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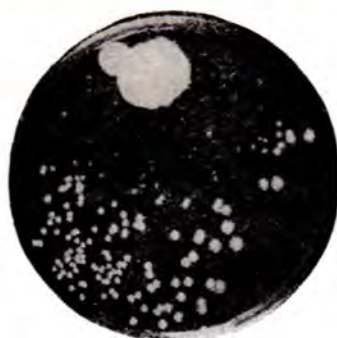
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## Penicillin

**T**HE story of Penicillin begins in 1928. Sir Alexander Fleming found, when working with the variations of staphylococcus colonies, that a mould colony had developed towards one side of a culture plate **FIGURE I**. Such contamination with a mould was not unusual, but



**FIGURE I**

what was astonishing was that in this particular culture plate the staphylococcus colonies for some considerable distance round the mould growth were obviously undergoing lysis. This had undoubtedly been often noticed before by bacteriologists! But Fleming had for years taken a special interest in naturally occurring antibacterial substances and, as he says himself, if this had not been the case the cultures would most probably have simply been discarded! The mould was soon identified as belonging to the genus *Penicillium* of the species *notatum* which had been found by Westling in decaying hyssop in Norway. The active substance which is still of unknown chemical constitution he christened "Penicillin". So was written the first chapter of this remarkable story of the "antibiotics".

As long ago as 1877 Pasteur and Joubert noticed that the growth of certain air-borne organisms inhibited the growth of the anthrax bacillus and suggested that this fact might be of importance in therapy (\*An address presented to the Academy of Medicine, London, Ont., April 19, 1945)

peutics. In 1899 Emerich and Loew<sup>3</sup> extracted "pyocyanase" from the *B. pyocyaneus*, and in 1939 Dubos<sup>4</sup> "gramicidin" from *B. Brevis*.

Fleming continued to investigate the properties of Penicillin in the laboratory and carry out a few clinical observations which permitted him to state in his original paper in 1929 that:

"It may be an efficient antiseptic for application to, or injection into, areas infected with Penicillin-sensitive microbes."

And again in 1931<sup>2</sup> in an article on the use of antiseptics:

"It is quite likely that it, or a chemical of a similar nature will be used in the treatment of septic wounds."

In 1938 Florey and his Oxford colleagues began to work on antibiotics in a systematic manner and chose "pyocyanase" and Penicillin for their first investigations. It is not my purpose this evening to review the preparation, purification and pharmacology of Penicillin, but I would recall the timidity and doubt of many that it would ever become possible to produce it in sufficient amounts to make it practical in medicine. The present proves the falsity of this prediction.

I do not think there has been a better example of the successful application of experimental laboratory work to therapeutic measures than that exemplified in the case of Penicillin. Some of the fundamentals of this work may be stated as follows:

(1) Practically all the human pathogenic organisms were early classified as Penicillin-sensitive and Penicillin-insensitive—(see table 1). Since then a few more sensitive organisms, such as the spirocheta pallida and the leptospira ictero-haemorrhagica, have been added, and the list is probably not yet complete.

TABLE I

SENSITIVE:	NON-SENSITIVE:
Pneumococcus	Hemophilus influenzae
Streptococcus haemolyticus	Escherichia coli
Staphylococcus	Bacillus typhosus
Meningococcus	Bacillus dysenteriae
Gonococcus	Bacillus proteus
Streptococcus viridans	Bacillus partyphosus A
Bacillus subtilis	Bacillus enteritidis
Clostridium welchii	Bacillus pyocyaneus
Vibrium septique	Bacillus fluorescens
Clostridium histolyticus	Bacillus prodigiosus
Bacillus sporogenes	Friedlander's bacillus

Bacillus oedematiens	Stephylococcus albus—1 strain
Bacillus sordelli	Micrococcus albus—1 strain
Lactobacillus	Monilia albicans
Cryptococcus hominis	Monilia kruzei
Spirochetæ Pallida	Monilia candida
Actinomycoses	
Bacillus Anthrax	

(2) It was equally important to know that the upper limit of dosage was not likely to be influenced by any toxic effect.

(3) That the oral administration of the unprotected drug would be ineffective because of its inactivation by the acid gastric juice.

(4) That frequent administration would be necessary because of the rapid concentration and excretion of Penicillin by the kidneys.

(5) That it would be unwise to prepare wounds for local application by cleaning with a number of the common antiseptics because of the inactivation of the Penicillin by heavy metals and by oxidation.

