EDITORIAL

The Annual Meeting of The Medical Society of Nova Scotia having taken place, and the Editorial Board of the Bulletin having resigned, the Nominating Committee saw fit to appoint a new Editorial Board made up of Doctors W. K. House, H. C. Still and C. J. W. Beckwith.

The new Editorial Board has been tardy in expressing to the members recently resigned, and for this we apologize, but are none the less sincere in expressing to them thanks, appreciation and respect for the labor which they must have endured in maintaining the standard of the Bulletin during their term of office.

The present Editorial Board take pride in being asked to carry on; it could be a pleasant and instructive experience, but the experience of editing the first two issues leaves serious doubts in our minds.

We feel, and believe it is with justification, that the Bulletin should represent the efforts of all members of The Medical Society. Early in October a letter was sent to each member, appointed by local medical societies to the Editorial Board, requesting articles for publication and news items. As of this date there has been received in reply one letter, no article and one news item.

While it is true that the year is yet young, and our experience, or lack of it, in these matters is not great, nevertheless the prospects of inanition through malnutrition has prompted us to bring this to the attention of the members of The Medical Society. It should be obvious that the Bulletin provides a medium for expression of thought, for the publication of articles and case reports, which will be of benefit alike to the contributor and the reader. It should be obvious, also, that a "balanced" issue, with articles of diversified matter, depends on the material available—at least four articles are required for each issue. These do not grow on trees, but represent honest endeavor.

The purpose, therefore, of these remarks is first to express sincere appreciation and respect for the retiring editors and to appeal for the support of the Bulletin by its members through active participation in providing material for publication.

Determinate Variability In Bacterial Infections*

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OUR present time is commonly referred to as "the Atomic Age", which is in reality an anticipation, with as little justification as previous periods are called "the Bronze Age" and "the Iron Age." Except for the political influence and the deterrence of war, the commanding significance of atomic fission has yet to be developed. In biology and medicine the value of isotope tracers and controlled radiation is in a stage of enthusiasm for what is new and will settle to its proper place in the ordered fitness of constructive thought with time and experience. This has been the history of many innovations in the field of medicine, such as bleeding, mercury, pH determinations, sulphonamides and the present gradual evaluation of antibiotics, but when all has been refined there is left a residue of proven knowledge wherewith to modulate both speculation and practice to prevent extravagance.

In truth we may more aptly say we live in the "Age of Science", for the discoveries in the laboratory are now quickly translated to every range of human interest and necessity. Even so, the rapid advance and far reaching scope of the ever increasing penetration of research is well nigh bewildering, and the borders of what were distinct sciences have become so diffuse that extreme specialization becomes a necessity, accompanied by technical terminologies that are almost new languages. The writing of an elegant prescription prompted by a clinical impression is a thing of the past, and, were it done, an apothecary to fill it might be sought in vain. It has become difficult to make a diagnosis or decide upon a treatment without numberless laboratory tests and various technical examinations, and the greater the specialization the more imperative these refinements become.

This is not an accurate picture of modern medical practice but it seems to be the impression that big centres evoke; it formulates an ideal that is not humanly attainable, however desirable, but even its partial accomplishment meets a public demand arising from the wide dissemination of supposedly spectacular medical news. None the less, there is a continuous thoughtful and searching incorporation of new knowledge in clinical procedures and therapeutic measures, based on accurate observation and experiment, which in their expansion bring new information on the processes of disease. Unconsorted empiricism may give unexpectedly valuable information, as much by its misses as by its hits, and at times, because it delimits safety or emphasizes character, it ultimately provides a reason for planned research.

Advances are not made uniformly along the whole front of medical enquiry and certain lines are set back for varying periods for several reasons; because of no immediate means of proceeding, because of supervening interest in other directions, because of seeming solutions giving an apparent measure of control, at times for what appears to be in fashion at the moment,

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or because of stimulated wide interest purveyed by statistical interpretation of prevailing morbidity or mortality. Any of these reasons may instigate the availability of funds and facilities directed to a limited line of enquiry which inveigles an undue proportion of the research competency. Fortunately there is always a remainder of independent minds who pursue their own bent, and I believe it is still true that these are the inspiring explorers whose trails break the way for the fulsome organized teams of compilers of details.

The discovery of the microbial cause of disease in the latter part of the 19th century did not merely dominate medical thought, its development introduced entirely new concepts that transformed almost every aspect of medicine, to make the descriptive term Medical Science supplant the old proudly exclusive subterfuge of The Art of Medicine. The progress of bacteriology initiated the first real experimental medicine, it made a reality of the idea that disease had a cause and this has extended to other than infections, it introduced and brought preventive medicine to marvellous accomplishment, it discovered an entire science in immunology, it made modern surgery possible, it enlivened pathology to see more than the mere forms of things in a corpse, and now it is developing a knowledge of the individual cell and its internal functions that is pervading physiology, biochemistry and genetics. This catalogue is far from complete, even in medicine, and neglects entirely the wide range of bacteriological interests completely unrelated to pathogenicity.

The prevalence, the high morbidity and in some instances the striking mortality of bacterial infections, enforce taking into account every facet of the processes of disease caused by these independent forms of life which exhibit unpredictable activity. To many practitioners it was a burden to be required to take into account so much detail, even to minutiae of antigenic structure of sero-types, for the proper handling of cases. In many specialties the incursion of bacteria seemed a mere nuisance, requiring complicating and impeding precautions. Thus the advent of sulphonamides and antibiotics, with the unreasoning hope of a completely effective and undiscriminating ideal disinfectant, that required nothing more complicated than signing an order for its administration, was a subject for rejoicing. No new dream! for before Lister we read:

> "Fetishlich hir fyngres / were fretted with golde wyre,
> And there-on red rubyes / as red as any glede,
> And diamantz of derrest pris / and double manere safferes,
> Orientales and ewages / envenymes to destroye."

or that "Richard Preston, citizen and grocer, gave to the shrine of St. Erkenwald his best sapphire stone, for curing of infirmities of the eyes." Perhaps even that peripatetic annoyance, the bacteriologist, could be dispensed with. Even Examination Boards for Licence to Practice Medicine took the view that antibiotics rendered it unnecessary to require candidates to have more than a smattering of bacteriology. Bacteriologists have actually been excluded from the panels of examiners.

But these fond hopes were not part of the natural order of events and the advantage bacteria can make of their environment and circumstances, together with the possibilities of the nature of antibiotic actions, have introduced problems that will not be elucidated for some time to come. Although many

lives have been saved and remarkable advantages otherwise obtained with antibiotics, they have not by any means solved the problems of bacterial diseases.

So, as is right, proper and desirable, we must return from this flight into the realms of fancy to the laborious and systematic study of bacterial diseases; in this our aim is to learn more about the bacteria themselves, to understand the response of the host to infection with its defects and excesses, to appreciate the interdependencies and antagonisms of host and parasite processes, to know the reasons for death or recovery or chronic infection. Many of the problems involved can only be investigated by cooperation between the laboratory and the ward, for neither of them is sufficient of themselves. Many diseases are peculiarly human and of those that can be produced in experimental animals many are then not adequately characteristic. It is also imperative that the entire resources of both clinical and laboratory methods are available to accumulate the relevant data for interpretation of the ever changing complexity of situations in the sick body.

The initial requirement for research is the definition of the problem and this often imposes surprising difficulty, for the value and penetration of the investigation depends on the clarity and discernment with which a problem is selected and the work planned. To this end it is valuable not only to survey a situation but to speculate judiciously on the influences that might determine the manifestations and circumstances that have been observed.

Many years of experience covering a wide range of bacterial diseases have left me sorely puzzled that so little is known of the striking circumstantial or incidental variants in cases of any kind of infection. We are all very well aware that apart from minor variations in the clinical picture of the average case, there are fulminant cases on the one extreme and mild cases on the other, either of which may present serious difficulty in making a diagnosis. There are occasional indications of reasons which suggest that a fuller knowledge would be of great value, but even a quick mental review of examples within the experience of each of us should leave no doubt that the subject is interesting and puzzling.

It is quite easy to dismiss the question smugly by invoking variation in virulence of the infecting strain. Beyond doubt there are intrinsic qualities possessed by bacteria which can be augmented or depressed experimentally, and which play a demonstrable part in establishing infection as well as in influencing its progress and mortality. Its influence is not so frankly observed now as in the days of "laudable pus" when patients having a wound with a sero-sanguineous exudate were rapidly transferred to the septic ward; a situation which prevailed to a lesser degree in my own student days. Accounts of the Franco-Prussian War (1870) tell that it was most dangerous for even a trivial wound to be dressed by a surgeon and this may be interpreted as increased streptococcal virulence by transfer from patient to patient. The important and much neglected work of Charles White of Manchester published in 1773, and the more acknowledged work of Holmes in 1843 and of Semmelweiss in 1847 to 1861, all emphasized the fatality of puerperal fever transferred from sick patients or from the post mortem room, with what was called "sickening in rows" and it is again probable that this was in large part a question

of streptococcal virulence. In these instances there would seem to be a progressive regional increase in severity of disease in which the intrinsic microbial qualities of virulence dominated.

Attractive as it may be as an explanation of variation in severity of disease, bacterial virulence alone does not account for all situations, though it surely must be a contributing factor. The comprehensive examination of the subject shows that virulence cannot be regarded as expressing a vital peculiarity essentially a property of the bacterium itself. Virulence as ordinarily measured is the ultimate expression of a diversity of competing influences contributed simultaneously by both parasite and host. Under experimental conditions with certain bacteria it is possible to depress or augment either the host factors or the bacterial factors independently. Thus it is possible to show an apparent increase or decrease of virulence without interfering in any way with the bacteria themselves. It is also important to realize that the intrinsic bacterial or virus factors of virulence not only can be raised but can be depressed by animal passage. This is illustrated by rabies, virus, by vaccinia, by embryonated egg passage of rinderpest and it has been shown with *Erysepelothrix*, with meningococcus, pneumococcus and *Listeria*.

