showed that 48% of the patients admitted receive some form of antbiotic; some of them receive multiple antibiotic regimes and many of them for prophylaxis alone (Table 4). As cross infections in the hospitals increase, more and more medical practitioners are resorting to prophylactic antibiotic therapy. This in turn

leads to further propagation of resistant infections and the vicious cycle goes on. The study identified the commonly used antibiotic as Penicillin (46%), Ampicillin (27%), Streptomycin (19%), Tetracycline (16%) and Chloramphenicol (10%). The resemblance of this pattern to Group I of the previous study is clear giving credence to the postulate that it is the overusage of some antibiotics that leads to the development of resistant strains. There is another sad facet to this story - and that is the role of the public in antibiotic abuse. A preliminary study conducted in one of the Pharmacies in Jaffna confirmed our suspicion that antibiotic usage and self prescriptions are rampant. Many drugs particularly Tetracycline, Ampicillin and Sulphonamides are sold without prescriptions and in some instances involved the sale of a single tablet or capsule of an antibiotic. Such abuse is detrimental not only to the user but more significantly to the community at large by inducing the development of transmissible antibiotic resistant traits. I am not being too pessimistic when I visualise the ominous prospect of an epidemic of some infection with an organism resistant to all known antibiotics. I wish to suggest that both at the Teaching Hospital and at the community level, a definitive policy of antibiotic usage is enforced with some control over its abuse.

(b) Anxiety neurosis and the chronic hyperventilation syndrome

Recent work in the division of Psychiatry of our faculty has shown that Jaffna has the highest suicidal rate in the world (10). This possibly reflects the stresses and strains existent in our society for some years. To this if one now adds the recent political turmoil, we have in our midst an ideal breeding ground for anxiety and tension. The extreme manifestation of this may well be a suicidal attempt but for every suicide attempted there ought to be thousands of others with minor manifestations of anxiety. Many of these patients do not present to the Psychiatrist but do so to the General Physician with some Physical symtoms. We have identified (11) one such presentation which appears to be quite common in Jaffna - viz. chronic hyperventilation syndrome. These include patients who manifest as their characteristic symtom a sense of suffocation or respiratory distress punctuated by a deep sigh. Many of them are often diagnosed as asthmatics or even as cardiac patients particularly as the ECG may show some non specific T wave changes in the inferior and anterior leades. Although the disorder has been labelled the chronic hyperventilation symdrome, the symptom of respiratory distress is so characteristic that a specific label of chronic sighing syndrome (பெருமூச்சு - syndrome) is more apt (12). It is common in the younger age group (mean age of 33 years) and is more than twice as common in the females than in the males. In addition to the deep sighing, the patients obtain some relief from their distress by either burping or yawning. Chest pain and palpitations are the other prominent symptoms. Non specific ECG changes are seen either in Lead III in the form of flat or inverted T waves or in the anterior chest leads in

the form of an upright and discordant T in V_1 and T wave inversions extending from $V_1 - V_4$ This specific syndrome is so prevalent in Jaffna that it should be correctly identified and appropriate therapy instituted by reassurance and (ஆத்மீக) β blockade and anxiolytic agents.

Many of these patients tend to fall into one of several sub - groups each of which is dependent on and identifies an underlying socio - economic problem in the community (13). I wish to mention three such examples (the terminologies are mine and are self explanatory):

i. "Pre and Post advanced level" neurosis involves young girls and boys presenting just before or soon after the advanced level examination or the release of the results of the examination.

ii. "Husband in Europe" neurosis is seen in young married females whose husbands have sought political asylum in many of the European countries leaving a group of lonely and anxious wives back in Jaffna.

iii. "Returned from Singapore" neurosis occurs in young females of poor economic status who at enormous expence had gone to Singapore to seek employment and having found the situation culturally and emotionally difficult to cope, had returned with classical anxiety neurosis.

Recently, the syndrome has been noticed in another sub - group - viz. University students. I hope it will not soon infect the University teachers !!

(c) Self poisoning with the seeds of Yellow Oleander (Thevetia peruviana)

Most cases of attempted suicides in Jaffna are cases of self poisoning with insecticides – a reflection of easy availability and accessibility. We have recently encountered (14) another pattern of poisoning that appears to be specific for this region – viz. that of Yellow Oleander ('Manchal Alari' in Tamil). Such poisoning in large numbers is a recent trend and illustrates the impact of news items on the behaviour pattern of a community. I had not seen a single case of such poisoning in the South of Sri Lanka or during the first two years of my stay here. However, subsequent to a news item in the local Tamil daily – viz. Eela Nadu - of an attempted suicide by two girls by the ingestion of these seeds, we have experienced a phenomenal increase in poisoning by this agent. The mean age of the patients was 22 years (range 13 – 40) and the female : male ratio was (range 2 : 1. The number of seeds ingested varied from ½ to 15 and the mean time interval between ingestion and admission to hospital was 6 . 3 hours (range ½ – 16 hours). The presenting symptoms were vomiting, dizziness, palpitations, diarrhoea and drowsiness. The significant abnormalities were in the cardiovascular system and in addition to the characteristic

saucer shaped depression of the ST segment (as in digitalis toxicity) varying types of cardiac dysarrhythmias were encountered including sinus bradycardia with sino atrial block, first and second degree heart blocks, junctional rhythms, atrial and ventricular ectopics and ventricular fibrillation. The only fatality was seen in a 20 years old male who had ingested 15 seeds. The poison is very likely a cardiac glucoside, as is seen in many members of the Family Apocyanaceae to which this plant belongs. Treatment should be instituted along the lines of digitalis toxicity. It is paradoxical that over 200 years after William Withering discovered the beneficial effect of foxglove in cardiac disease, we in Jaffna are experiencing the deleterious effect of a similar plant due to its cardiac toxicity.

I have so far illustrated examples of companion studies conducted mostly within the framework of clinical medicine. These have taken the form of analysis of basic data and common problems encountered in the community. I believe that such studies are essential to lay the foundation for further scientific research into the health problems of the community.

Biomedical research and the clinician

What then is the position of biomedical research in the academic clinician's research programme? There is no doubt of the utmost importance of basic scientific research, however irrelevant it may seem at that time to direct patient care. It therefore appears reasonable to expect even the busy clinician to contribute to biomedical research. This could be approached in one of two ways (Fig. X A, B). Firstly, a research 'companionship' could be established with one or more non clinical disciplines specialising in basic science or more ideally the clinical department could be developed into two sections - a clinical section and a basic research section. The first inter - disciplinary approach is welcome because it also helps to promote integrated research training programmes leading to postgraduate clinical research degrees. Such links with the basic science disciplines need not be confined to within the Faculty but could also extend to include the natural and even the social sciences.

I wish to illustrate three such links we have attempted, one within the Faculty and two outside it.

The Department of medicine and the Division of Parasitology have linked to analyse Hepatic Amoebiasis, a disorder of high prevalence in Northern Sri Lanka. The diagnosis has until recently been based solely on clinical grounds. On the basis of analysis of cases over the past two years, we have postulated a set of diagnostic criteria to enable the clinical diagnosis to be more objective (15). The criteria are divided into Hepatic and Extra hepatic features. Varying number of points are allocated to the different criteria as illustrated in tables 5 & 6. A diagnosis of Hepatic Amoebiasis could be entertained either with (a) 10 points from the Hepa-

tic criteria alone or (b) 11 points overall with at least 5 points from the Hepatic criteria and 1 point each from the sub divisions of the Extra hepatic criteria. We have currently validating these criteria using specific serological tests.