It is surprising how many times these fundamental observations have been neglected. Penicillin has been boomed by the lay press and magazines as a wonder drug which it is, and the cure of all infections, which it isn't! It will soon take its place beside aspirin, sulpha drugs and sex hormones in the family bathroom drug cabinet for all members to take, irrespective of age or sex, to combat the sundry miseries of mankind. The sulpha drugs have had their day. I would not be very bold to wager that five years ago 99 out of every hundred febrile cases were given sulpha drugs irrespective of what was the infecting organism. In fact the prostitute and her freelance sisters took them as a routine as did their boy friends as a chemical prophylactic of considerable merit for the joy of all concerned until the wily gonococcus became stubborn and resistant—which was not playing the game! The same may be the destiny of Penicillin to be circumvented by both the gonococcus and spirocheta pallida.

#### HOW DOES PENICILLIN ACT?

It must be appreciated that up to the present but a comparatively small amount of almost pure Penicillin (85%) has been available for the critical study of some of its more fundamental clinical properties. It was believed at first that its action was mostly bacteriostatic and it was suggested that it acted on sensitive organisms by preventing their multiplication when the cells were dividing, i.e. in young cultures. But the effect of temperature and the almost uniform susceptibility of cells from both old and young cultures are against this concept. Furthermore, there is accumulating evidence which would support the possibility that Penicillin has bacteriocidal properties also. Like other

antiseptics, Penicillin has an accelerated action in temperatures between 4° and 42°. But, on the other hand, its action decreases with changing pH from 7.0 to 5.0. With the acidity of its medium, either in vivo or vitro, approaching the latter it practically becomes inert. The presence of certain chemical antiseptics and sulphonamides reduces the effect although it continues to act in the presence of pus and necrotic tissues.

#### HOW TO USE PENICILLIN

In common with other antiseptics, it is necessary for Penicillin to come in contact with the pathogenic organisms. It is obvious, therefore, that it must reach them either through the blood stream or by local application or injection. In superficial infections of the skin or mucous membranes local application is often the most economical and effective. This may be accomplished by sprays with the Penicillin in solution or in a medium of an ointment, but it must always be certain that the Penicillin is brought in contact with the pathological organism. For instance, in the case of a carbuncle or an anthrax pustule, the mere application of the Penicillin to the surface is a poor method and little likely of success as compared to the systematic route. The same applies to deeper wounds. If the infected area in soft tissues can be laid bare and all the crevices exposed the local introduction of Penicillin with primary suture gives excellent results with much less pain, rapid and complete restoration of function, smooth and painless scars and the prevention of sloughing and loss of valuable tissues, as, for instance, in the hand when this treatment is used at the first operation. In wounds with compound fractures and penetrating brain injuries there are deep and often inaccessible foci of infection when both local and systematic therapy are indicated. It is not proper to draw definite conclusions from the earlier reports, as in 1942 and even in the first half of 1944 the amount available was limited and its indiscriminate use rigidly controlled. Out of this work two fundamental principles were obvious, namely proper surgical procedures and the earliest possible administration of Penicillin after a proper manner to reach the infected area. Penicillin would not save the face of sloppy and irrational surgery, but good surgery would be made better by the proper use of Penicillin.

In these days of intravenous therapy there is apt to be a blind belief that all agents may reach the desired destination without thought of certain peculiarities of some tissues. Whereas Penicillin is highly concentrated and rapidly excreted by the kidneys, its passage into the serous, synovial and meningeal fluids from the blood stream is slight. Therefore, infections in these cavities must be treated by the direct approach through removing some of the infected fluid and replacing it by a solution of Penicillin. The basis for this relative impermeability of these membranes remains to be explained. A recent

publication would indicate that in nephrosis it passes into the peritoneal and pleural fluid, but this is an unusual form of oedema and may not be comparable to inflammation.

Another factor of importance to be kept in mind is the rapid excretion of Penicillin by the kidneys. If it be given intermittently either by the intravenous or intramuscular route there is a high blood level or peak within a few minutes, after which the concentration rapidly declines; and in a few hours, depending upon the route and the amount given, it returns almost to zero, but during all of this period there is a high concentration in the urine from which it may be recovered in a comparatively pure form.