These considerations bring into relief only some of the antagonistic and concurrent influences of both host and pathogen, whereby each of them may contribute to its own destruction, but they are sufficient to indicate the improbability of virulence alone determining variability in manifest disease. It thus ceases to be surprising that in an epidemic of bubonic plague there are ambulatory cases so mild that taken by themselves they might not be recognized and are only confirmed by finding the plague-spot at the site of the infecting bite, and at the same time there appear fulminant haemorrhagic cases scattered among the normal bubonic type. It also removes any incongruity from cases where symptoms of cholera have only developed after a fatiguing journey or after purging or following any extravagant excesses. But these, like the more ordinary variants of *Staphylococcus pyogenes* infections (pimples, boils, pyodermia, pyaemia, osteomyelitis, etc.) or those shown in cerebrospinal fever, gonorrhoea, relapsing fever, and many another, still require explanation.

Apart from the host participation in virulence, there are without doubt additional inborn qualities in the host which find expression in the rather vague terms susceptibility and resistance. This is a constitutional disposition more easily recognized in a study of the liability to particular infections exhibited by different species than it is in race, siblings or individuals. This is unrelated to immunity in its strict sense and it must not be confused with variations imposed by risks of exposure, vector distribution and climatic requirements. Similarly, bacteria exhibit natural propensities that allow them limited power to selectively determine infectivity, choice of host and character of disease. Here again there is an interplay allowing of a gamut ranging from the complete insusceptibility of man to rinderpest through every degree to the extreme severity of diseases introduced to people not previously exposed to them. This is in itself a separate problem; but, in conjunction with virulence, it takes a share in the variability of infections; it is complicated by hereditary qualities which in turn participate in a Darwinian natural selection, when not inter-

fered with by the procedures of preventive medicine, which also have to be taken into account.

The ordinary way of life exposes each of us to a considerable range of major and minor infections all of which leave their individual impression in the form of a derangement of our original physiological state. That we may have completely recovered without residual recognizable lesions still does not preclude rearrangement or disturbance of intricate balances of functions of cells and organs. Some we suspect, often without too convincing evidence; such as the liability to subacutebacterial endocarditis depending on a history of rheumatic fever, also the predisposition to other infections that measles in infancy is supposed to induce. In any case, all these various infecting agents of disease have their particular antigenic constitution and consequently induce an active immunity, which though varying in degree is none the less permanent. It is immaterial whether this immunity is of a final protective character or merely the presence of specific antibodies without evident protective activity; there is a debatable point whether immune-body globulin is or is not equivalent in some degree to a foreign protein. Be that as it may, it is abundantly clear that even when the antibodies are protective they may be produced sparsely or abundantly and persist in adequate concentration for a short or long time in different individuals. This of itself does play a considerable part in the character of disease the partially immune person may contract and must be taken into account.

Before prophylactic immunization became widespread, diphtheria exhibited everything from the carrier state without visible lesion through the average faucial membranous case to the bull-neck type of great severity. There is some evidence of the toxigenicity of strains influencing the syndrome, but it cannot account fully for the situation, for strains isolated from carriers very often are producers of highly potent toxins. Some degree of immunity induced by sub-clinical infection in persons with some form of natural resistance may too have played a part. Immunity that is sufficient to prevent the evolution of declared disease does not necessarily prevent the implantation and persistence of pathogens and these individuals are effective distributors of the organisms. There is a great difference in degree of response by individuals to active immunization with diphtheria toxoid, and the maintenance or fading away of whatever immunity is produced may be over a short or a long time. Immunized individuals may thus be liable to some degree of declared disease, or to establishing a temporary or prolonged carrier state, though most seem to be completely protected. It has not been uncommon to see immunized children with a sero-sanguineous nasal exudate yielding profuse cultures of fully toxigenic *Corynebacterium diphtheriae*. These are cases of diphtheria and are frequently overlooked or not clinically accepted as such in spite of the bacteriological evidence. They correspond in nature to modified smallpox in vaccinated people and to "contact fever" which is developed by vaccinia immunized people coming in contact with smallpox patients.

Similar situations prevail in other diseases and demonstrate the modifying influence of degrees of immunity. Faecal carriers of poliomyelitis virus have been shown to have homologous antibodies in their blood and volunteers with antibodies in their blood have been made alimentary carriers by being

fed virus. The situation has been paralleled in apes and it has been demonstrated that the frequency and duration of the experimental carrier state by feeding is inversely proportional to the concentration of serum antibodies. In the studies of hog-cholera and dog distemper there are indications that serologically immune animals may become temporary carriers on exposure to these viruses, as seems to be the case with human influenza and poliomyelitis, which is consistent with the epidemiology of these diseases. In the use of live Newcastle disease vaccines both the vaccine strain and field strains of virus have been isolated from diagnostic specimens from fowls. Coexistence of virus and their immune bodies seems to be the rule in human serumhepatitis and infections anaemia of horses.

I have had several opportunities to observe the development of bactericidal antibodies in sub-acute *Streptococcus salivarius* endocarditis, before the days of antibiotics. The method was to allow the patient's blood to clot in the 37°C. incubator and culture it the next day. In the early stages of the disease there was not enough antibody to kill the bacteria present in the patient's blood; but in the late stages up to the time of death, the antibodies present would kill not only those naturally there but relatively enormous added numbers of streptococci from a fresh primary culture of the patient's own strain. In one case it was possible to give the patient 200 cc. a day of freshly collected human serum intravenously, and, without other treatment, this brought about spectacular improvement. The experiment was ruined by a dentist extracting a tooth with an apical abscess, contrary to emphatic instructions, which caused a rapidly fatal overwhelming septicaemia. These observations support other evidence that there is no complement as such in the circulating blood, and in these cases the presence of abundant bactericidal antibodies was ineffective.

In relapsing fever due to *Borrelia carteri* it has been shown that the antigenic type of the spirochaete changes with each relapse, and that the antibodies in the serum due to the types of the preceding relapses persist and may even increase. It is probable that the essential relapsing character of this disease is determined by the type specific immunity, corresponding to the capacity of the spirochaete to transform its type under the duress thus imposed. We hope to publish soon some interesting findings on specific antigen transformations brought about by antibiotics, not only experimentally but in treated patients.

Degrees and character of immunity can evidently play some determining part in the form of infectious disease. Immunity response and maintenance being unpredictable in any individual, and as these features differ with different antigens in any one individual, so it is evident that the scale of possible variants in clinical features is correspondingly large. In this connection it must be borne in mind that any degree of immunity whatsoever can be overcome by a large enough dose of a sufficiently pathogenic microbe.

The age distribution of *Haemophilus influenzae* meningitis is strangely almost confined to infants and steadily decreases with age in childhood to become almost non-existent in adolescents and adults. This has been shown not to be due to maturation, but is a question of the presence of specific antibodies in the blood, which increase with age and exposure. However this is a feature

of disease and there are variations in susceptibility related to age. It is not necessary to more than recall that it is common speech to speak of diseases of childhood. The converse is shown by resistance of infants to infection, as instanced by smallpox. There must be, too, some matter of maturation of cells and tissues. Suckling mice are susceptible to experimental infection with Rickettsia and viruses which the adult mouse resists and cultures can be established in embryonated hens eggs of organisms which will not infect chicks or fowls. Metchnikoff produced typical cholera in suckling rabbits which he could not do in adults. Pneumococcus pneumonia was (and probably still is) far more serious after middle age than ever it proved in childhood. Such situations can be multiplied but their explanation is not evident, nor is it necessarily the same in all instances.

Maturity with ageing is not the only influence of the physiological state of the host on the character of infectious disease. Physiological differences between individuals and deranged physiology are probably of proper importance. It is well founded that diabetics are unusually prone to severe infections, but it is very doubtful that this is simply due to the increased sugar in their blood. Many such observations are merely accepted without questioning what they depend upon. The free use of A.C.T.H. and Cortisone has brought to light not only that they suppress antibody formation but that they bring about an acute dissemination of infection, sometimes disastrously. Listeriosis has been observed to develop suddenly when a patient was treated with Cortisone for other reasons, and similar effects have been observed with tuberculosis and other diseases.

In experimental animals increased susceptibility to meningococcus, to various viruses and to other organisms, has been shown repeatedly with these hormones. It has been assumed by some that fulminant purpuric meningococcus septicaemia is due to suppression of these hormones because in a small number of such cases there are suprarenal lesions. It seems to me much more likely that the initial trouble may well be hyperactive suprarenal function and that subsequent to the damage done by the septicaemia suprarenal function may be depressed in some cases. In these then Cortisone treatment may at a relatively late stage show good effects. In what is referred to as the "Waterhouse-Frederichsen Syndrome" and which is no more than was long known as fulminant purpuric meningococcus septicaemia, there is maintenance of the sodium chloride level without raised potassium, which does not suggest adrenal cortex deficiency. The appearance of shock seems not to be related to haemoconcentration nor to diminished venous return to the heart. It has been said of this "intense infection with profound circulatory collapse" that these result in "an intensity and rapidity of progression unparalleled among bacterial diseases." The contrast between this state and the ordinary run of cases of cerebro-spinal fever is amazing, and the more so because of the innocuity of heavy infection in carriers. But some cases of plague and of cholera are no less overwhelming and offer surprising contrasts with more ordinary types of case.

Although it is a matter of old observation, almost as old as bacteriology, that there are antagonisms and synergies between different species of bacteria, its application and general recognition is recent. Present clinical interest

arises from the probability that antibiotic treatment often kills our friendly bacteria to favour others that do harm. There are many instances of these oecological balances being upset by antibiotics, but for present purposes they only serve to emphasize that these synergies and antagonisms do exist. It has long been known that in the company of *Proteus* in a local lesion the pyogenic cocci can spread to give a septicaemia more easily. I have seen three cases of surgical wounds infected heavily with both *Streptococcus pyogenes* and *Staphylococcus pyogenes*, in which there was a persistent bacteraemia of only the *Streptococcus*, and which yielded consistently negative blood cultures when the *Staphylococcus* in the wound was brought under control with antitoxin. This is synergy in the character of disease developed in mixed infections and other types of combinations can be cited, such as the complete antagonistic replacement of meningococcus in meningitis by pneumococcus. Synergy of mixtures of organisms is also evident in treatment with sylphonamides, when the resistant *Staphylococcus* will protect the highly sensitive *Streptococcus* from the drug. This is a different matter and I have seen several cases in which this action was beyond dispute. This protective action has been shown using experimental cultures in test-tubes with exactly comparable results. Unless the *Staphylococcus* and *Streptococcus* strains were isolated and tested separately, it might be wrongly surmised that the *Streptococcus* had developed drug resistance, which is an extremely rare occurrence.