A link was also established with the Department of Botany of the Science Faculty in the conduct of the bacteriological studies to evaluate antibiotic resistance as mentioned earlier. Occasionally the link involves a discipline that appears to be far removed from clinical medicine - eg. Department of Mathematics. Such a link with the Mathematics Department at Peradeniya was utilised to design a normogram to calculate the electrical axis of the heart from an Electrocardiogram (16, 17). Using the mathematical formula,

$$\frac{\text{Cos } \phi}{\text{Cos } 60 - \phi} = \frac{X}{Y} = R$$

where, x is the voltage of the complex in Lead I

y is the voltage of the complex in Lead II

ϕ is the angle made by the mean electrical axis with the horizontal

an R value is derived for ϕ at one degree increments.

This is illustrated (Table 7). Since such accuracy, although useful for research purposes, is not essential for clinical practice, the normogram has been further modified (Table 8) to include the R values at 10 degree increments. This modified normogram could be utilised to calculate the electrical axis with accuracy acceptable for patient care.

As illustrated earlier (Fig. X B), the ultimate objective of an academic clinical department should be the development within its own framework a biomedical research section. This section should have its own complement of scientists and research workers as well as clinicians working part time in biomedical research. It could incorporate in addition, research scientists from other disciplines within and outside the Faculty. With this objective in mind and as the first step the Faculty has approved the establishment of a Clinical Investigation Unit which I hope will function as the basic research section for all the clinical discipline of the Faculty. The establishment of such combind clinical departments is a priority area in many of the developed countries. One such department is the Department of Cardiovascular Studies at the University of Leeds in U. K. established under the auspices of the British Heart Foundation and where I was fortunate enough to be employed, The department basically

consists of a clinical section - Cardiology - and a basic science section - Cardiovascular Physiology. The trainees are given option of working full time in either of the sections or be attached to both sections. I chose the latter alternative and was initiated to one aspect of conducting companion studies . I shall briefly illustrate an area of interest.

Atrial receptors and Urine flow

Atrial receptors are stretch receptors situated in the low pressure chambers of the heart - viz. the atria. They are concentrated around the openings of the veins into the atria, particularly at the left pulmonary vein - atrial junction. Stimulation of these receptors (eg. when the atrium dilates) causes, among other effects, an increase in urine flow and a concomitant increase in sodium excretion. The atrial receptors have been identified in several animal species as well as in humans. For obvious ethical reasons one cannot attempt to stimulate these receptors in humans. Whenever the clinician comes across a problem which for ethical reasons or otherwise cannot be carried out in humans, he resorts to the use of animal experiments It should be stressed that animal experiments receive the same ethical considerations and that one should not resort to such experiments unless for definite scientific advancement. All efforts should be made to conduct such experiments with the minimum of discomfort to the animals. We used anaesthetised dogs as the experimental model in this instance and devised a method to stretch these receptors by introducing small balloons into the left pulmonary vein - atrial junctions and then distending them with saline. (Fig. XI). We evaluated the role of the renal nerves in the urinary response to stimulation of atrial receptors by analysing the changes in urine flow and sodium excretion in dogs with one kidney surgically denervated while the other kidney functioned as the innervated control (18). An example of an experiment is illustrated in (Fig. XII) An analysis of twelve experiments revealed that the increases in urine flow and sodium excretion were significantly greater in the innervated kidneys, showing clearly that the renal nerves are important mediators of this urine response However, a significant increase in urine flow and sodium excretion occured in the denervated kidneys as well, giving credence to an additional humoral mechanism. It was also observed that stimulation of atrial receptors resulted in a reflex increase in heart and it could therefore be argued with some justification that the urinary response seen in the denervated kidneys was the result of the increases in cardiac output and renal blood flow rather than due to an underlying hormone. In order to resolve this, we stimulated the atrial receptors in dogs after injection of Bretylium, Atropine and Atenolol, thus pharmacologically denervating the heart and kidneys (19). An experiment is illustrated in Fig. XIII. An analysis of eleven experiments showed that stimulation of atrial receptors without increases in heart rate resulted in an increase in urine flow but did not cause a concomitant increase in sodium excretion. It therefore is

clear that the hormonal agent is solely diuretic and the natriuresis seen in the absence of renal nerves was most likely due to a haemodynamic component.

Thus, here is a marvelous system of receptors, acting as watch dogs in the atria, and which on stimulation causes increases in urine flow and sodium excretion from the kidneys by three distinct mechanisms - the renal nerves, the hormonal agent and a haemodynamic component, each affecting the urine flow and sodium excretion in varying proportions. The atrial receptors therefore exert a significant physiological control over circulatory blood volume. This pathway is also of clinical importance in many pathological states - eg. in the diuresis that follows episodes of paroxysmal atrial tachycardia.

Such reflex pathways are numerous in the human body. They keep a delicate balance of all the physiological processes in the body - so that every action (here the stimulation of atrial receptors due to increased blood volume) tends to have a reaction in the opposite direction (here a reduction of the blood volume by increasing the urine output). What a resemblance to Newton's third law! Or could these reflex arcs of actions and reactions be carrying a message viz. the basis of the cosmic balance albeit in a miniature form within the body?

I finally wish to illustrate with studies conducted in another clinical cum research department in U. K. - the cardiac Research Unit attached to the Regional Cardiothoracic Centre in Leeds.

Evaluation of antiplatelet drugs

For the clinician concerned with the human body as a whole, researching into the platelets, the tiny cellular elements of the blood, affords the opportunity of realising the very basis of human existence - that not only the human body but this whole universe is made up of billions and billions of minute particles - living and dead - atomic and sub atomic - the very basis of modern physics and certainly the very basis of Vedantic philosophy.

The platelets are so tiny that one has to search very carefully to find them in a blood film under the light microscope (Fig XIV) However, the advent of the electron microscope and the scanning microscope showed that these tiny cells have elaborate structural and biochemicalsy stems (Fig. XV). The main function of the platelets is in the formationof a platelet clot to help arrest bleeding. But occasionally this physiological function gets out of hand and clots may form within the body leading to serious disturbances such as heart attacks and strokes (Fig. XVI). Such clotting may also occur when the blood comes into contact with an artificial surface - eg. heart valves, renal dialysis membranes.

Because of such deleterious effects and since biochemical pathways are abundant in platelet metabolism, search was made for drugs that could inhibit platelet function through such biochemical systems. Surprisingly it was found that the commonly used Asprin in low doses has a significant antiplatelet action. The other popular antiplatelet drug is Dipyridamole (persantin). It is now thought that antiplatelet therapy could significantly reduce platelet clots formation. We have demonstrated the beneficial effect antiplatelet regimes in three groups of patients susceptible to platelet clots- viz. patients with artificial heart valves (20), patients on renal dialysis (21) and patients with semoro - popliteal dacron grafts (22). Thus, on account of the possible beneficial effect of aspirin on cardiovascular morbidity, and mortality, the popular myth of "An apple a day keeps the doctor away" could be replaced by "An aspirin a day keeps the doctor away"! (Fig.XVII.)

Ladies and Gentlemen, I have attempted to present to you ways and means of conducting scientific studies within the framework of clinical medicine. Such studies could take the format of collection and analysis of clinical data and clinical case studies, may involve an inter and multi - disciplinary approach to clinical and biomedical research and should lead towards the ideal objective of a clinical cum research section with adequate supporting staff within the frame work of a clinical department. An academic clinician should be conscious of his role as a teacher and researcher but should in no way compromise on his primary obligation to his patient. The developing world offers an abundance of clinical material and scientific studies could and should be carried out by all clinicians as it provides an opportunity, perhaps the only opportunity, for international recognition of our medical fraternity in Jaffna.

Acknowledgements

I wish to acknowledge my indebtedness to the present and past members of my clinical Unit who by their dedication to patient care, teaching and research, are responsible in no small way for the basis of my talk today.