#### DISADVANTAGES OF PENICILLIN

The disadvantages of Penicillin are principally twofold. These are,—first, restricted action, as many organisms are non-sensitive to it. I grant it would be asking too much to expect it to be a panacea for all pathogenic agents and we should be thankful that it covers such a wide range. But a group of organisms, for instance the

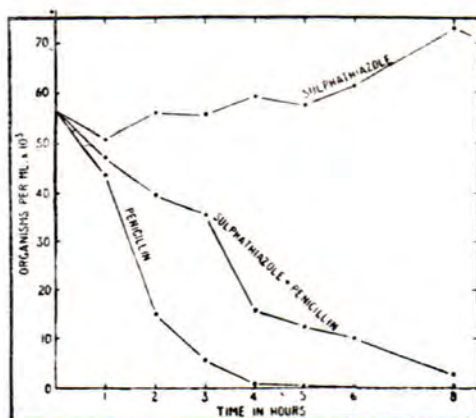


FIGURE II

streptococci, are not all equally sensitive and it has been amply proven in vitro that by growing sensitive cocci such as staphylococcus aureus in concentrations of Penicillin which are not inhibitory and gradually increasing this, that eventually an ordinary lethal concentration may be reached but the cocci continue to survive and grow. In other words, they become Penicillin non-sensitive or resistant. Until recently it was considered that in vitro this resistance continued indefinitely through many subcultures similar to sulpha-resistant strains. Recent work by Todd, Turner & Drew (1945)<sup>5</sup> has shown that staphylococci which have become resistant in vitro will rapidly revert to a non-resistant state. This would suggest the probability that such may occur in vivo if the drug is withdrawn for a period. This would seem



the only excuse for its intermittent use in a case where the original cultures were shown to be sensitive but later become resistant. Bigger (1944)<sup>6</sup> advanced the theory that Penicillin only kills dividing cells and that a very small proportion of dormant non-dividing cells which he terms "resistors" are liable to survive; these he advised should be permitted to grow by interrupting treatment if sterilization is to be complete. He also advanced the argument that Penicillin and Sulfonamides were synergistic. But this has not been confirmed, in fact the contrary is indicated by other workers. At the moment all available evidence points to the conclusion that Penicillin therapy should be continuous and not intermittent unless the organism acquires resistant qualities proven by proper methods.

The second disadvantage is the necessary use of the intravenous or intramuscular route for systematic therapy. There are obvious reasons why handicaps are inherent in these methods. It can be administered in either manner by a continuous or drip method, or by separate injections at various time intervals. To accomplish either of these successfully and without risk, constant nursing attendance or hospitalization—although not absolutely necessary—is considered advisable. The intravenous method required a comparatively pure preparation free of pyrogens and, in addition, its repeated or continuous intravenous use always carries a risk of thrombosis. There is little doubt that both of these untoward results are due to impurities which in time will be eliminated. The intramuscular drip or intermittent method is relatively free of both these objections, but at the same time it requires expert attendance which at the present time, and even in the predictable future, imposes restrictions which are difficult to overcome.

The ideal method, which gave sulphonamide therapy a preference over specific serum therapy as in pneumococcus pneumonia, is oral administration.

In the early days of Penicillin therapy this was tried without success. The failure was attributed to the high acidity of the stomach contents. However, this has always been considered as a challenge rather than a defeat and it has been expected that when investigators could get around to it the problem might be solved in spite of past failures. In February (1945) Little and Lumb<sup>7</sup> published in an unabridged form their results from an Army Laboratory in the Middle East. If these are substantiated they open up a new vista of clinical investigation. They found it more convenient to use Seitz-filtered urine of patients receiving parenteral Penicillin for the "gutter-plate" method of determining the sensitivity of organisms. It was observed that such urine filtrate retained its activity longer than saline solutions of the sodium salt of equal inhibiting power. It, however, seemed

probable that the substance excreted in the urine had been in some way stabilized by passage through the body. They continued their investigations to find out whether the urine Penicillin had increased resistance to heat and to extremes of pH. This was found to be the case.

In experimental animals sporadic experiments have been undertaken to the end of finding whether Penicillin could be absorbed from the intestinal tract as indicated by sufficiently high blood level from practical purposes. (Chain et al (1940)<sup>8</sup>; Abraham et al (1941)<sup>9</sup>; Florey and Florey (1943)<sup>10</sup>; and Rammelkamp and Keefer (1943)<sup>11</sup>.) Rammelkamp and Helm (1943)<sup>12</sup> reported a case of pernicious anaemia with achlorhydria which, with the ingestion of Penicillin, showed blood levels which were in the range of practical therapeutics.