The point at issue is that associations of organisms, according to their kinds, can vastly alter the nature of disease. This is well recognized by bacteriologists and is very well shown by the various species of gas-gangrene *Clostridium*. The great advantages that have accrued from the pure culture study of bacteria, and the absolute necessity of this procedure for many purposes, have induced a habit of mind which tends to neglect the fact that in a large proportion of instances infections are mixed. It is full time this was taken into account in the work of both the laboratory and the ward. There is no doubt that the character of disease is altered by the nature of the admixture of organisms involved; it is also true that in many instances the therapeutic procedures should be modified accordingly.

The concatenation of complexities resulting in chronic infection seems most difficult to unravel. It is not generally confined to particular species of bacteria, nor is there any indication that virulence attributes of the parasite are involved, and in many instances, such as *Staphylococcus* lesions of many kinds, immunity cannot be shown to dominate the situation. The localization and duration of lupus is in itself inexplicable, especially as the cultures isolated from it do not differ in any way from those in other forms of tuberculosis. That lupus precludes the establishment of other forms of tuberculosis in the patient may be an influence of immunity, but, though immunity may have some effect in later stages of the primary skin lesion, there must be some cutaneous character effective initially. Typhoid carriers and chronic meningococcus carriers must involve circumstances other than immunity. The indolent duration of gonorrhoea in the female during the child-bearing period of life is not due to a loss of infectivity, for it can be transmitted to the male and cause ophthalmia in the infant. Immunity is not likely to be operative in gonorrhoea since previous infections do not afford any protection. There are diseases,

such as syphilis in man, *Spirillum minus* and *Borrelia* infections in rodents, in which chronicity is a salient feature, but they offer no leading explanation of chronic cases of diseases that ordinarily are acute infections. The experimental approach is made difficult by the almost impossibility of producing chronic disease by any route of inoculation of healthy animals. It would seem that some important modulation of the host tissues is a required preparation, but only a close and exhaustive study of natural chronic cases will give us the urgently needed lead.

The speculations I have indulged in here do not exhaust either the kind or the scope of the influences which may alter the character of the syndrome any particular infection might exhibit. I have endeavoured to make it clear that there is a seriously important problem underlying the variability of infectious processes. The elucidation of the inter-relations of the multiple co-existing systems involved is bound to be difficult, if for no other reason than that the vital processes of at least two kinds of independent living beings are involved. It is quite evident too that the scope of the problem is not limited to the interests of bacteriologists and immunologists, it is quite as much the concern of all kinds of clinicians, pathologists, physiologists and biochemists. Many sides of the enquiry needs the interested cooperation of several or all of these various disciplines and that is perhaps the most difficult requirement to meet.

Had the question considered here been the subject of the judicial assemblage at Arlo, the judgment of the Greatest Goddesse Dame Nature would still have read thus:

> "I well consider all that ye have said,
> And find that all things stedfastnesse do hate
> And changed be; yet, being rightly wayd,
> They are not changed from their first estate;"

Some Observations on Prognosis and Treatment of Emergencies in the Aged *

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AT birth, the individual is given an amazing margin of reserve (energy potential), the amount of which is specific for each individual, and which cannot be accurately measured by the crude methods available at the clinical or even research level. It is a useful concept that ageing represents the lessening of this reserve by the constant expenditure of energy without complete replacement throughout the life span. Thus, the problem of old age becomes an individual one, in each case being determined not only by the original endowment, including perhaps particularly, the endocrine status, hereditary factors, but also a great many unknown factors, as well as the many stresses of life; for example, the illnesses, the injuries, the over or under-nutrition, the periods of prolonged fatigue from excess of work or play.

The ability to withstand acute stress or emergency in the aged then can be expected to vary a great deal from person to person, being greatest in those who have had the best start with the fewest and least intensive or prolonged insults throughout life. Quantitative assessment of this is difficult in any one case, but clinical experience and research study have given the physician considerable guidance.

The response to stress or emergency by the aged person exhibits for the most part the same pattern as that of the younger person—any difference being quantitative rather than qualitative; the defense mechanism being most efficient in the healthy young and least protective in the poor risk aged. An emergency, for example, a gastric haemorrhage, which may produce moderate weakness, dyspnoea, and minimal shock in a young man, may be responsible for moderate shock and perhaps slight confusion in the healthy aged, but in the elderly poor risk, may precipitate severe shock, confusion, semi-consciousness, or severe permanent damage, such as blindness, cerebral thrombosis, hemiplegia, coronary occlusion, or terminal renal failure. However, many clinical reports have shown that the mortality rate following severe stress, for example, coronary infarction, cholecystectomy, femoral neck fracture or severe infection is approximately the same for good risk patients, regardless of age.

We can say then that the prognosis of the elderly good risk patient to recover from an acute emergency approaches very closely that of the young or middle aged patient providing that therapy is initiated relatively promptly and adequately. This was not always so, but has come about because of the increasing availability of accurate laboratory determinations, electrolyte and endocrine assessment, blood, plasma, antibiotics, and improved anaesthesia and surgical technique.

But these new and improved diagnostic and therapeutic procedures, along with better standards of living, have been largely responsible for a new challenge to the medical profession. The number of poor risk patients over sixty with their chronic cardiovascular renal disease, chronic bronchitis, pul-

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monary fibrosis and emphysema, and mental infirmity is increasing rapidly and the majority of acute emergencies in the aged must be considered to be in this group. Fortunately, although their adaptative response to stress is quantitatively low and their homeostatic mechanism of defense may fail early and rapidly even with a moderate insult, experience has shown that their reserve is often greater than was suspected in the past and is adequate to allow salvage of a great many of them, if the emergency is not too grave, or the stress too prolonged. Treatment must be instituted at once. As is well known, in this group, the appearance of a shock syndrome may be the first sign that anything is wrong although an acute infection, bleeding, intestinal obstruction, urinary obstruction, or myocardial infarction may have been present for one or more days.

Blood loss may require urgent replacement. At first, we may be deceived by the early rise of blood pressure which may occur and bleeding may be allowed to go on to postural syncope. Again, in concealed slow blood loss, the break in tolerance may be very sharp and shortness of breath, weakness or unconsciousness may be the first sign. But, in the aged, a relatively small loss —perhaps of 400-500 cc may give this picture and one unit (500 cc) of blood may give clinical recovery, while two units may precipitate overloading of the heart or kidneys. Whole blood is better than plasma or plasma expanders—the increased oxygenation necessary, particularly to the brain, is so very important. Of course, these latter, along with glucose and water or saline may have to be used while a supply of blood is being made available.

The general rule of minimal quantities to prevent overloading must especially be observed when blood is used where there is no blood loss, for example, shock of acute coronary infarction.

Where there has been previous loss of weight from intercurrent disease or malnutrition with anaemia and hypovolemia, blood becomes very important. However, one unit per day is usually adequate until blood volume is restored and anaemia corrected. Packed red cells may be useful particularly when there has been previous anaemia, because of the decreased sodium content as well as the lesser volume.

The necessity of accurate electrolyte deficit assessment and replacement is well known. Ten to fifteen years ago, we used a great deal more saline parenterally in quantity that we now look on as dangerous. However, we must not overlook the possibility of over-enthusiasm in its restriction in the aged, particularly in cases with increased sweat loss, some cases of chronic renal disease and mercurial refractory congestive heart failure.

Oxygen is a very important therapeutic aid in many emergencies. It is a helpful adjunct in blood loss, coronary thrombosis, cerebrovascular accidents, acute cardiac arrhythmias and acute heart failure. It is particularly useful in trauma to the chest and head. Nasal catheter oxygen is often adequate—it causes less apprehension in acute emergencies than the oxygen tent and it permits the necessary handling of the patient by the nurse and physician; in cerebral vascular accidents although it does not give the optimum fifty per cent, it may be better tolerated at least for the first day or two.

Respiratory acidosis must be guarded against in patients with pulmonary emphysema and fibrosis. Again oxygen by nasal catheter is less likely to

result in carbon dioxide intoxication. If it occurs, pneumoperitoneum has been used successfully and should be tried if a suitable respirator is not available. Expiratory positive pressure oxygen is very valuable in acute attacks of left ventricular failure with pulmonary oedema, and one hundred per cent oxygen given with mask has been advised for severe pain in coronary occlusion.

Analgesics must be used in reduced dosage because of reduced tolerance in the aged. Morphine is exceedingly dangerous and even Demerol must be used with caution if the patient is an asthmatic. Local and regional blocks are very useful in traumatic cases—particularly multiple rib fractures where they are a valuable measure in controlling and preventing "wet lung."

There is a reduced tolerance for digitalis and full dosage must be used with caution; for example, in the acute auricular tachycardias, where it may be the drug of choice, if it has not been used previously, half the usual digitalizing dose may be given; for example, 0.6 to 0.8 mg. of cedilanid intravenously is often sufficient. If not, further dosage may be given in two or three hours if necessary.

Paroxysmal auricular tachycardia frequently requires urgent treatment, as, in the elderly, failure may rapidly supervene if the attack is not abolished. Digitalis, as above, is probably safer than carotid sinus pressure if simpler methods such as ocular pressure and the gag reflex fail. Demerol or morphine in small dosage may allay anxiety and spontaneous remission often occurs. Mecholyl and Neosynephrine have been advocated for this arrhythmia. They are probably over-dangerous in the aged. Strophanthin is particularly useful if failure has supervened before the arrhythmia is controlled. Quinidine, while useful to prevent repeated attacks, is too unpredictable for urgent, immediate use.

Chronic auricular fibrillation is common in the elderly and frequently requires no treatment unless failure is present. On the other hand, acute paroxysmal attacks may require urgent treatment. Again, digitalis is to be preferred although quinidine may be used for control of repeated attacks. Quite occasionally, auricular fibrillation occurs shortly after the onset of coronary thrombosis, is often transient and may require no treatment. However, the occurrence of frequent ventricular extra systoles after an acute coronary is probably an indication for immediate quinidine therapy unless there is evidence of bundle branch or A-V block, usually considered a contraindication.