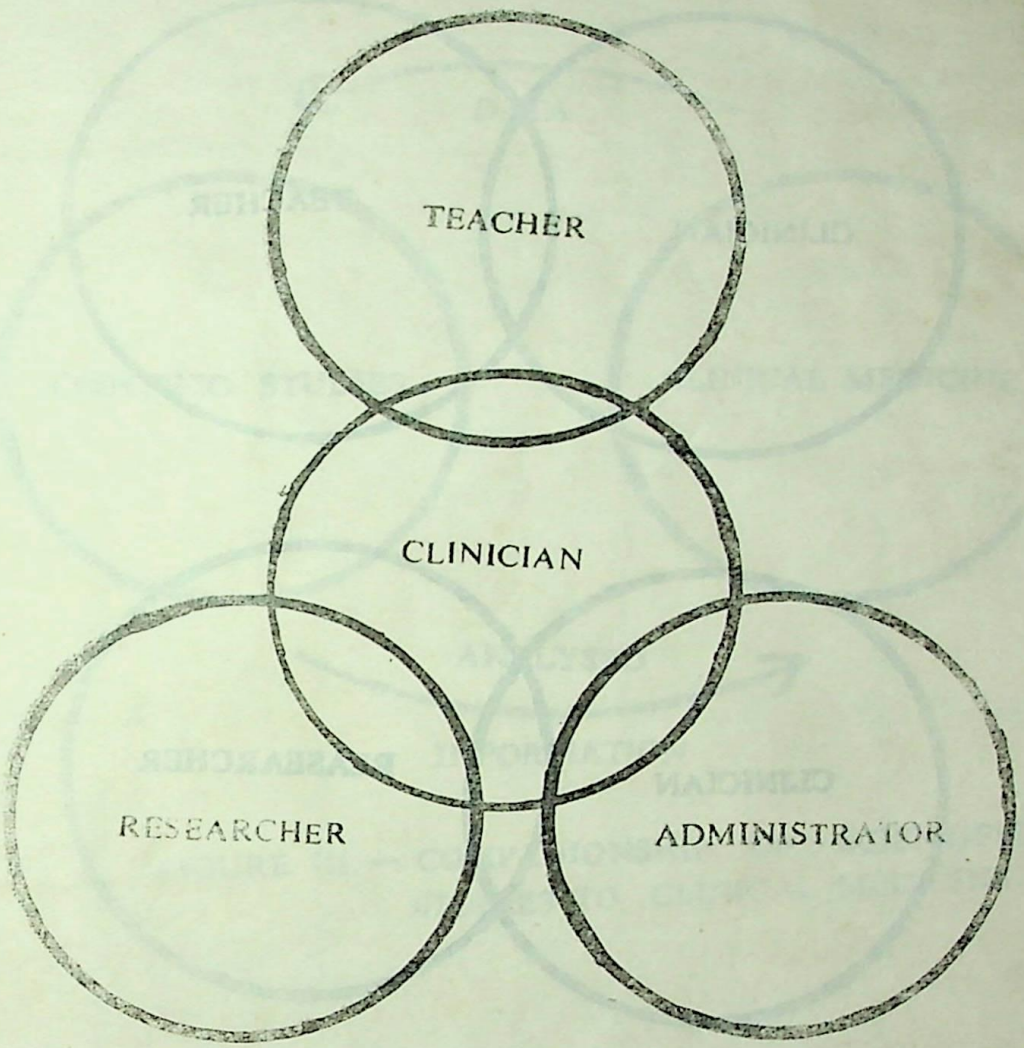


FIGURE 1 ROLE OF AN ACADEMIC CLINICIAN.

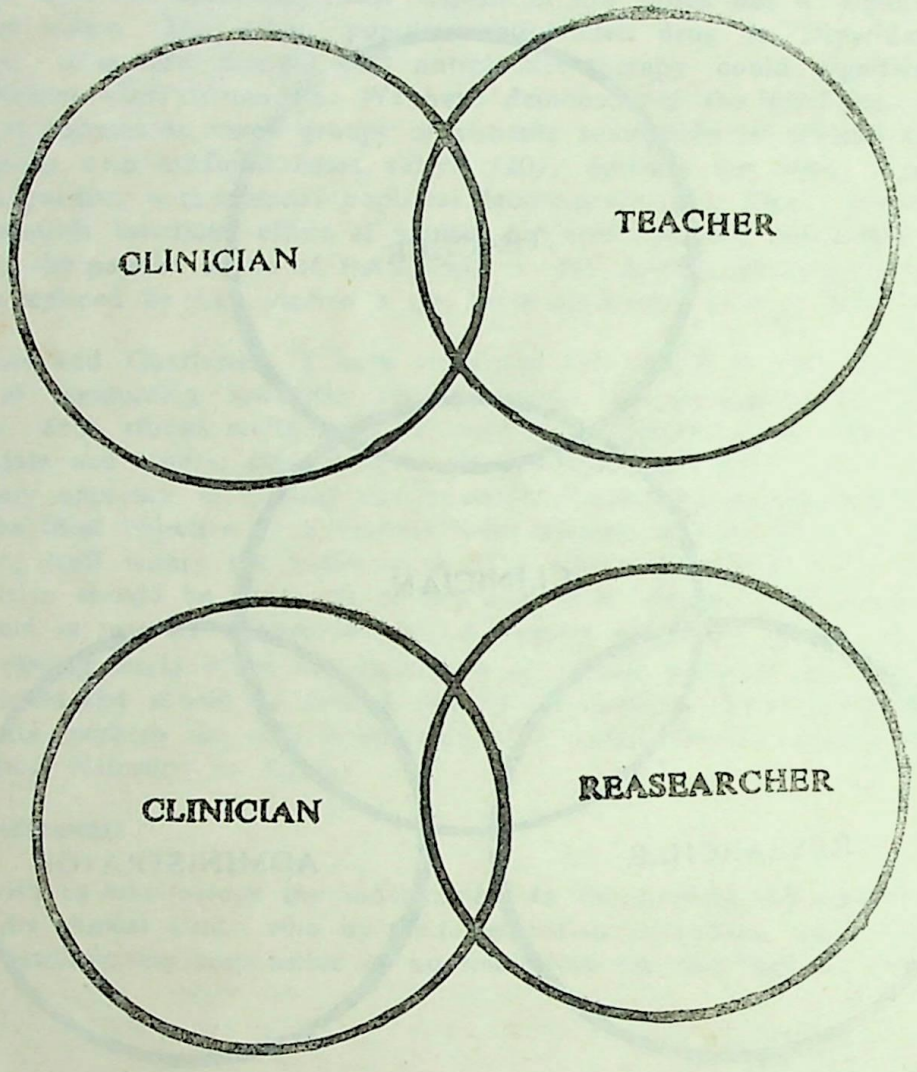


FIGURE II — COMPANION ROLES.