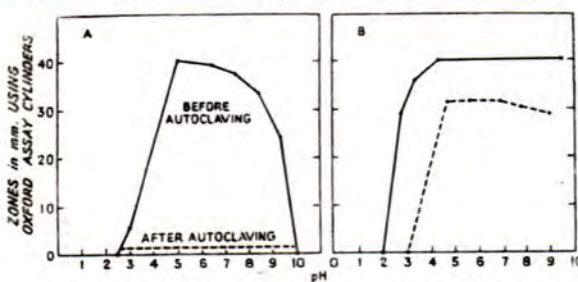


FIGURE III

Little and Lumb (1945)<sup>7</sup>—being convinced that Penicillin was made more stable by passing through the body, set out to find, if possible, the “stabilizing agents”. It would seem a large order, but they were influenced by two leads, first that Penicillin is excreted in appreciable quantities in the bile, and, second, that Col. Pulvertaft, former commandant of their unit, suspected that sulphur-containing elements could render it more resistant to heat. There is not time to review all their work, but, in brief, they found that admixing Penicillin with raw egg made it more resistant to heat and alterations to pH. It is not to be concluded that the change in Penicillin produced by this admixture with egg albumin is the same as that which occurs by passage through the body, but the resistance is of the same kind. Penicillin was given by mouth admixed with egg albumin with a preceding two drams of sodium bicarbonate or magnesium trisillate and compared with the intra-muscular injection of the same amount.

The comparative blood levels are shown in Figure IV. If this be a true finding, there is no comparison as to the relative therapeutic value of the two methods. Chow and McKeen (1945)<sup>13</sup> showed that Penicillin combined with human serum albumin retains its antibiotic activity. It is possible that in this combination it may prove more resistant to changes in pH than ordinary Penicillin and might be capable of being given by mouth with satisfactory results.

It has now been demonstrated by several investigators that Penicillin given by mouth in patients with pernicious anaemia and achlorhydria was excreted in the urine with relatively high blood levels. Charney et al. (1945)<sup>14</sup> using trisodium citrate as a buffer with Penicillin two hours after breakfast, showed that there followed an appreciable urinary excretion which was taken as an index that it was absorbed from the gastro-intestinal tract. In clinical trials they found that Penicillin given by mouth in combination with trisodium citrate was therapeutically effective in a series of cases of gonorrhoea. The effective doses were comparable with the amounts given parenterally and this combination with the buffer gave greater and more prolonged blood levels than when Penicillin was given without it.<sup>15</sup>

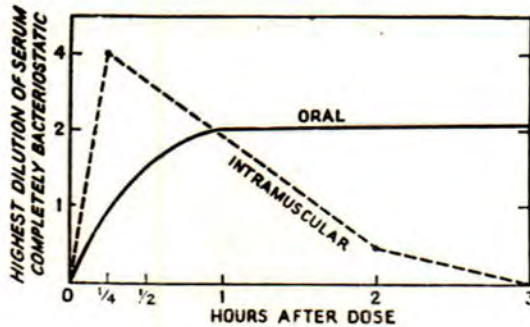


FIGURE IV

These investigations would seem to suggest that the oral use of Penicillin may be within the realm of practical therapeutics. The time is now ripe with these leads for careful and intelligent clinical investigation. This is within the province of any who have the facilities of following Penicillin blood levels at frequent intervals. If these controls are not carried out I feel sure that the medical literature may be flooded with uncritical conclusions based upon clinical impressions of a few successful cases. The bug-bear of therapeutics will be reinvited! The blind spot of wishful thinking will plague us through not giving failures their proper weight. Medical literature is grotesquely flooded with transient therapeutic successes which do not stand the test of time or critical statistical analysis.

#### INDICATIONS AND DOSAGE

In the early part of this address I made reference to organisms which were sensitive and non-sensitive to Penicillin. There has been a tendency to ignore this fundamental factor and to give Penicillin in all and sundry febrile and even non-febrile infectious and non-infectious conditions on the mere chance that it might do some good. Such therapy once in a thousand times may hit a bull's-eye, but these

can not be accepted as true bells as so many others may recover in spite of treatment that the really effective results are lost in the shuffle. But there are a large number of specific lesions which are easily recognized and their bacterial cause fairly accurately determined or reasonably surmised.