Aminophylline and morphine or Demerol are valuable in acute pulmonary embolism. Papaverine which has been used a great deal in the past is considered by many to be of doubtful value. Of course, the advisability of anticoagulant therapy with or without vein ligation must be decided at once. Anticoagulants are used in the usual dosage in the aged with the same precautions as in the younger, remembering that certain contraindications, for example, recent cerebral haemorrhage or possible dissecting aneurysm, are more likely to be present. Anticoagulant therapy probably should also be used in acute coronary infarction with marked hypotensive shock; on the other hand, it may be dangerous in cases where blood pressure is maintained.

Quinidine and Pronestyl are particularly valuable in ventricular tachycardia which is a very serious happening in the aged, regardless of the etiological factors. They may have to be tried even if the attack is initiated by syncope of the Stokes-Adams type with A-V block. Recently Isuprel sublingually has been suggested in these cases. Adrenalin continues to be the drug of choice in Stokes-Adams attacks with ventricular slowing or asystole although Isuprel may also be tried.

In emergencies with severe hypotensive shock, Paredrine or Neosynephrine in small doses subcutaneously may be given as necessary. Norepinephrine 4 mgs. in 1000 cc. glucose and water may be life-saving when given slowly intravenously with the rate adjusted to maintain blood pressure at about 100; it is often advised in the treatment of severe hypotension in coronary thrombosis, but it must be used with great caution and with a physician in attendance, as the least subcutaneous leak can produce severe ischaemic necrosis, and the blood pressure must be under constant supervision.

Aminophylline .25 to .5 gms. very slowly intravenously is often helpful in acute left ventricular failure along with oxygen therapy and morphine or Demerol. Acute congestive failure due to hyperthyroidism may come under control more rapidly with Iodine rather than with antithyroid drugs.

The great value of the antibiotic group of drugs to the geriatric patient is beyond question. Acute infections may be present with minimal early signs or symptoms and these drugs should be given at the earliest suspicion. For example, acute bronchitis or bronchiolar disease occurring in a case of chronic emphysema may exhibit only severe dyspnoea and intractable cardiac failure unless the underlying infection responds to treatment. On the other hand, prophylactic antibiotic treatment must be used with caution as the suppression of the commoner pathogenic organisms may result in the implantation of bacteria which may require the less commonly used and more toxic antibiotics which are poorly tolerated, especially where there is chronic renal disease.

The steroid hormones, carefully administered may be very valuable, as in status asthmaticus refractory to adrenalin and continuous drip aminophylline. They may have to be used as replacement therapy more frequently than formerly because of the radical palliative surgery sometimes used in cancer. Cortisone has been reported recently to be of value in the immediate treatment of "strokes" with earlier improvement in the paralytic signs as well as the emotional state. It is hoped that the newer, less toxic, low dosage preparation, for example, metacorten will prove of value.

It may be better of two evils to postpone surgical intervention in emergencies for a few hours or longer until the adverse nitrogen balance, under hydration and anaemia is corrected or improved, but they must not be overcorrected. Post-operative over-hydration and excessive blood by transfusion is more dangerous than minimal under-supply and the earlier the patient can be allowed to use his homeostatic repair mechanism, the better. Similarly, Wangensteen suction which should be started early, usually pre-operatively, should be terminated at the earliest possible moment.

It is well known that generally speaking, the quicker the patient can be gotten out of bed, the better; for example, few will deny the advantages of early armchair treatment of acute coronary infarction as advocated in selected

cases by Levine. Frequently, however, in acute emergencies, perhaps because of previous physical infirmity, early ambulation is not possible. This is where adequate complete twenty-four hour nursing care is imperative to prevent gravitational oedema in lung or elsewhere.

Post-accident and post-operative atelectasis particularly require energetic and continuous treatment whether with postural drainage, expectorants, antibiotics, carbon dioxide inhalation and bronchoscopic suction.

Summary

The number of elderly poor risk patients requiring urgent medical attention is increasing. It has been found that although their reaction to severe illness or injury may be very alarming, prompt and careful therapy will result in many recoveries. On the other hand late or incautious over treatment will more often be unsuccessful.

NOTICE OF V CONGRESS OF PAN AMERICAN MEDICAL WOMEN'S ALLIANCE

The V Congress of Pan American Medical Women's Alliance will be held in Santiago and Vina de Mar, Chile, March 6 - 14, 1956.

Papers on the subjects of: Medical Problems of Women in Medicine, Infertility, Family Security, Cancer, Miscellaneous Subjects will be presented.

Opportunities for sight seeing in Mexico, Salvador, Panama, Chile, Bolivia, and Peru have been arranged.

Information may be obtained from the Secretary, Dr. Eva F. Dodge, 2124 West 11th St., Little Rock, Arkansas, or from the Program Chairman, Dr. Eva Cutright, Wooster, Ohio.

Anti-Bios

J. D. Gray, M.D.
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WHEN Erlich expressed the hope that some day a "Steriliza Magnans" would be discovered, most of his contemporaries considered that he was merely competing with Jules Verne for first place as romanticist of his century. However, the work of Domagk, Flemming and Waksman has, as well as the benefits provided, demonstrated that the difference between the pedestrian scientist and one of the very great is the ability of the latter to combine with his scientific passion the imagination of the poet.

We have our "Steriliza Magnans", or rather a plethora of them. The sulphonamides, penicillin, streptomycin, aureomycin, terramycin, chloromycetin and erythromycin. These are the constant therapeutic companions, others lurk in the background—Tyrothricin, Bacitracin, Polymycin etc.—but because of their specificity and toxicity are only called upon in particular cases.

The definition of a "Steriliza Magnans" was that of a substance lethal to bacteria but without injury to the patient's tissue. It seems to me that we should take stock from time to time to see how applicable the definition remains. Broadly speaking, the enquiry breaks neatly into two parts; the effect of the anti-bacterial substance on the hosts tissue and the effect of the anti-bacterial substance on the pathogenic micro-organisms.

The Effect of Antibacterial Substances on Tissue

Sulfonamides

With the introduction of the more spectular and expensive antibiotics much of what was learned of the sulfonamides is in danger of being forgotten.

The administration of any of these compounds may be followed by agranulocytosis often ending in the death of the patient. In general it may be said that it is most likely to occur with high prolonged dosages, although not necessarily so. Less common in adults than in children is the onset of an acute and devastating hemolytic anaemia and purpura due to mega-karyocytic destruction. Acute porphyrinuria whose onset is definitely related to the taking of a sulfonamide has been reported in a fair number of cases.

Rich, who reviewed the autopsy data of the Johns Hopkins hospital, states that since the introduction of the sulfa drugs there has been an increase by twelve fold in the mortality rate for Polyarteritis nodosa; the association between disease and drug has been known for some years, but I doubt if the frequency with which the one may follow the other is widely appreciated.

Two lesser evils that may appear are drug fever, which often simulates the pyrexia of a septicaemia, and dermatitis. This latter varies from measly rashes or bullous eruptions to an exfoliative dermatitis; the bullous type may be related to porphyrinaemia percipitated by the drug.

On reviewing this list it is evident that most if not all of the toxic effects of sulfonamides are due to tissue sensitivity reactions, the particular clinical picture observed depending on the type of tissue in which the allergic reaction occurs. It is worth noting that in the body the sulfa-compounds are closely

bound to plasma albumin which probably accounts for these immunological sensitizations.

Lastly, there is the uncomfortable habit of sulfonamide and its derivatives to precipitate as crystalline conglomerates in the urine, which may block the urinary flow at any place between the straight tubules in the nephron and the urethral lumen.

Penicillin

In the first nine years of penicillin therapy, only two deaths directly attributable to the exhibition of this antibiotic were reported. Between 1952 and 1953 the number of published cases of penicillin induced deaths were 15. It is estimated in the U.S. alone that between thirty and sixty people died in 1954 from penicillin anaphylactoid shock, a figure which I think too low. The assessed incidence of hypersensitivity reactions of all types in patients treated with this antibiotic in the United Kingdom is calculated to be about 8 per cent at the upper limit and in the United States 10. These reactions may vary from localized plaques of urticaria to angio-neurotic oedemna, a serum sickness like disease and anyphylactic shock; a more recently noted complication is that of anuria of which four cases have been reported, all occurring in children.

Epidermally speaking, penicillin is such a potent inducer of contact dermatitis that its topical application is of questionable value.

The explanation for the bizarre immunological responses induced by penicillin follows the same line as that for the sulfonamides. Penicillin combines with serum albumin to form a complex which is no longer identified by the reticulo-endothelial system as a native protein. The protein-pencillin-complex acts as an antigen and the antibodies produced may become attached to the tissue cells. When this sessile antibody reacts with further antigen an explosive release of histamine occurs which presents clinically as an allergic reaction.

There are two other points worth noting. First, the speed with which penicillin induced anyphylactaic shock sets in is remarkable. In a personally observed case the patient showed signs of intense distress in about a minute and a half after injection, was desperately ill within five minutes and recovery was slow. Secondly, the deaths following the injection of procaine penicillin may be due to a different mechanism than that evoked by the crystalline salt, for it has been shown experimentally that the introduction of the former into a vein is followed by multiple pulmonary emboli.

Streptomycin and Dihydrostreptomycin

The toxicity of these drugs is similar and consists most commonly of allergic reactions, particularly of the skin. It is more potent than penicillin in producing contact dermatitis and deaths have been reported from a condition resembling a severe erythema multiforme. Less intense reactions show periorbital oedema, pruritus and denudation of the skin over the areas most exposed to the drug. About 7% of all cases in which this antibiotic is given develop manifestations of epidermal sensitivity of varying degrees of intensity. The figure for the same type of reactions in personnel administering the antibiotic has been reported as high as 25 per cent. The effect of streptomycin on the

8th nerve is fairly widely known. Dihydrostreptomycin appears to be more toxic for the auditory branch of the nerve than streptomycin while the reverse is true concerning the vestibular branch.