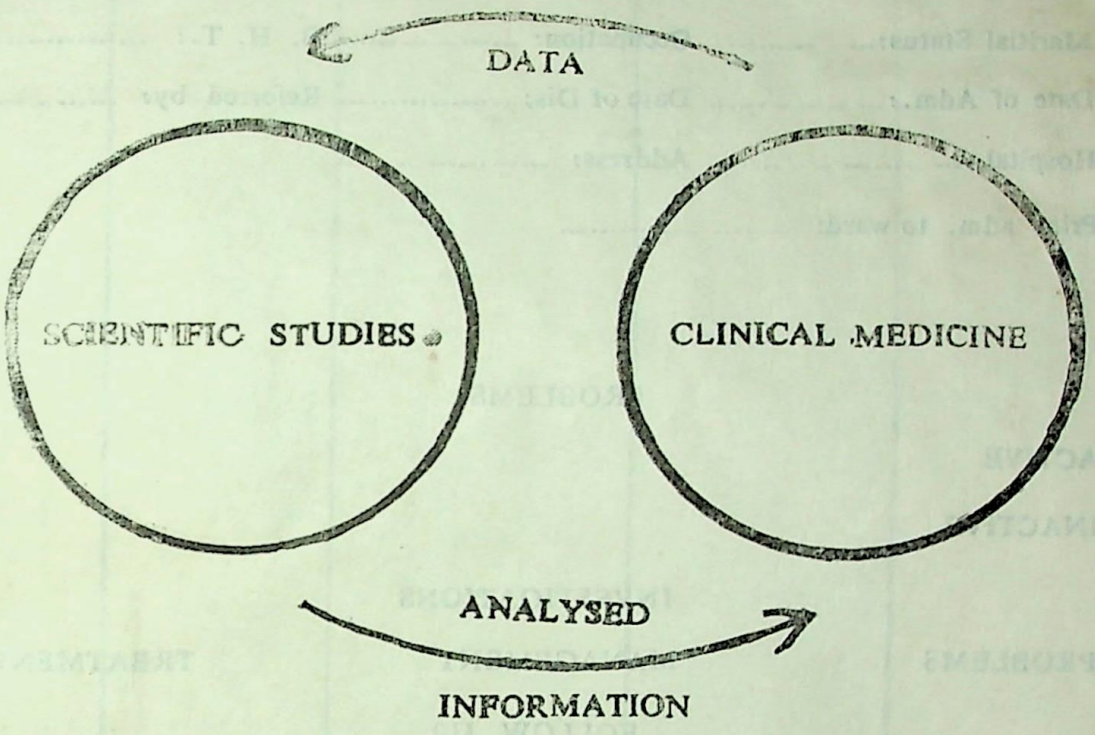


FIGURE III — COMPANIONSHIP OF SCIENTIFIC STUDIES TO CLINICAL MEDICINE.

DEPARTMENT OF MEDICINE

University of Jaffna.

Name: ..... Age; ... . Sex: ... .

Maritial Status:... ..... Occupation: ..... B. H. T.: .....

Date of Adm.:..... Date of Dis;..... Referred by: .....

Hospital: ..... Address: ....

Prior adm. to ward: ... .

PROBLEMS

ACTIVE

INACTIVE

INVESTIGATIONS

PROBLEMS MANAGEMENT TREATMENT

FOLLOW UP

Figure IV - SUMMARY SHEET

UNIVERSITY MEDICAL UNIT

Date	Problem List	Plan of Action		Progress Notes
		Investigation	Therapy	

Figure V — Problem Oriented Medical Record

Figure VIII- **Patient with rhinocerebral mucormycosis showing ptosis and periorbital oedema of the right eye and a blood stained discharge from the right nostril.**

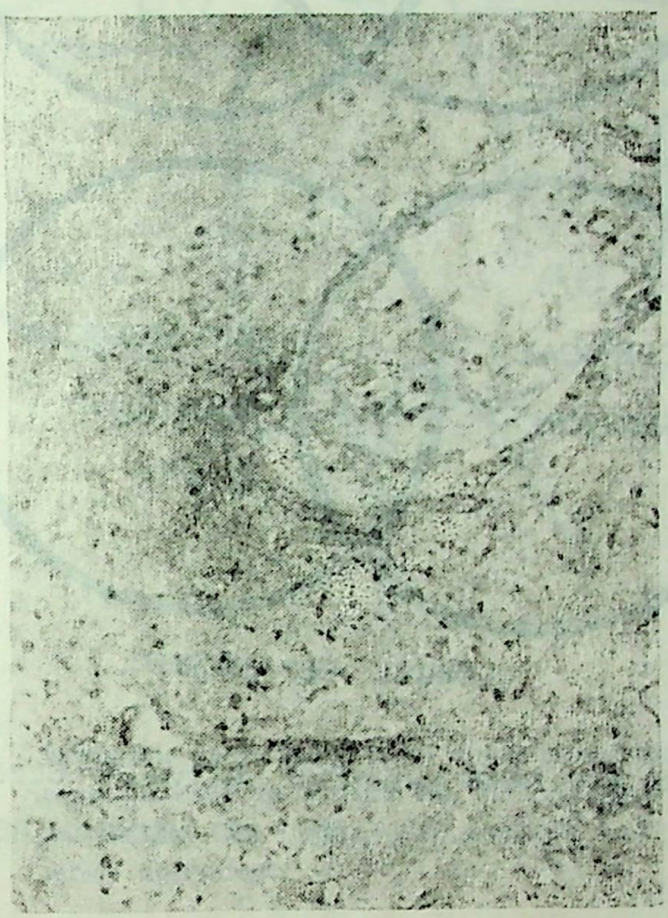
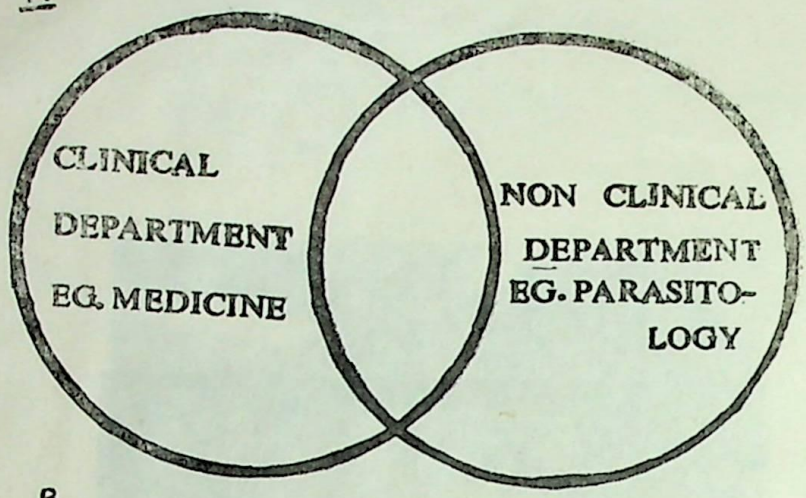
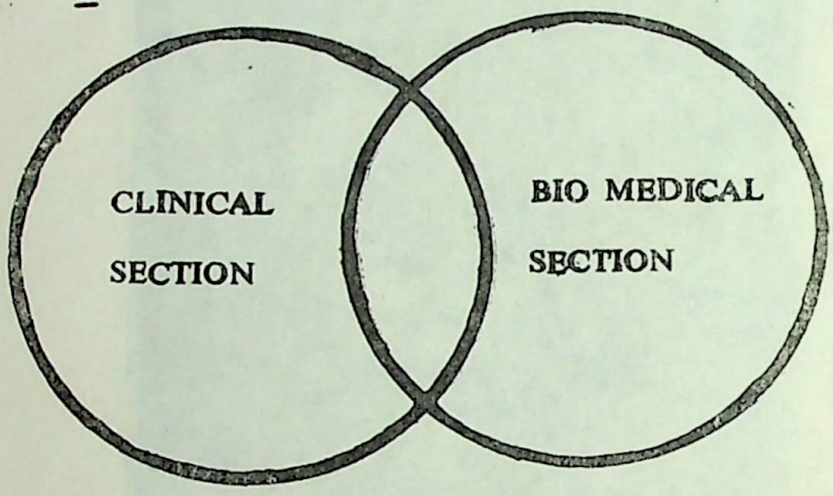


Fig. IX- Histological section of the Nasal Mucosa showing several hyphae of the fungus particularly around and invading a blood vessel.

A



B



CLINICAL DEPARTMENT

FIGURE X — COMPANIONSHIP BETWEEN CLINICAL AND BIO MEDICAL RESEARCH.