#### METHODS OF ADMINISTRATION AND DOSAGE

In contra-distinction to the sulphonamides, Penicillin has certain restrictions which are of the greatest importance. The sulphonamides can be given by mouth or intravenously and permeate all tissues more or less equally. They have, however, two characteristics in common, namely that a high blood level can be attained by intravenous therapy and they are efficacious by topical administration. But the differences are of great importance and are as follows:—(a) It is not as yet proven that Penicillin can be efficacious by the oral route. (b) It does not diffuse from the blood into the meningeal fluid, the serous cavities, through synovial membranes, and is not excreted by the tears or the

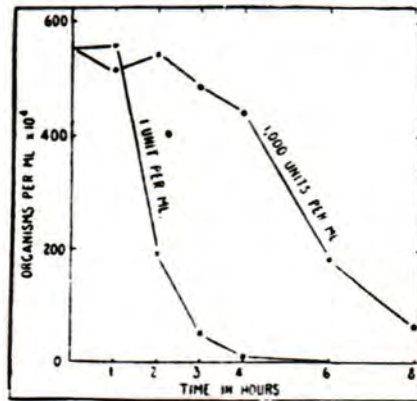


FIGURE V

saliva. (c) It is rapidly excreted by the urine in concentrated form, and apparently undergoes a change in quality. It is important to bear these facts in mind, as they will naturally influence the method of its administration under particular conditions.

The dose of Penicillin is as yet somewhat in a state of flux. The reason is that, until recent months, the amount available was strictly limited and what was released was used for the greatest good to the greatest numbers under emergency conditions. In fact, the principal efforts were extended to determine the normal adequate or effective dosage. Not because this drug is toxic, but to conserve its supply to the utmost so as to extend its use over the broadest area and at the same time to learn how it could be used to the best purpose.

In addition to these factors, it must be appreciated that Penicillin is not yet available in a pure state. It is true that as each month

passes it is being produced with less and less impurities. It is safe to conclude that most, if not all, of the untoward reactions which have been reported are due to these impurities rather than to the drug itself. This is important in local or topical applications. It might be reasoned that, if one unit applied locally does  $x$  amount of good 1000 times as much will have 1000 $x$  times this effect. This may not be so, even the contrary may be the case, unless the drug be of great purity.

Furthermore, there is accumulating evidence to suggest that certain organisms which are considered non-sensitive to Penicillin may be adversely affected by enormously increased concentrations. The truth of this lies in the future.

It would be impossible to cover all the different lesions which are amenable to Penicillin. But they may in great part be grouped according to certain general principles.

External lesions, such as those of the eye, are best treated by direct instillations or ointments with additional parenteral therapy if the lesion has extended beyond the conjunctival sac and external appendages. The same may be said of lesions of the ear, and the accessory sinuses. If the infection is in the deeper cavities, however, insertion of small rubber tube drains for irrigation with Penicillin solutions give excellent results. In all severe cases with systematic reactions parenteral injections should be employed, and it is of great assistance to have blood cultures taken if there be any suspicion of septic thrombosis or systematic spread.

In lesions of the mouth and fauces, ranging from trench mouth to streptococcus angina, lozenges composed of Agar-Agar impregnated with 5 to 10 per cent. Penicillin are most useful. These can be sucked frequently and enrich the secretions of the mouth with the drug, as it must be appreciated that the saliva does not contain Penicillin.

Visceral lesions, apart from those of the meninges, serous and synovial cavities, are best treated by the parenteral route. The amounts employed may vary considerably with the virulence of the infection, and it must always be understood that all organisms are not equally sensitive to the drug. It is important to appreciate this, as the exact bacteriology may not be ascertainable and often good clinical results are taken at their face value without critical reservations. This is of particular importance in lesions of the lung. In my experience some cases of pulmonary abscess of long duration have made most spectacular recoveries, while in others where equally good results should be expected but little improvement has occurred. One of the difficulties to be experienced in such cases is the multiplicity of organisms which may be found in the purulent sputum, and often the *Haemophilus Influenza* may be overgrown by organisms which are really saprophytes.

The use of Penicillin in culture media may be of the greatest value in the investigation of such cases, as it will inhibit the growth of many of the cocci and permit an otherwise masked H. Influenzae infection to be detected. In the acute pneumococcus pulmonary lesions the brilliant results obtained by sulphonamides do not as a rule justify the use of Penicillin unless the individual be sensitive to the former or there be any suggestion of a leukopenia. It must be thoroughly appreciated that Penicillin has no effect on the Haemophilus Influenzae, nor is there any evidence that it is at all effective against viruses. Therefore, it should not be used in cases of atypical pneumonia unless there be a proven secondary infection which is sensitive to this drug.