Thomas reporting to the Royal Society of Medicine observed the onset of vertigo in the streptomycin treated cases of tuberculosis on a two grams dose per day. He found 14 out of 23 developed vertigo on or about the 22nd day of the course. On a one gram per day dose the onset of vertigo appeared about the 45th day with a reduction in the attack rate by 3/4. It is felt that any recovery of vestibular function which may appear after cessation of therapy is due to compensatory mechanisms rather than anatomical restoration. As far as damage to the auditory branch of the 8th nerve is concerned personal experience in following a series of cases of tubercular meningitis treated by streptomycin or the dihydro compound is that about 1 in every 10 develop absolute deafness; "Delayed deafness" has been reported following the use of the dihydro salt, becoming obvious weeks after treatment was stopped. There is some question as to whether this deafness is truly delayed or is actually a slow progressive auditory nerve degeneration. Whichever the case may be the result as far as the patient is concerned is the same. Streptomycin has nephrotoxic potentialities, Farrington, using a compound that was 95 per cent pure noted casts in the urine in all sixteen patients under treatment with a reduction in renal function in two, one of which subsequently showed recovery of kidney function. Lastly streptomycin has apparently been involved in an occasional case of aplastic anaemia.

Aureomycin, Terramycin and Tetracycline

Because of their chemical affinity these three antibacterial substances have been grouped together.

Toxic reactions in the sense used to describe those following the administration of the sulfonamides, penicillin or streptomycin are not to be found in this class of antimicrobial agents. That is not to say they are free of danger for there are a growing number of cases in which they have precipitated a desperate or even fatal illness. This arises from three factors; firstly, these drugs are indiscriminate in the type of bacteria they kill, hence administration is followed by a profound depression in the normal bacterial flora in man's respiratory tract and gut, secondly they are not fungicidal, and thirdly a number of strains of staph. aureus are now resistant to their effect. This combination has led to the occurrence of two illnesses of extremely serious import and increasing frequency.

The first of these is pulmonary moniliasis. This group of antibiotics practically annihilate the normal upper respiratory tract flora but have no fungicidal effect; Candida albicans normally an inhabitant of the upper air passages proliferates without bacterial check and in certain cases this may be followed by an invasion of the yeast cells into the bronchial epithelium setting up an inflammatory reaction in the lung tissue, resulting in a long continued debilitating illness which may end fatally.

The second and more dramatic is the occurrence of a staphylococcus aureus enterocolitis. The antibiotics depress the normal gut flora, and this may lead to their replacement by strains of S. aureus resistant to these antibacterial substances; a fulminating entero-colitis follows in which sloughing

of the gut mucosa takes place. Death usually follows within 72 hours due to a combination of bacterial toxins and extreme electrolyte and water loss.

Lastly this group may produce an uncomfortable stomatitis, vaginitis, or perianal and bladder irritation. There is an assumption that they are primarily due to a proliferation of yeasts in the mouth, gut or vagina and a loss of vitamin B following the destruction of the gut coliforms. It is my opinion that an irritant factor is present in the antibiotics themselves which in the susceptibles lead to local irritation.

Chloromycetin

This antibiotic has been undeservedly given a bad name. Next to erythromycin it is the least toxic of all antibacterial compounds. Because its molecule contains nitro-benzine ring it will in the occasional patient produce an aplastic anaemia. Between 1952 and 53 a survey conducted in the United States unearthed 44 cases with 23 deaths of aplastic anaemia in which chloromycetin alone could be blamed. A year later a second survey showed 26 deaths from the same cause. Oddly enough the sex ratio shows a 3 to 1 preponderance of females affected over males with 1/3 of the cases occurring before the age of 10. In England a similar survey made in 1954 described a total of 24 fatal cases. As far as can be determined there has been no overall increase in the total number of cases of aplastic anaemia occurring in either country since the introduction of this antibiotic, suggesting that there is a pool of individuals with an inherently unstable hematopoetic system whose fate is to die of aplastic anaemia where the specific stimulus or stimuli are met.

It appears that approximately one patient in every four hundred thousand treated with chloromycetin will die of an aplastic anaemia.

Erythromycin

I have never met and can find no reference to toxic reactions following the use of this antibiotic.

The Effects of the Antibacterial Substance on Pathogenic Micro-organisms

The sensitivity of bacteria to the lethal power of antimicrobial substances is the core of this part of the whole problem. Has the sensitivity of organisms changed, or is it changing? Unfortunately, there can be but one answer, that some of the commonest bacteria causing disease in man are no longer killed by many of our antibiotics in ordinary therapeutic dosages.

In this hospital 80% of staphylococcus pyogenes isolated are penicillin resistant, 70% are resistant to Aureomycin, Terramycin and Tetracycline and about 5 per cent to Chloromycetin; so far only an occasional strain has been encountered which is Erythromycin resistant. This is not true of the pathogenic streptococci most of which are still sensitive to the popular antibiotics.

There are some properties of the individual antibiotics in relation to bacterial resistance which are of interest. Streptomycin breeds resistant mutants most readily both in vitro and vivo in most of the bacteria against which it has been used. In the tetracycline group cross resistance is almost invariable, that is an organism acquiring resistance to aureomycin becomes automatically resistant to terramycin and tetracycline at the same time, although the two

latter antibiotics may not have been used in the treatment of the particular infection. This cross resistance does not seem to spread to chloromycetin.

Resistance develops rapidly to erythromycin, particularly by the staphylococci; the fact that it has not been seen to any great extent in this laboratory appears to be a reflection of its infrequent use and not to any particular virtue in the parochial organisms. In general it may be said that continued use of any antibacterial compound in low dosages will lead to strains of resistant organisms emerging.

The continued isolation of pathogenic organism from the stools after a good therapeutic response to antibiotic treatment of a Salmonella or Dysenteric infection has been obtained is not necessarily an indication of increased bacterial resistance to that antibiotic. It may often be due to an adequate tissue concentration essential for combating the infection in the face of a low gut concentration due to the almost complete absorption of the antibiotic. This is particularly true of chloromycetin where in the treatment of Typhoid Fever there is clinical evidence of adequate response when examination of the stools may show pathogenic bacteria; over 90 per cent of a given dosage of this antibiotic is absorbed and the residual left never reaches a high enough concentration per cubic centimeter of gut contents to kill the organisms in the lumen.

That we have departed from Erlich's conception of the perfect "Steriliza Magnans" there can be little question, for in our attempt to cure the patient of his infection we may kill him, in other words—"antibios"; further in many cases we can no longer destroy the invading bacteria plaguing his tissues.

When faced with the problem of treating a case suffering from an infection there are, to me, six basic questions which the physician should put to himself and seek the answers before employing his remedy. It may be that the severity of the illness is such that time becomes the overriding factor, and it behoves him then to use those weapons that from his past experience have been found most effective in similar situations, but even so it is incumbent upon him to remember the six variables so that if the expected response to his therapy does not occur, or an anti-bios effect sets in, he is not unprepared for the unwanted. The six basic factors are:—

1. The severity of the illness.
2. The tissues invaded.
3. The stage of the inflammatory process.
4. The organism and its sensitivity.
5. The toxicity of the drug.
6. The diathesis of the patient.

The Severity of the Illness

The lack of discrimination in the choice of illness to treat or otherwise, is probably more responsible for the difficulties which now beset antibiotic therapy than any other factor. Most inflammatory diseases are self-limiting and the body defense mechanisms are quite able to cope without outside help.

The giving of antibiotics for coryza, pharyngitis, mild tonsillitis, furunculosis, cervical adenitis, localizing subcutaneous infections, and possibly for minimal lesions of Tuberculosis, is unwarranted except in special circumstances such as tonsillitis in the presence of mitral valvular disease or congenital heart-

disease. The use of antibacterial substances as an "umbrella" in cold surgery has much for condemnation and little for recommendation, as well as being irrational if it leads to carelessness in aseptic technique.

The criterion for therapeutic interference should rest on the balance between the severity of the illness and the potential toxicity of the anti-microbial substances, and where one outweighs the other the question is settled. Exhibition of the antibiotics in mild infections may lead to the sensitization of the patient when their help may be in desperate need at a later date, or it may induce a toxic reaction whose effects may be disastrous and lastly it will add to the growing pool of antibiotic resistant organisms in the community.

The Invaded Tissues

The optimum therapeutic effect of the antibacterial compound is only achieved when the specific tissue reacting to bacterial invasion achieves its maximum concentration of the drug. It is an unwarrantable assumption that high blood antibiotic levels reflect the same concentration throughout all body tissues. Unfortunately, the concentration varies from tissue to tissue, from antibiotic to antibiotic.

Penicillin penetrates pleural, pericardial and synovial membranes poorly, it does not penetrate the blood-brain barrier unless inflammation is present, it does not reach the brain, nerve tissue, the eye, bone, sweat or saliva glands. Chloromycetin reaches high concentrations in the brain, passes through the choroid plexus readily, reaches high amounts in the spleen and kidneys, moderate concentrations in the lung and liver and low in the gut lumen. Streptomycin enters brain and nerve tissue poorly but passes inflamed meninges readily,does not enter the liver, is high in renal tissue, moderate in lung and muscle and is virtually excreted unabsorbed when taken by mouth. Erythromycin does not pass the blood-brain barrier in the absence of inflammation, is concentrated in the liver, appears readily in ascitic and pleural fluids and reaches therapeutic levels in kidney tissue. This antibiotic is irregularly absorbed.

Aureomycin passes the blood-brain barrier and the serous coats readily, is found in reasonable levels in the liver, kidney, lung and spleen and reaches high concentration in the bowel lumen.

Terramycin patterns aureomycin closely except that it does not pass the blood-brain barrier in the absence of inflammation and absorption from the gut ceases when the oral dose reaches about 75 mgs. per kilo per day.

Tetracycline is similar to aureomycin.

The stage of the Inflammatory Process

If there is fibrosis and loculation as in pericariditis, bronchiectasis, empyema, chronic infection of the antra or an abcess of some duration, a theorectically effective antibiotic probably will not penetrate to the causal organism.

It should be borne in mind that in order to get an antibiotic into a tissue suffering from inflammation an effective blood supply to that tissue is essential. Where nature has thrombosed the capillary net-work surrounding an inflammatory locus it is not possible to get the antibacterial substance into that part; it is for this reason that the antibiotic treatment of boils is a failure.

That is not to say however that an infection in the spreading pre-necrotic stage cannot be successfully dealt with, for here the capillary blood supply is abundant thus allowing a lethal concentration of the drug of choice to be readily achieved in the affected tissue.

Treatment is unnecessary and unhelpful in a declining infection, as example in the stage of resolution and absorption of a pneumonic process already dealt with by nature, and may interfere with the formation of natural antibodies.