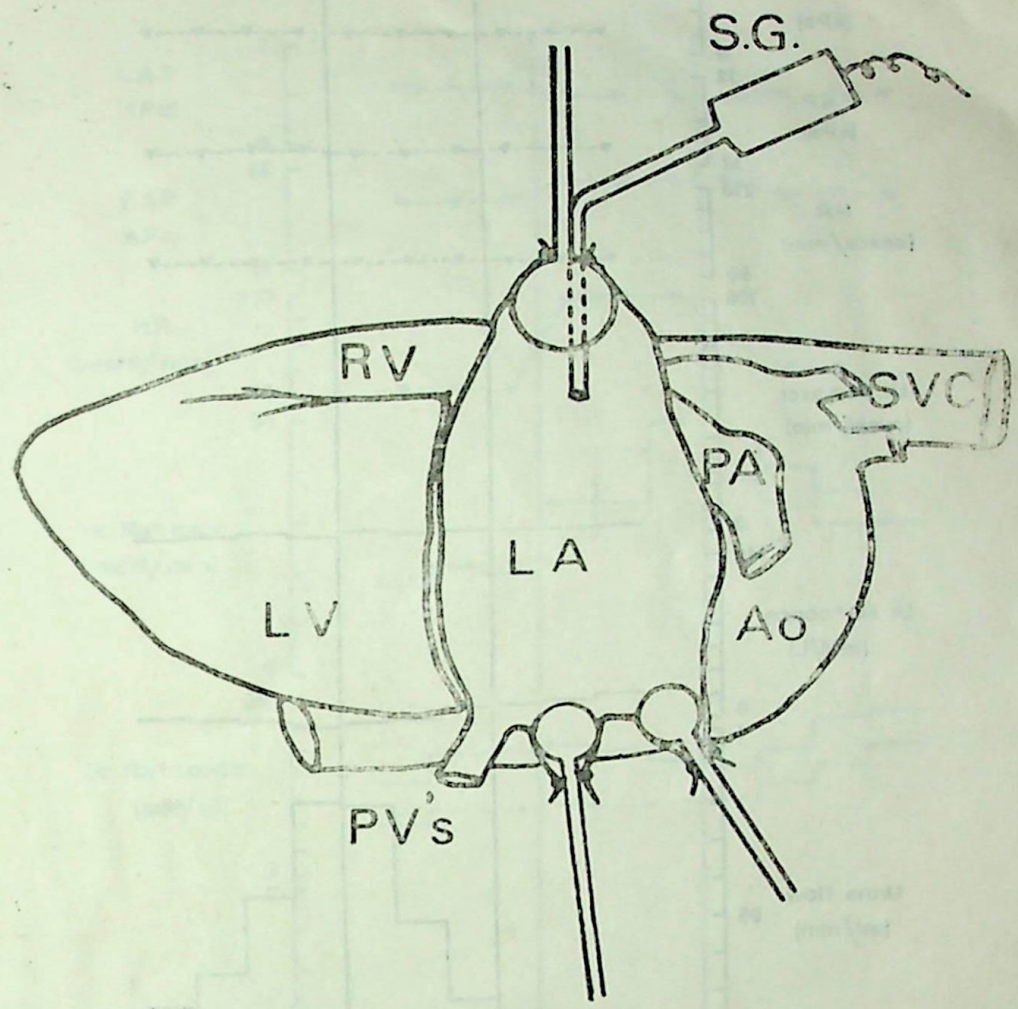


Figure: XI - Schematic representation of the experimental preparation used to distend the superior and middle pulmonary vein - left atrial junctions and the left atrial appendage.

LA - left atrium; LV - left ventricle;
AO - Aorta; RV - right ventricle;
PA . Pulmonary artery; SVC - Superior vena cava;
PV's - Pulmonary veins.

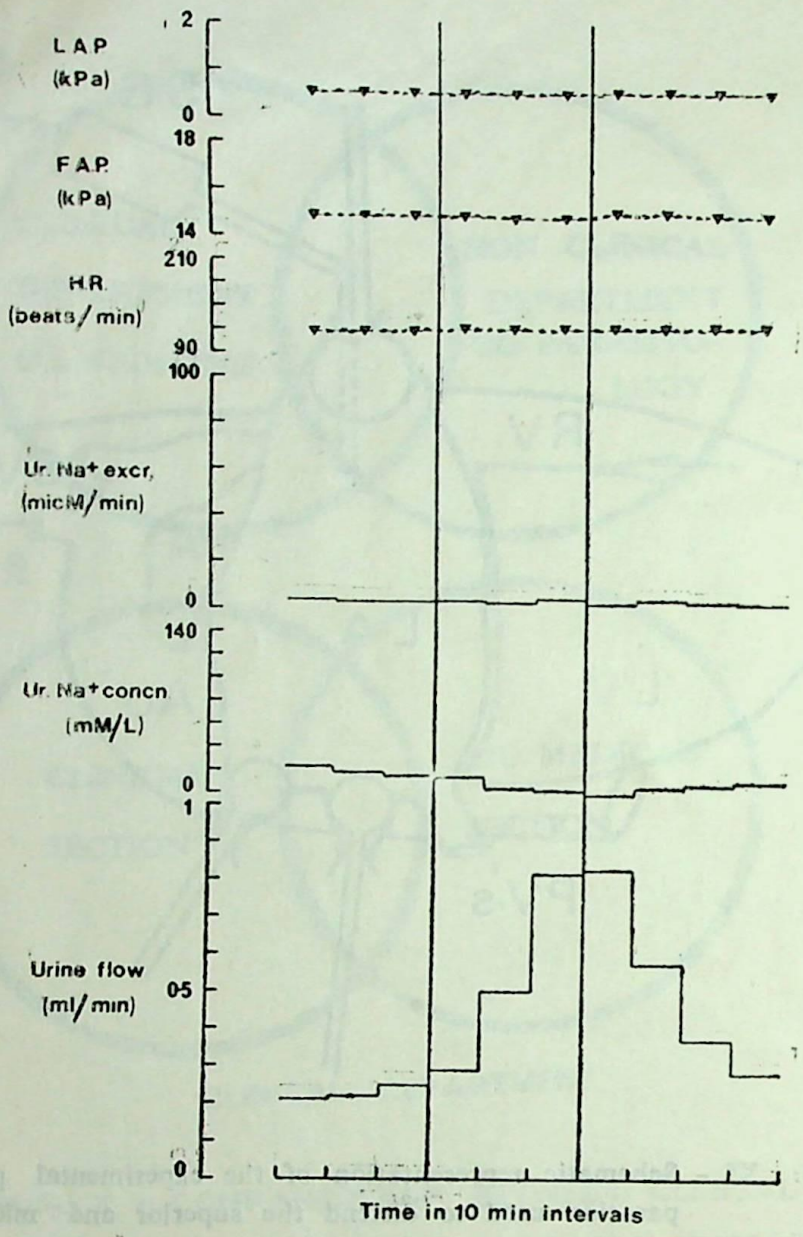


Figure XII – An experiment showing the effect of stimulating the atrial receptors on Urine flow.

The ordinate depicts, from above downwards, the left atrial pressure in kPa (L.A.P.), the arterial pressure in kPa (F.A.P.), the heart rate in beats/min (H.R.), the urinary sodium excretion, the urinary sodium concentration and the urine flow. The time course is shown in the abscissa. The responses of the innervated and denervated kidneys are illustrated in continuous and interrupted lines respectively. The period distension of the balloons is included within the two vertical lines.