In all cases of meningitis—whether due to the pneumococcus, meningococcus, staphylococcus or streptococcus, the intrathecal administration of Penicillin in amounts of 10,000 to 20,000 units daily has given excellent results. As in the most infections, the earlier the drug is used the more favorable will be the outcome. Some workers have reported the presence of Penicillin in the spinal fluid after very large doses intravenously, but the amount is only a fraction of that in the blood stream and, therefore, time should not be lost before introducing the drug intrathecally. The results already obtained with the use of sulphonamides in meningococcal meningitis have been excellent and it is doubtful whether Penicillin therapy can improve on this. In the more fulminating cases Penicillin has produced dramatic improvement. The treatment of pneumococcal meningitis, however, has been relatively less satisfactory. Whereas occasional cases of pneumococcal meningitis have been cured with sulphonamides, it may now be taken that the death rate with the use of Penicillin can be reduced to under 50%, which is almost equivalent to that of pneumococcal pneumonia in pre-serum days. All bacteraemias due to these organisms should be treated with Penicillin. The period of treatment is comparatively short, except in cases of bacterial endocarditis. All deep foci such as abscesses, septic thrombi, etc., should be handled surgically.

Subacute bacterial endocarditis has been one of the medical diseases which up to the present have resisted all forms of therapy. It is true that sulphonamides have rendered blood cultures negative, but in the long run there have been very few cases that could be taken as cured. In the early days of Penicillin therapy similar disappointing results were obtained, but during the past year the results have been much more encouraging. The introduction of Heparin in the treatment of this disease was considered by many as a distinct step forward. I have always had grave doubts as to its use being justified. Before any case was reported in the literature I used Heparin on 3 occasions with disastrous results, namely cerebral haemorrhages that were the immediate cause of death. I acknowledge I did not have the courage to publish these results.

The report published recently by Loewe (1945)<sup>16</sup> is most encouraging, and the incidence of untoward effects from Heparin are few. On the other hand, it would be very much better if we could have a more simplified technique in the treatment of this disease. His results have to some extent been confirmed by Dawson & Hunter (1945).<sup>17</sup> They report 20 cases in which Heparin was employed in the majority as an adjuvant to Penicillin. The results were apparently successful in 15, all of which were clinically and bacteriologically free from infection after some months. In addendum to the same article they report seven additional patients, in five of whom Heparin was not used. The results indicated that the results were as favorable in the group without Heparin as when it was used. In six of the cases the infection had apparently been terminated. They found that higher blood levels were obtained by giving the Penicillin by continuous intramuscular drip than by the continuous intravenous drip and, as the former is better tolerated and the technique is simpler, it would seem to be the method of choice. The dosage of Penicillin in these cases has ranged from 500,000 to a million units per day, and it may be advisable to use even larger amounts. It cannot be denied that the prolonged intravenous or intramuscular therapy required in these cases is a great handicap, as the treatment must be continued for many weeks. Therefore, it is to be hoped that the oral method of its use will be solved in the very near future.

Probably the most dramatic result that has been obtained with Penicillin is in the treatment of gonorrhoea. When one considers the long and tedious invalidism which resulted from this infection and compares this with the present day—when a case can be cured in eight hours, it has reduced this disease as of less inconvenience than the common cold. There has been much investigation as to the proper dosage, but I think, taking it all in all, the administration of 30,000 units every two hours for five doses will cure 99% of the acute cases.

In his early work Fleming pointed out that the Anthrax Bacillus was Penicillin-sensitive.<sup>1</sup> In December, 1944, Murphy et al<sup>18</sup> reported three cases of cutaneous anthrax which responded favorably to Penicillin therapy. The amounts used averaged about 100,000 to 150,000 units in 24 hours. In two cases this treatment was sufficient, and in the third a little over two days' treatment was required. It is true that these cases were all non-bacteraemic, but it holds out hope that, in sufficiently large amounts Penicillin may control even bacteraemic anthrax infections.

A few words about clostridial infections, I think, are indicated. It has been most difficult to arrive at a definite assessment of any specific therapy in this condition. The primary reason for this indecision is the difficulty of determining the actual degree or even presence of

this infection in any specific case. Further, the mere recognition of these pathogens does not necessarily indicate that either "anaerobic cellulitis" or "gas gangrene" may develop. Anti-gas gangrene serum has seemed to be beneficial, and so have sulphonamides, but the following technique has given the best results.

It seems advisable to consider all badly infected wounds as liable to these infections with or without associated pyogenic organisms for which Penicillin is most efficacious. It is, therefore, recommended in all such cases that, as soon as possible, the intramuscular injection of Penicillin be started—(15,000 units every 3 hours, for 10 to 15 days). There should also be incision of wounds with removal of all necrotic muscle, to be followed by anti-gas gangrene serum and the local application of Penicillin paste. This regime should be continued even after all systematic reaction has ended, as the clostridia may persist for some time without being recognized. A short or interrupted course of Penicillin may control local signs of gas infection, but not a general toxæmia, and such procedures may completely befog the true condition.