The Organism and its Sensitivity

Recent work has shown that the antibiotics are bactericidal and in fact there are a number of workers in this field who doubt the validity of bacteriostasis as a concept.

It has been shown that penicillin, streptomycin and chloromycetin kill 99.5 per cent of a young actively growing culture in six hours, the balance of 0.5% called persisters take one to seven days to die; these organisms are considered to be in a dormant non-dividing state.

In general there is a relationship between the effective antibiotic concentration and the number of organisms; the greater the number the higher the concentration per unit of tissue required to bring about bacterial death and vice-versa. Whenever the bacterial population is static at the time of contact with the antibotics, that is, organisms in tissue in the non-dividing state, the death rate is measured in days and not hours. Their eventual disappearance depends on the space-food stimulus to multiply in the presence of the antibacterial compound. Therefore if the successful treament of an infection is to be achieved, tissue antibiotic concentration must be optimally present for at least six days and the organisms caught during their proliferative phase. The longer the infection has been present before treatment the more difficult is eradication.

The determination of the sensitivity of the organism to the antibiotics is the sine qua non of rational therapy. This sensitivity must be related to the concentration of antibacterial substance achievable in the body and sensitivity as a term is relevant to this point. With the growing number of "resistant" bacteria every use should be made of laboratory facilities in the determination of the choice of antibiotic.

The Toxicity of the Drug and the Diathesis of the Patient

These two factors can be discussed together because of their basic interelationship. Enough has already been said to demonstrate that all our antibacterial compounds except one can be "toxic" to the patient—the anti-bios effect. These reactions are fundamentally allergic responses with the exception of staphylococcal entero-colitis.

Much could be done to prevent their occurrence if before prescribing antibiotics a careful assessment was made of the patient's history and the practise of using antibacterial compounds in combinations were avoided.

The patient with a definite allergic diathesis who has had penicillin or streptomycin previously is an excellent candidate for an anaphylactic reaction, serum-like sickness or dermatitis. He is safer with a tetracycline. It has been

suggested that all patients who are allergic should be skin tested before either of these drugs are given, an impracticable council of perfection.

The number of cases of toxic reactions following the combination of antibiotics or antibiotics and sulfa drugs, arsenicals, analgesics, anti-convulsants, barbiturates or antipyretics is much higher than when an antibiotic has been used alone. Obviously this restriction must be combined with common sense but surely it is not necessary to include all the antibacterials in the pharmacopea, even though this polypharmacy has been supported by the idea that some antibiotic combinations show synergism. The proof of the latter does not seem to be very convincing.

The dosage scheme in use for penicillin and streptomycin are well established and need no comment. However, for the tetracyclines, chloromycetin and erythromycin the dose should be rationalized on tissue mass and the knowledge of bacterial persisters; the amount given should be not less than 50 mgs. per kilo per day and not more than 75.

Whatever antibiotic is administered it should be continued in full dosage for seven days.

The prescribing of antibiotics is not easy, contrary to what the drug houses would have us believe. Successful use demands a visualization of many factors which vary from patient to patient each of which has to be assessed before a proper course is selected if anti-bios is to be avoided and an antibiotic effect attained.

How Canada Handled The Salk Vaccine*

Robert Crichton
New York

THERE were some anxious faces on the morning of May 9 at the Canadian Department of National Health and Welfare in Ottawa. The early editions of the Toronto Star had arrived, featuring prominently on page one a story about a boy who, after receiving a shot of Canadian-made Salk vaccine, had come down with bulbar poliomyelitis.

One of the first to see the item was George Carty, the young executive assistant to Paul Martin, Minister of National Health and Welfare. He telephoned Martin immediately, and Martin gave instructions for Doctor G. D. W. Cameron, Deputy Minister of Health and the career civil-service officer who actually administers national health policy, to alert the ten provincial ministers of health.

"I can remember muttering aloud, 'God help us, this is the start of it,' " Carty has recalled. "I hadn't the least doubt the panic was on for us, just the way it was down below."

The panic was on indeed "down below." On May 7, two days before Canada recorded its first polio case of the year, U. S. Surgeon General Leonard A. Scheele requested a halt in the U. S. immunization programme. On that day Canada's Health Minister Martin asked Doctor R. D. Defries, director of Toronto's Connaught Laboratories, which were producing all of Canada's Salk vaccine, to fly to Washington and try to find out what was going wrong with the U. S. programme. In the meantime Martin and Cameron talked the situation over with every provincial health official they could reach. On Sunday, May 8, Martin had a talk with Doctor Defries about what he had learned in Washington and reached the final answer to a crucial question: Should Canada stop its immunization programme and see what developed in Washington, or should it go ahead alone?

That same evening Martin announced to the Canadian people that the Department of Health would not only go ahead with its immunization programme but would step it up just as fast as compliance with rigid safety regulations would allow.

The bold announcement was received throughout Canada with pride and confidence. None of this, of course, was displeasing to the Minister of Health and Welfare. Fifty-two-year-old Paul Joseph James Martin, the son of an Irish steelworker from Ontario, is both aggressive and ambitious in his administration of one of Canada's most highly prized political offices. But if the news from Toronto on the morning of Monday, May 9, meant that Canada was about to duplicate its neighbour's recent vaccine difficulties, both the nation's pride and Martin's political stock were in for a drastic deflation.

Before notifying the provincial ministers of health, Carty had checked with Toronto for a more complete version of the story. Some months before, Toronto had set up a flying squad of experts whose job was to evaluate any new cases of polio that might develop. The team consisted of an epidemiologist,

* Reprinted by permission of the author from the July 14 issue of The Reporter, New York.

a bacteriologist with virological training, and a doctor with previous polio epidemic experience. Even before Carty's call, the team had been able to determine that the boy in the news had contracted a mild form of polio four days before receiving his shot. Canada finally had its first case of polio, but the Connaught vaccine was cleared of any suspicion.

The record, as this is written, remains unblemished. Of course the Canadian programme is smaller—a little less than a million children vaccinated as against nearly eight million in the United States—but in the United States 168 cases of post-vaccination polio had been reported by June 18. Canadian health officials and scientists, reluctant to be drawn into making any invidious comparisons with the U. S. programme and profoundly grateful for the American generosity in including them in all phases of the Salk vaccine development, will usually go no further than to say that they have been lucky. They point to Canada's smaller population and later polio season. But Canada's luck, if luck it was, also involved having a Cabinet officer in charge of the programme who, unlike his opposite number in the United States, *did* foresee "the great public demand for the Salk vaccine."

Most private citizens in Canada are not at all reluctant to say why their polio vaccination programme has gone so well. As they see it, there are three main factors:

Early conferences between scientists and government officials, thoroughly co-ordinated by the federal Department of Health.

Federal control of manufacturing and distribution.

Thorough vaccine safety testing standards.

A National Emergency

Canada has participated in the development of a polio vaccine from the beginning. Doctor J. F. Morgan of the Connaught Laboratories contributed significantly to the work of Doctor John Franklin Enders of Harvard, who in 1949 succeeded in keeping polio viruses alive in non-nervous tissue. In 1953, as preparations were being made for the 1954 field trials, the U. S. National Foundation for Infantile Paralysis gave Connaught the contract to supply almost all the live virus strains needed to produce the vaccine. Shortly before the field trials, the Foundation invited Canada to participate on a limited basis when it was found that more vaccine was available than had been anticipated. Health Minister Martin consulted the ten provincial health ministers, and Manitoba, Alberta, and Nova Scotia were the first to accept.

Health and welfare have always been big issues in Canadian politics, as is evidenced by the Canadian budget. Last year Martin's department received $1.2 billion, the second largest item (after Defence). The budget for Mrs. Hobby's Department of Health, Education and Welfare was almost twice as large, but the U. S. population is more than ten times that of Canada.

Although Canadian health programmes are traditionally administered by the provinces, their general organization has tended more and more to be concentrated in the Department of National Health and Welfare. This portfolio, considered a juicy plum for a rising politician, was created in 1944. As in Britain, the Minister is drawn from the ranks of Commons and is responsible for policy. Beneath the Minister is a career civil-service officer, at present

Doctor Cameron, who is responsible to the Minister for seeing that policy is carried out.

Each of the ten provinces has the same set up, the provincial minister of health coming from the local legislatures and backed by a civil-service officer.

The basic federal structure is similar to that of the United States. Martin's department does not dictate policy. The provinces are as jealous of their rights as states are, and the Minister is authorized to intrude in local affairs only when it can be clearly established that it is in the national interest to do so. At most he advises and persuades. His means of persuasion, similar to those of the U. S. Surgeon General, if he chooses to use them, are talent and money. The federal department has access to the best medical advice, and its policies are almost always followed in the provinces. Furthermore, under the National Health Grant Programme, which was established in 1948, the federal government makes large grants to the provinces for special needs. Recently, for example, $41 million was made available in three grants to provinces for such things as improved laboratory and radiological services. Martin has enjoyed the fullest co-operation from the provinces.

When Canada was invited to participate in the field trials of 1954, its Department of Health set up a standing group of experts to study the vaccine and its problems and also began work on a pilot plan for its eventual manufacture and distribution. Six months later, in October, after being informed of the group's findings, Martin called a meeting of the Dominion Council of Health. This is a conference of the deputy health ministers from all the provinces, the men who in the end must advise the provincial ministers, many of whom are not medical men. The Department of National Health had a complete programme drawn up and ready to go. By all calculations, the Salk vaccine seemed certain to be a success. Doctor Defries estimated that if Connaught Laboratories went into production right then, enough vaccine could be ready in the spring to inoculate all Canadian children between five and seven, the most vulnerable age group. For some 550,000 two-shot treatments the cost was estimated at about $750,000.

Martin asked for sweeping powers. This, he declared, certainly qualified as a national emergency. The provinces were asked to relinquish their traditional prerogatives in this case and authorize the federal government to run the polio programme. The federal government would advance half the cost (outside of grants) if the provinces would meet the other half on a basis of population.

The provincial deputy ministers found Martin's reasoning persuasive. They formed their own committee to report back to the Council with a plan for national production and distribution. Others were persuaded too. The Canadian Medical Association went along with the plan; there were no cries of "socialized medicine" in Canada. The commercial pharmaceutical houses, clearly not equipped to produce vaccine to meet Martin's schedule, did not protest the granting of a contract to the nonprofit Connaught Laboratories, which are attached to the University of Toronto Medical School.