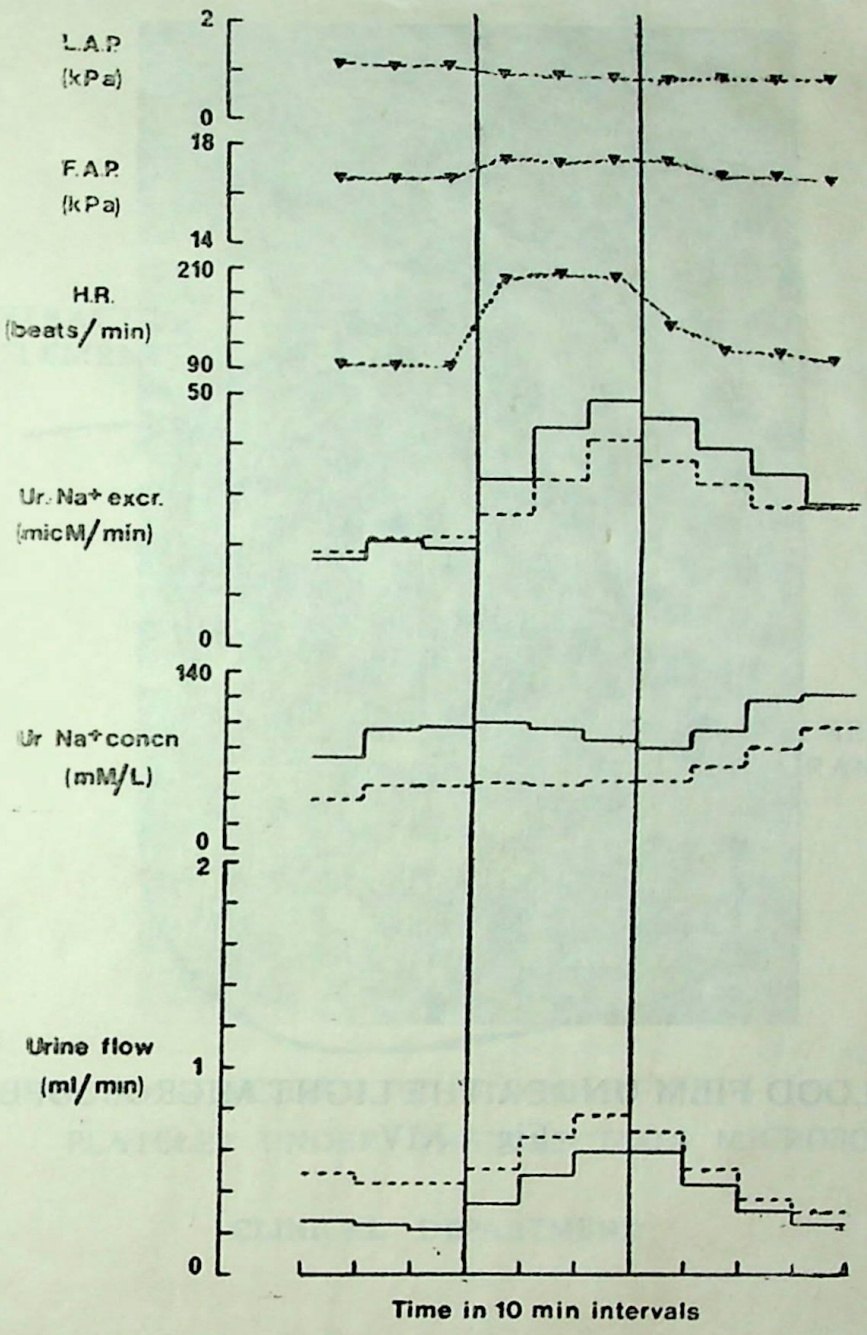


Fig: XIII - An example of an experiment in a Pharmacolo - gically denervated animal.

The ordinate and abscissa are represented as in fig: XII

BLOOD FILM UNDER THE LIGHT MICROSCOPE
Fig: XIV

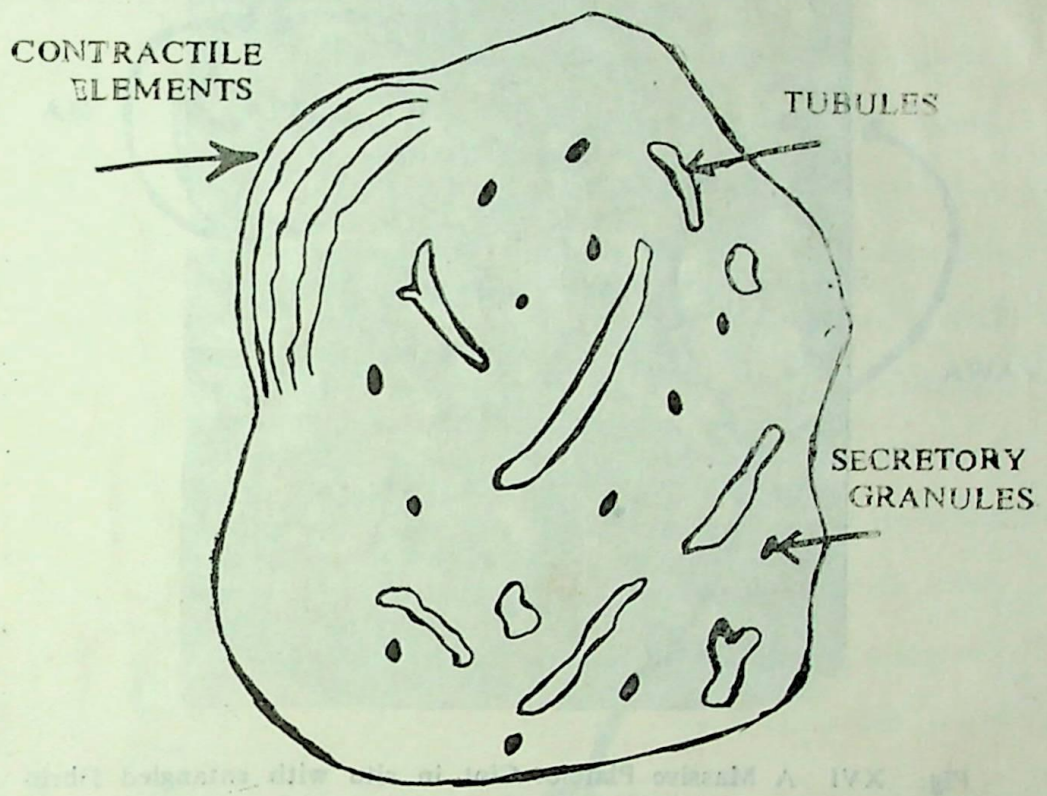


FIGURE XV – SCHEMATIC DIAGRAM OF A PLATELET UNDER THE ELECTRON MICROSCOPE.