When Penicillin was first introduced it was considered that it would only be useful in the treatment of bacterial infections. Those who knew of the early and confidential reports of Mahoney, and its spectacular therapeutic effect in syphilis, could hardly believe that it was true; and, in fact, many workers are still somewhat skeptical. Many clinical experiments are continuing as to the proper combination, if this be advisable, with the arsenicals and heavy metals, as well as combinations with fever therapy, etc. The optimum dosage has not yet been determined, but it again will be noted that there has been a constant attempt to find the minimal dose which would be effective. At the present time this seems hardly justified, as the supply of Penicillin is now equal to, and will soon be much greater than the demand. There is little doubt that moderate amounts, 150,000 units per day, continued for a matter of 7 to 14 days, produces what appears to be an immediate cure. The *spirocheta pallida* disappears from the lesions within a few hours, and the Wasserman reaction becomes negative within a few weeks. The final test will be whether such cures are permanent; and, if so, there would seem no reason to expose patients to the hazards of arsenicals and the inconveniences of mercury to accomplish this simple cure, particularly if a trustworthy oral method can be devised.

In addition to syphilis, infectious hepatitis (Weil's Disease) due to leptospira ictero-haemorrhagica has responded most brilliantly to Penicillin therapy. It should be given early and in relatively large doses, 40,000 units every 3 hours, either intramuscularly or intra-



venously, up to a total of 1 to 2 million units. It is important that it be given early, so as to forestall the irreversible hepatic and renal lesions.

Rat-bite fever, although a relatively rare disease, is one that often resists all forms of therapy. There are two aetiological agents, the *Spirochaeta Morsus Muris* and the *Streptobacillus Moniliformis*. The former responds well to arsenical therapy, but no satisfactory chemotherapeutic agent has been available for the latter. In vitro, Penicillin has a powerful bacteriostatic effect on the *Streptobacillus Moniliformis*. In three cases reported by Altemeier, Schneider & Howe (1945)<sup>19</sup> there was a prompt and dramatic response followed by a complete recovery. The dose was 10,000 to 15,000 units every 3 hours, continued for at least 7 days. Although the number of cases reported is few, the spectacular results warrant its being used for this disease in the future and indicate also that it might be of value in the treatment of Haverhill fever. Laboratory studies suggest that Penicillin may be effective against the spirillum of relapsing fever. It is doubtful whether it will be more efficacious than Arsphenamine, but it might be useful in cases which are sensitive to the latter.

The reports to hand would indicate that at least we have a specific therapeutic agent against Actinomycosis. This was first indicated by Fleming in his early work when he reported that Penicillin was bacteriostatic in vitro for this fungus. The few cases reported in the literature would encourage the conclusion that this may possibly be correct. It is a disease, however, which will require a long period of observation to be certain that a definite cure has been obtained.

It is not to be expected that Penicillin will effect cures without all accessory means being used to enhance its value. I mean by this that rational surgery cannot be replaced by Penicillin alone, but that both should be used with an intelligent understanding of their respective virtues and interdependence. Penicillin must be allowed to reach the infecting organisms. It cannot work miracles in necrotic tissue to which it has not access, nor can it effect clearance of bacteria from chronic lesions which are but superficially exposed. This is particularly important in chronic cases of osteomyelitis. Sane, but conservative surgery must prepare the way for Penicillin action.

There is one condition where its use has more far-reaching effects than merely the control of the infection. Its local application has given brilliant results in burns by controlling infection. In areas where severe contractures or dense scar tissues are expected to cause serious deformity, Penicillin has done much to prevent sloughing and loss of valuable tissues, and in the promotion of smooth and painless scar tissues with comparatively little deformity—which minimizes the long and tedious treatment by plastic surgery, which by itself has attained such brilliant results.

So this is the story of "Penicillin". A review of such a subject must necessarily be sketchy due to the time at our disposal. But I have tried to bring out the general principles without too much detail, and at the same time to emphasize peculiarities of this drug which must be borne in mind if it is to be used after a rational manner. Careful clinical investigations are still required if we are to reach full knowledge of the value of this therapeutic agent.