Before the Dominion Council of Health had adjourned, the committee had already reported back a plan for approval. The committee suggested free inoculations as the fairest form of distribution and devised a method whereby

all provinces would be assured of simultaneous and equitable distribution under federal surveillance. It was further suggested that a stringent code of safety procedures be worked out by the Health Department's Laboratory of Hygiene in Ottawa and representatives from Connaught. The committee's proposals were adopted unanimously.

Six months before Doctor Thomas Francis, Jr., gave his evaluation of the Salk vaccine at Ann Arbor last April, Canada had established a programme for vaccine production and distribution adequate to national needs, with a clearly defined chain of command and centre of responsibility.

Fishing for Guppies

Canada went ahead, after the alarm in May, because Canadians had confidence in the Salk vaccine their doctors were using. The United States called a halt because that confidence had been shaken. A comparison of the two countries' safety procedures in producing Salk vaccine may help to explain the differing attitudes.

In the United States a new biological can be licensed if, after testing and a review of safety procedure, the product turns out to meet Public Health standards. In Canada, the federal Laboratory of Hygiene goes through the same steps the manufacturer did and actually produces the drug; if any potential flaws are found in the process, even though the product rates highly, the Laboratory advises the manufacturer that changes must be made if he is to be licensed.

Connaught established safety procedures for the manufacture of polio vaccine that borrowed heavily from the methods established by the U. S. National Institutes of Health for the 1954 field-trial vaccines and then presented them to the Laboratory of Hygiene at Ottawa, for appraisal. The final approved test was not much different from that established for U. S. vaccine producers, except for one striking difference:

In Canada safety tests have been applied to lots of up to 120 liters, enough vaccine for 120,000 shots, whereas in the United States these basically similar quantitative tests have been applied to lots of up to 1,200 liters, enough vaccine for 1,200,000 shots.

Because of certain special problems in the manufacture of Salk vaccine, this difference becomes vitally important. Salk vaccine, as many people know by this time, is produced from three distinct virus strains. Before being pooled for the final vaccine, these strains are individually treated with formaldehyde, which, theoretically, will inactivate or "kill" live virus in the strains.

But as Doctor Scheele stated in his June 9 report to Mrs. Hobby on reasons for the vaccine stoppage, there is now evidence that formaldehyde sometimes fails to reach or penetrate minute particles of live virus. Thus a supposedly finished lot might still be speckled through with dangerous spots of live virus—as, indeed, numerous lots have been. It becomes obvious that as the size of the batch to be tested increases, the chances of discovering dangerous live virus decreases. The problem has been compared with that of trying to discover whether there are any guppies in two dark containers. Ten sweeps with a small net through a barrel is not much of a test, but ten through a bucket might provide a guppy or two if there are any to be caught.

In the United States it has been argued that safety lies in production methods rather than in testing, but the fact remains that Canadian safety tests provide up to twenty times more chances of finding something wrong.

It was to meet this safety problem that the U. S. government was finally forced to take official action. The Public Health Service tightened safety procedures on May 25, but Canada is still ahead, and Martin has announced that at least the same relative standards will be maintained as larger lots are produced.

The second significant difference between the Canadian and American procedures concerns the touchy issue of the double check. The Scheele report notes that in four "supposedly inactivated lots of vaccine" produced for the field trials, live virus was discovered on triple-checking.

It is possible that subsequent checks simply made more certain that any live virus that had failed to be inactivated by formaldehyde would be found. There is a theory, however, that something can happen to a lot of vaccine between the time it is cleared and the time it is ready to be bottled for distribution. Some of the viruses may be only "stunned," or they may gather in "clumps" so that only the outside viruses are affected by the formaldehyde, or some of them may be vaporized and then somehow find their way back into the vaccine after final safety checks.

Whatever the explanation may be, the possibility that some live virus can survive the formaldehyde "cooking" has convinced the Canadians that a complete double check is warranted even after the vaccine has passed stringent tests. They insist that this is not a luxury but a necessity if a vaccine is to be made as safe as humanly possible. As of this writing, four lots of carefully tested Connaught vaccine, enough to inoculate 400,000 children, have been rejected and dumped after double checks at the Health Department's Laboratory of Hygiene in Ottawa. Since U. S. manufacturers are not now required to double-check, these suspicious lots of vaccine would in all probability have been set out for use in the United States.

Even under the revised safety regulations in the United States, the basic check by the Laboratory of Biologics Control still consists in asking the manufacturer to supply detailed data on just what steps he followed in producing his last lot of vaccine. These are called "protocols." If the protocols read correctly, the lot is then released for use. Under revised standards, the Laboratory is now conducting spot checks on various lots, but in his report to the President Surgeon General Scheele stated: "Great emphasis will not be placed on simple repetition of the testing already done in individual laboratories, since this adds little to the safety factor."

This statement differs sharply with the Canadian view. The Canadian experts are convinced the double check is the backbone of their safety programme. Of course the Canadians great advantage in the double check is the much smaller amounts they deal with. In the United States, to institute a double check would call for so much expansion in trained personnel and facilities that the mass polio programme might have to be suspended for a year or even two years. The revised safety standards of May 25 have already slowed down the production of fresh vaccine to a trickle.

Where Are The Missing Monkeys?

One other item that showed significant difference between the two nations immunization programmes came to light in one of the first Canadian encounters with commercially produced American vaccine. Canada invited all six participating U. S. firms to apply for licenses to sell in Canada. Five of them replied and sent along particulars, varying in details, about their operations. Particulars supplied by three firms were not adequate enough to warrant issuing a license at the time. Two firms, the Eli Lilly Company and Parke, Davis, were requested to send protocols and batches for testing. The first Lilly protocol became the object of much subdued wrangling. Although information on tests with twenty-four monkeys was requested, data on only eighteen were forthcoming. Ottawa wanted to know what had happened to the other six monkeys. Had they perchance dropped dead?

The U. S. government did not bother to ask any searching questions such as after the field trials. Of course the pharmaceutical houses were not anxious to advertise their failures, but as a result much valuable information on vaccine production was certainly lost. Only by complete records could any worthwhile yardstick be applied to test the effectiveness of production methods. If one firm was botching up three batches out of every five (although Washington only saw a report on the two good lots), it might be reasonable to assume that the firm's methods were not all they might be.

Aside from theatrics at Ann Arbor when the vaccine was cleared by Doctor Francis—which the Canadians felt was both undignified and dangerous in that it tended to sell people the idea that the vaccine was one hundred per cent effective—the aspect of the U. S. programme that raises most Canadian comment (and eyebrows) is price. When Connaught began production, it charged $1.50 for three inoculations. Since then the price has dropped to $1.25. When the Institute of Microbiology at the University of Montreal gets into production this autumn, the price is expected to drop below a dollar.

In the United States the retail price of private doctors for three shots may run as high as $6.60. In wholesale lots the average price for private doctors will be about $4.50. What actual cost may be is hard to determine, but Canadians who have seen the elaborate facilities of some of our big pharmaceutical plants find it hard to believe that U. S. costs could be much higher than the Connaught's, especially taking into account that U. S. vaccine is manufactured in bulk lots of 1,200,000 cubic centimeters. One explanation may be that the highly competitive drug firms traditionally try to get their investment in a new product back within a year or two. After that the price might drop considerably. Another is that a nonprofit laboratory like Connaught does not get involved in the enormous public relations campaigns that U. S. drug firms wage.

Free Enterprise Till It Hurts

In the United States little or no official guidance is now given to the private doctor. With inadequate advice, conflicting information, and sweeping claims and counterclaims about the vaccine hanging in the air unresolved, he is asked to take upon himself the responsibility of inoculating children. This had led to situations such as that in New Jersey, where some counties have de-

cided to go ahead and some have decided to stop, where some towns within the counties have programmes and others don't. In some counties all responsibility has been left to the parents. The parent who decides not to allow his child to be vaccinated this year and whose child then contracts polio presumably must blame himself for having given the wrong answer to a highly complicated medical problem. And what of the scarcely better-informed doctor who decides to go ahead with an immunization programme during the summer polio season and finds that he has induced paralysis in children who were carrying polio virus held in check by natural antibodies? The possibilities of personal tragedy are everywhere present in a programme that has no co-ordinated direction.

The present U. S. government policy holds that halting the programme again would deprive millions of children of protection in order to prevent a rather remote risk for a handful. Surely another consideration is that a long halt in the programme might set back public confidence in the vaccine for a decade. There may also be a few political considerations involved. Having started with big claims, the programme has to go on being big.

In the light of what has happened recently in the United States, the Canadian experience with its immunization programme would seem to bear out Health Minister Martin's original claim: The introduction of anything so important as a new polio vaccine amounts to a national emergency and calls for some form of national control.

ANIMAL CARE PANEL

A meeting of the Animal Care Panel will be held on December 1st and 2nd, at the Henry Hudson Hotel (353 West 57th Street), New York City.

The Animal Care Panel is an organization of investigators, administrators of animal quarters, animal breeders, food and cage manufacturers; in short, individuals interested in the care of experimental animals. The programme will consist of papers dealing with the physiology and behaviour of laboratory animals, their diseases, nutrition and related problems.

Further information may be obtained from L. R. Christensen, Ph.D., Director, New York University, Bellevue Medical Centre of New York University, 550 First Avenue, New York 16, N. Y.

Dalhousie University Appeal
Faculty of Medicine

For the first time the Dalhousie Medical School is specifically appealing to the doctors for financial assistance. Up to now money has flowed from the general university funds in increasing amounts in order to give a medical education to the doctors of this and other provinces. The financial drain has been heavy.

Some time ago several members of our profession met and delved into costs of a medical education, particularly in relation to that paid by the medical graduate. To our surprise we were shown that the expenditure in the medical training of a doctor amounted to over $11,000. The contribution in fees by the student to the university amounted to only $2,000. The government contributes approximately another $2,000, but the bulk, or other $7,000 largely is provided through the generosity of benefactors.

Does it not seem reasonable at this time that the University appeals to members of our profession for financial assistance, particularly in view of the money expended in their behalf?