CLINICAL DEPARTMENT

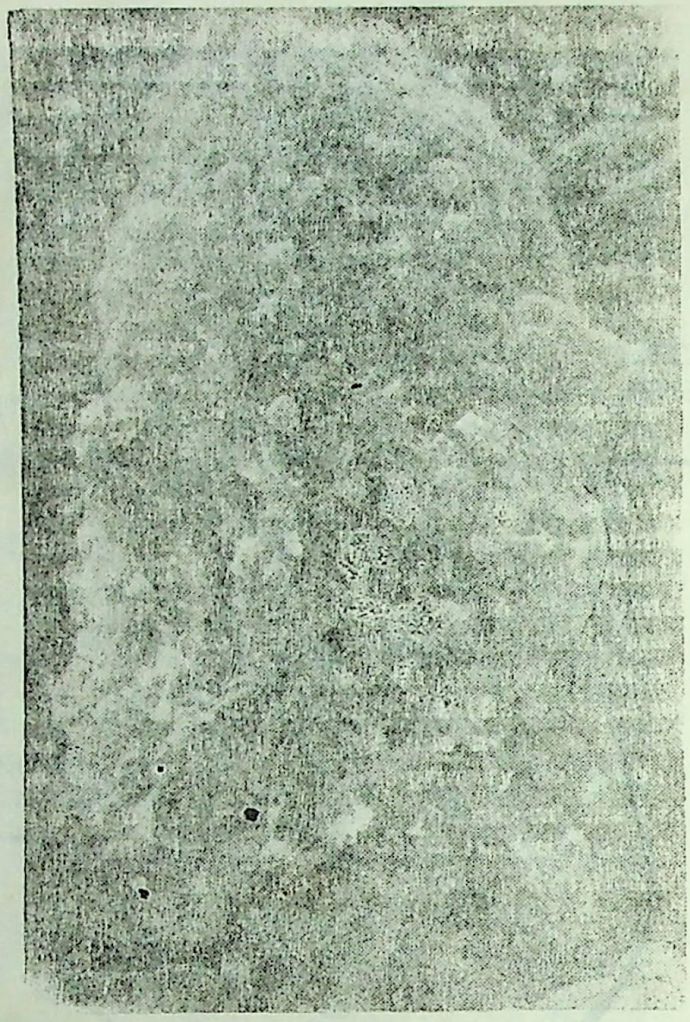


Fig: XVI A Massive Platelet Clot in situ with entangled fibrin network and red cells.

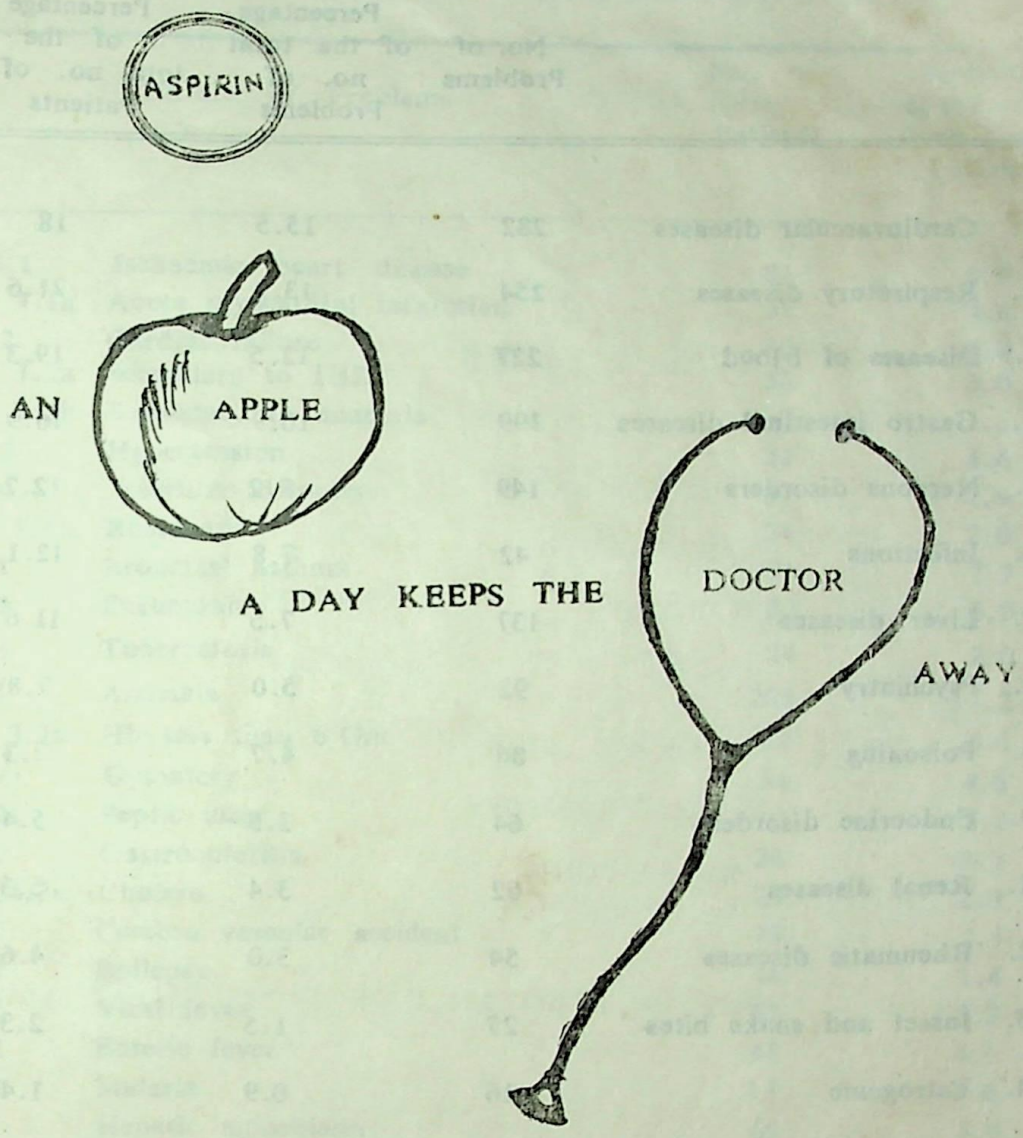


FIGURE XVII — THE ASPIRIN
REPLACES THE APPLE!!

	No. of Problems	Percentage of the total no. of Problems	Percentage of the total no. of Patients
1. Cardiovascular diseases	282	15.5	18
2. Respiratory diseases	254	13.9	21.6
3. Diseases of blood	227	12.5	19.3
4. Gastro intestinal diseases	199	10.9	16.9
5. Nervous disorders	149	8.2	12.7
6. Infections	42	7.8	12.1
7. Liver diseases	137	7.5	11.6
8. Psychiatry	92	5.0	7.8
9. Poisoning	86	4.7	7.3
10. Endocrine disorders	64	3.5	5.4
11. Renal diseases	62	3.4	5.3
12. Rheumatic diseases	54	3.0	4.6
13. Insect and snake bites	27	1.5	2.3
14. Latrogenic	16	0.9	1.4
15. Unclassified	31	1.7	2.6

TABLE 3

DISTRIBUTION OF HEALTH PROBLEMS

	Nature of Problems	No. of Patients	Percentage of the total no. of Patients
15.1	Ischaemic heart disease	81	6.9
1.1a	Acute myocardial infarction	21	1.8
1.2	Cardiac failure	80	6.8
1.2a	Secondary to IHD	35	3.0
1.2b	Secondary to anaemia	9	1.6
1.3	Hypertension	52	4.4
1.4	Valvular disorders	31	1.6
1.4a	Rheumatic	24	2.0
2.1	Bronchial asthma	91	7.7
2.2	Pneumonias	70	5.9
2.3	Tuberculosis	24	2.0
3.1	Anaemia	203	17.2
3.1a	Hb less than 6 Gm	78	6.6
4.1	Dysentery	54	4.6
4.2	Peptic ulcer	44	3.4
4.3	Gastroenteritis	36	3.1
4.3a	Cholera	23	2.0
5.1	Cerebro vascular accident	30	2.5
5.2	Epilepsy	16	1.4
6.1	Viral fever	62	5.3
6.2	Enteric fever	48	4.1
6.3	Malaria	17	1.4
7.1	Hepatic amoebiasis	69	5.9
7.2	Cirrhosis	24	2.0
7.3	Viral hepatitis	20	1.7
8.1	Depression	32	2.7
8.2	Anxiety	17	1.4
9.1	Poisoning with O. P.	45	3.8
9.2	Poisoning with oils	19	1.6
10.1	Diabetes mellitus	44	3.1
11.1	Urinary infections	23	2.0
13.1	Snake bite	21	1.8