With these thoughts in view all members of the profession will be approached in the near future in the hope that sufficient funds will be obtained to keep the standard of the Dalhousie Medical School at the highest level.

The objective from the profession in Nova Scotia is $500,000. This means an average of $1,000 per doctor. As it is anticipated that some will not be giving, it will be necessary if the objective is to be reached that more be obtained from those who are financially in a favourable position.

The campaign in Halifax is well under way. The results to date have been most gratifying. Indeed donations up to $5,000 have been received, spread, of course, over several years.

It is anticipated that many donations will be spread over a considerable period of time and that quite possibly the younger doctors might wish to spread theirs over five, ten or even more years. While it is desirable to obtain large contributions which can be considered as capital, spread over a three year period, contributions of a smaller amount given annually would be quite acceptable and appreciated.

One doctor who was recently canvassed made this statement: "I am not in a big income group but I am going to give what I can, and that is to an extent that pinches a little." He gave $200 a year for five years.

The Medical School solicits and hopes for your generous support.

C. B. Stewart, M.D.
Dean, Faculty of Medicine,
Dalhousie University.

Clarence L. Gosse, M.D.
Chairman,
Medical Campaign Committee.

Report of the Medical Economics Committee

AS chairman of the Medical Economics Committee of Nova Scotia, I attended two meetings in Toronto of Canadian Medical Committee on Economics, on November 29th and 30th, 1954, and April 22nd and 23rd, 1955. The following topics were discussed.

A. *Sick Mariners Fund.*

There has been no change since 1954 Annual Report, but there is some hope that changes in the Canada Shipping Act may modernize and improve this service to all concerned.

B. *D. V. A. Schedule of Fees.*

Here the Economics Committee had looked for a one dollar increase in home, office and night calls, as well as a twenty per cent increase in the surgical fees. This was met by a fifty cent increase in home, office and night calls and no increase in surgical fees. The Economics Committee is, however, still pressing for a reconsideration of the entire schedule, and it is hoped that something constructive will be forthcoming during the coming year.

C. *Indian Affairs.*

The Committee has not accepted the schedule of fees put forward by the Indian Health Services because they regard it as a scale of fees for indigents, and they feel that when the Federal Government has assumed responsibility for the payment of medical services, then it should use a single schedule of fees as a basis for payment of fees by all Government departments.

D. *Principles Relating to Health Insurance.*

A great deal of time was spent on hammering out these principles which were printed in the February issue of the Nova Scotia Medical Bulletin, and have been accepted by The Canadian Medical Association on much the same form.

E. *The Alberta Plan.*

Basically what the Alberta government plans to do, is to contribute one third of the premiums of all persons insured in the non-profit insurance agencies, and in April it looked as though M. S. I. would be the sole carrier.

Provincially, the Medical Economics Committee met twice in Halifax, on October 26, 1954 and April 6, 1955.

At the October meeting we suggested that benefits be increased to the welfare group, to include hospital medical or surgical care to a maximum of $25.00. This was put into effect. The Federal Health grants were fully discussed by Doctor G. Simms, Assistant Deputy Minister of Health and the minutes of this meeting were published in the November issue of the Nova Scotia Medical Bulletin.

The resolution from the Western Counties Medical Society dealing with income tax was discussed and later was discussed with Doctor A. D. Kelly, but as yet nothing has been accomplished in this matter and the prospects on any action in the future is not too bright.

At the April meeting the main topic of discussion was the proposal to give complete medical and surgical coverage to the wards of Children's Aid Societies, and the proposal put forward by the Economics Committee was reported in detail in the May issue of the Bulletin. This matter has been followed up, and in July Mr. F. R. MacKinnon reported that as yet all the Societies had not agreed to participate, but that there would be a meeting in September and following that he hoped to have the consent of all the Societies, and be able to go ahead with the contract.

At this meeting we also suggested that the surgical coverage for the Welfare Group be increased to a maximum of $50.00 and this I understand has been accepted.

F. *Provincial Welfare Funds.*

On January 1, 1955, the surplus in this fund was $27,482.15, following the introduction of the increased benefits above mentioned, the surplus on July 31, 1955, was $2,202.44. This surplus should decrease more rapidly in the months to come, as the monthly expenditures since March, 1955, have exceeded the monthly net revenues.

This year we had the Assistant Deputy Minister of Health sit in on our meeting, and I must say that he has made a tremendous difference in our understanding of the Federal Health Grants and how they are utilized.

Your chairman also acted as representative of The Medical Society on a panel discussion on Health Insurance held in Sydney, February 20, 1955, under the auspices of the St. Francis Xavier Extension movement. (I assure you it was most interesting).

In conclusion, I would like to thank Doctors A. L. Sutherland, T. B. Murphy, D. M. MacRae, J. B. Tompkins, the members of the Economics Committee, Doctor Graham Simms and Mr. D. C. Macneill for their interest and help all through the year.

(Sgd.) H. J. Devereux
Chairman, Medical Economics Committee

The Post-Graduate Committee of the Faculty of Medicine of Dalhousie University in co-operation with the Department of Obstetrics and Gynaecology and the Department of Paediatrics presents a

"WEEK IN OBSTETRICS, GYNAECOLOGY AND PAEDIATRICS"

November 28th - December 2nd, 1955

With attendance restricted to ten, this course provides the candidate with the maximum of practical experience, in addition to didactic material.

Programme: Week In Obstetrics, Gynaecology and Paediatrics

Monday, November 28th, 1955.

9.00-10.00	Problems of Obstetrics—Dr. H. B. Atlee.
10.00-11.30	The Place of X-Ray in Obstetrics.—Dr. I. A. Perlin.
11.30- 1.00	Symposium: (a) Minor Complaints in Pregnancy.—Dr. J. McD. Corston. (b) Diabetes in Pregnancy.—Dr. W. G. Colwell. (c) Cardiac Disease in Pregnancy.—Dr. K. M. Grant.
2.00- 4.00	Gynaecological Procedures in Office Practice.—Dr. M. G. Tompkins.
4.00- 5.00	Film—Abnormal Obstetrics.—Dr. E. Woloschuk.

Tuesday, November 29th, 1955.

9.00-11.00	Case Presentations.—A Review of Common Respiratory Infections. Diagnosis and Treatment. Moderator—Dr. N. B. Coward.
11.00-12.00	Fluid Balance. Demonstration of Paediatric Procedures.—Dr. J. M. Crosby, Dr. R. S. Grant.
2.00- 3.00	Conditioning for Childbirth: (a) Nurse and Hospital.—Mrs. P. Cook. (b) Doctor's Responsibility.—Dr. W. R. C. Tupper.
3.00- 4.00	Problems of Prenatal Care.—Dr. W. R. C. Tupper.
4.00- 5.00	Film—Physiology of Normal Menstruation.—Dr. M. G. Tompkins.
5.00- 6.00	Problem Cases—Obs. Gyn. Staff.

Wednesday, November 30th, 1955.

9.00-10.00	Ward Walk—5th Floor West, V.G.H.—Dr. H. B. Atlee.
10.00-12.00	Demonstration in Operating Room (a) Cauterization; (b) Conization; (c) Biopsy of Cervix; (d) Insertion of Pessary; (e) Removal of Bartholin's glands; (f) D & C; (g) Emptying Incomplete Abortion.
12.00- 1.00	Symposium—Uterine Bleeding: (a) Organic Causes.—Dr. J. McD. Corston. (b) Functional Bleeding.—Dr. K. M. Grant. Discussion by Staff.
2.00- 3.30	Paediatric X-rays—Discussion of Techniques and Interpretation—Dr. R. L. Smith.
3.30- 4.30	Common Emotional Disturbances in Children.—Dr. F. A. Dunsworth.
4.30- 5.30	Surgical Ward Rounds.—Surgical Staff.

Thursday, December 1st, 1955.

9.00-10.00	The Problem of Sterility.—Dr. M. G. Tompkins.
10.00-11.00	Proper Application of Forceps Head and Breech.—Dr. H. B. Atlee.
11.00-12.30	Symposium: (a) Ante Partum Bleeding.—Dr. W. G. Colwell. (b) Post-Partum Complications.—Dr. W. R. C. Tupper.
2.00- 3.00	The Vomiting Infant—illustrated by Kodachrome Slides.—Dr. R. S. Grant.
3.00- 5.00	Symposium: Recent Advances in Paediatrics. (a) Nephrosis. (b) Erythroblastosis. (c) Poisoning. Dr. G. B. Wiswell, Dr. H. B. Ross, Dr. H. Hunter, Dr. P. Sigsworth.

Friday, December 2nd, 1955.

9.00-10.00	Paediatric Dermatology—The Common Skin Conditions—Diagnosis and Treatment.—Dr. D. R. S. Howell.
10.00-12.00	Weekly Medical Ward Rounds.—Moderator: Dr. G. B. Wiswell. The Medical Staff, Children's Hospital.
2.00- 3.00	Problems of Abnormal Uterine Action.—Dr. I. A. Perlin.
3.00- 5.00	Symposium: (a) Post Maturity.—Dr. C. S. Robinson. (b) Virus Infections (Measles)—Dr. C.F. Brennan. (c) Toxaemias of Pregnancy—Dr. K.M. Grant. (d) Eclampsia.—Dr. J. McD. Corston.

Committee on Maritime Medical Care Incorporated

At the Annual Meeting of The Medical Society of Nova Scotia a Committee was established to study the set up of Maritime Medical Care Incorporated in its relationship to The Medical Society. The Chairman of the Committee is Doctor J. F. L. Woodbury of Halifax. The other members of the Committee are Doctor J. W. Merritt of Halifax, Doctor J. A. McDonald of Glace Bay, Doctor D. F. Macdonald of Yarmouth and Doctor W. A. Hewat of Lunenburg.

Any member of The Medical Society who has any ideas or opinions in regard to this question which he feels would be of value to the Committee in their study are asked to communicate the same to any member of the Committee or he may write to the Secretary of The Medical Society.

As this is a very important matter all members are asked to give it careful consideration.

Post-Graduate Activities

Under the auspices of the Medical Post-Graduate Committee of Dalhousie University, a Regional Refresher Course for the members of the Lunenburg-Queens Medical Society was instigated at Bridgewater on November 7th, 1955.

This course on Obstetrics, Gynaecology and Paediatrics will continue weekly for the next six weeks.