Table: 2

PROFILE OF COMMON HEALTH PROBLEMS

	ANTIBIOTIC	% OF ORGANISMS RESISTANT TO ANTIBIOTIC
GROUP I		
	CO - TRIMOXAZOLE	85%
	STREPTOMYCIN	85%
	SUPHONAMIDE	72%
	TETRACYCLINE	71%
	AMPICILLIN	71%
GROUP II		
	NALIDIXIC ACID	38%
	NITROFURANTOIN	10%
	GENTAMYCIN	2%

TABLE III — ANTIBIOTIC RESISTANCE OF ENTEROBACTERIACEAE

No. of patients sampled	—	600
No. on Antibiotics	—	286 (48%)
a) Therapeutic indication	—	168 patients (57%)
Prophylactic indication	—	123 patients (43%)
b) Single antibiotic	—	171 patients (60%)
Two antibiotics	—	80 patients (28%)
Three or more antibiotics	—	35 patients (12%)
c) Common antibiotics used:		
Penicillin	—	132 patients (46%)
Ampicillin	—	76 patients (27%)
Streptomycin	—	53 patients (19%)
Tetracycline	—	46 patients (16%)
Chloramphenicol	—	30 patients (10%)

Table: 4 Antibiotic prescribing habits in G. H. Jaffna.

		Points
i.	Right hypochondrial pain	1
ii.	Enlarged tender liver	3
	or	
	Tender epigastric lump	5
iii.	Right intercostal space	
	Tender & full	5
	Definite tenderness	4
	Ill defined tenderness	1
iv.	Elevation of right dome of diaphragm	3
v.	Aspiration of amoebic pus	10
vi.	Alanine transaminase -	
	Normal	1
	Mild elevation	½
	Over 60 I. U.	(-)1
vii.	Definite clinical jaundice	(-)1

Table 5

HEPATIC CRITERIA

		Points
(A) i)	Fever – 38°C	1
	– 38.1°C	2
ii)	Neutrophil count - 7 - 10 × $10^9/_I$	1
	10 × $10^9/_I$	2
(B) i)	Definite alcoholic history	1
ii)	Blood and mucus diarrhoea within 6 months	1
iii)	Right shoulder tip pain	1
iv)	Right basal lung signs	1
v)	ESR – 100 mm/hr	2
	50 – 99 mm/hr.	1

Table 6

EXTRA HEPATIC CRITERIA

R	ϕ	R	ϕ	R	θ
0.00	90	1.02	29(-151)	-49.11	-31(149)
0.02	89(- 91)	1.04	28(-152)	-24.30	-32(148)
0.04	88(- 92)	1.06	27(-153)	-16.02	-33(147)
0.06	87(- 93)	1.08	26(-154)	-11.88	-34(146)
0.08	86(- 94)	1.11	25(-155)	- 9.40	-35(145)
0.10	85(- 95)	1.13	24(-156)	- 7.74	-36(144)
0.11	84(- 96)	1.15	23(-157)	- 6.55	-37(143)
0.13	83(- 97)	1.18	22(-158)	- 5.66	-38(142)
0.15	82(- 98)	1.20	21(-159)	- 4.97	-39(141)
0.17	81(- 99)	1.23	20(-160)	- 4.41	-40(140)
0.18	80(-100)	1.25	19(-161)	- 3.96	-41(138)
0.20	79(-101)	1.28	18(-162)	- 3 57	-42(138)
0.22	78(-102)	1.31	17(-163)	- 3.25	-43(137)
0.24	77(-103)	1.34	16(-164)	- 2.97	-44(136)
0.25	76(-104)	1.37	15(165)	- 2.73	-45(135)
0.27	75(-105)	1.40	14(-166)	- 2.52	-49(134)
0.28	74(-106)	1.43	13(-167)	- 2.33	-47(133)
0.30	73(-107)	1.46	12(-168)	- 2.17	-48(132)
0.32	72(-108)	1.50	11(-169)	- 2.02	-49(131)
0.33	71(-109)	1.53	10(-170)	- 1.88	-50(130)
0.35	70(-110)	1.57	9(-171)	- 1.76	51(129)
0.36	69(-111)	1.61	8(-172)	- 1.64	-52(128)
0.38	68(-112)	1.65	7(-173)	- 1.54	-53(127)
0 39	67(-113)	1.69	6(-174)	- 1.45	-54(126)
0.41	66(-114)	1.74	5(-175)	- 1.36	-55(125)
0.42	65(-115)	1.78	4(-176)	- 1.28	-56(124)
0.44	64(-116)	1.83	3(-177)	- 1.20	-57(123)
0.45	63(-117)	1.89	2(-178)	- 1.13	-58(122)
0.47	62(-118)	1.94	1(-179)	- 1.06	-59(121)
0.48	61(-119)	2.00	0(-180)	- 1.00	-60(120)
0.50	60(-120)	2.06	-1(179)	- 0.94	-61(119)
0.52	59(-121)	2.13	-2(178)	- 0.89	-62(118)
0.53	58(-122)	2.20	-3(177)	- 0.83	-63(117)
0.55	57(-123)	2.28	-4(176)	- 0.78	-64(116)
0.56	56(-124)	2.36	-5(175)	- 0,74	-65(115)
0.58	55(-125)	2.45	-6(174)	- 0.69	-66(114)
0.59	54(-126)	2.54	-7(173)	- 0.65	-67(113)
0.61	53(-127)	2.64	-8(172)	- 0.61	-68(112)
0.62	52(-128)	2.76	-9(171)	- 0.57	-69(111)
0.64	51(-129)	2.88	-10(170)	- 0.53	-70(110)
0.65	50(-130)	3.02	-11(169)	- 0 50	-71(109)
0.67	49(-131)	3.17	-12(168)	- 0.46	-72(108)

continued in page 37

0.68	48(-132)	3.33	-13(167)	- 0.43	-73(107)
0.70	47(-133)	3.52	-14(166)	- 0.40	-74(106)
0.72	46(-134)	3.73	-15(165)	- 0.37	-75(105)
0.73	45(135)	3.97	-16(164)	- 0.34	76(104)
0.75	44(-136)	4.25	-17(163)	- 0.31	-77(103)
0.76	43(-137)	4.57	-18(162)	- 0.28	-78(102)
0.78	42(-138)	4.96	-19(161)	- 0.25	-79(101)
0.80	41(-139)	5.41	-20(160)	- 0.23	-80(100)
0.82	40(-140)	5.97	-21(159)	- 0.20	-81(99)
0.83	39(-141)	6.66	-22(158)	- 0.18	-82(98)
0.85	38(-142)	7.55	-24(157)	- 0.15	83(97)
0.87	37(-143)	8.74	-25(156)	- 0.13	-84(96)
0.89	36(-144)	10.40	-26(155)	- 0.11	-85(95)
0.90	35(-145)	12.88	-27(154)	- 0.08	-86(94)
0.92	34(-156)	17.02	-28(153)	- 0.06	-87(93)
0.94	33(-147)	25.30	-29(152)	- 0.02	-88(92)
0.96	32(-148)	50.11	-30(151)	- 0.04	-89(91)
0.98	31(-149)	E		- 0.00	-90
1.00	30(-150)				

Table; 7

Normogram to calculate Electrical Axis of the Heart

R	ϕ	R	ϕ
0.00	90°	2.88	-10°
0.18	80°	5.41	-20°
0.35	70°	E	-30°
0.50	60°	-4.41	-40°
0.65	50°	-1.88	-50°
0.82	40°	-1.00	-60°
1.00	30°	-0.53	-70°
1.23	20°	-0.23	-80°
1.53	10°	-0.00	-90°
2.00	0°		

Table: 8

Modified Normogram to calculate electrical axis of the heart.

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