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## LEGENDS FOR TABLE AND FIGURES

TABLE I—Lists of Penicillin-sensitive and non-sensitive organisms.—After Hobby, Meyer & Chaffee, Proc. Soc. Exp. Biol. & Med. 1942, 4, 277.

FIGURE I—This photograph shows the original contaminated culture which led to the discovery of penicillin. The patch at the top is the growth of mould (*Penicillium notatum*). In the lower third, normal staphylococcal colonies are seen. For some distance around the mould, the growth of staphylococci has been suppressed. (Alexander Fleming—Brit. Jour. Exper. Path., 1929, x, 226.)

FIGURE II—Numbers of surviving *Staph. Aureus* in broth at 37°C. containing (1) 0.2% sulphathiazole; (2) 10 units penicillin per ml.; (3) both of the drugs. (L. P. Garrod—Brit. Med. Jour., Jan. 27, 1945, 107.)

FIGURE III—Activity of penicillin (A) in saline solution (25 units per c.cm.) and (B) in patient's urine (approx. 25 units per c.cm.) at various pH, before and after autoclaving at 15 lb. for 15 min. (C. J. H. Little and G. Lumb, Lancet, Feb. 17, 1945, 205.)

FIGURE IV—Bacteriostatic activity of serum after oral administration and intramuscular injection of penicillin. The curve for oral administration is based on table II. The intramuscular dose was 15,000 units. (C. J. H. Little and G. Lumb, Lancet—Feb. 17, 1945, 205.)

FIGURE V—Numbers of surviving *Staph. Aureus* in broth at 37°C. containing penicillin (TRCIO) in concentrations of 1 unit and 1,000 units per ml. (L. P. Garrod—Brit. Med. Jour., Jan. 27, 1945, 107.)

# Present Day Management of Rheumatic Fever\*

By J. C. MEAKINS, C.B.E., M.D., LL.D.

## INTRODUCTION

THE term "Rheumatism" was first used by Guillaume de Baillon but Sydenham gave the first good clinical description in 1676 with some, or all, of the following symptoms and signs—arthritis or arthralgia, pyrexia, various skin manifestations, and in many cases a following carditis which might include the myocardium, pericardium and endocardium. The mitral valve was most frequently involved, leading to mitral stenosis, which is now considered to be almost a specific lesion of this disease. It would serve no particularly useful purpose today to describe in full detail the symptomatology of this disease but there are several general features that should be borne in mind. The first is that there is hardly a tissue of the body which may not be affected in some degree and be manifest clinically in an occasional case. Therefore, it is in a true sense a systemic disease. Secondly, there is a pernicious quality of recurring and it may be truly said that, "once rheumatic always rheumatic". This tendency to recur is most characteristic of this disease. Thirdly, these recurrences may be almost symptomless or at least unrecognizable by any acceptable criteria, as may the initial attack. On the contrary the disease may manifest explosive qualities of the most malignant severity. Fourthly, there may be neither rheumatic pains nor fever, and for this reason according to our present concept "Rheumatic Fever" is a misnomer. "Rheumatic State" has been suggested in its place but this seems to me to be no better. It is hard for us to get away from the term "Rheumatic" as it is endorsed by custom and tradition. Its menace lies in the emphasis placed upon the arthritis or arthralgia which are uncomfortable features but are transient and benign. The "carditis" is the most dreaded lesion but holds in its nosography a secondary place. As we have "Sydenham's chorea", why not "Sydenham's carditis"?—as it is this lesion we strive to prevent or arrest its progress. But this may be considered as destructive criticism which I acknowledge with the reservation that we must stress the heart and place the joints in their proper place—as an air-raid warning of the destruction which is likely to follow.

## AETIOLOGY

The search for a specific agent as a cause for this disease has been long and disappointing. This may have been due to the tendency

(\*An address presented to the Academy of Medicine, London, Ont., April 18, 1945)

to concentrate attention upon the traditional concept of the causation of diseases which appear at first sight to be of an infectious origin, whether this might be a virus, a bacterium, or an agent of even higher species. But many workers have not neglected other aspects which today are beginning to press their claims for consideration in the over-all picture of this disease.

#### FAMILIAL CONSIDERATIONS

Cheadle<sup>1</sup> in 1889 wrote a monograph on acute rheumatic fever which was a classic at its time. Indeed, there has been little added to the subject since. He pointed out that the disease was apt to occur in families. He did not hold that it occurred in epidemic form or was definitely communicable but rather that there was what might be called a "family tendency". In the experience of practitioners who have had the opportunity of watching families in which there have been one or more cases of this disease either in one generation or in a series of generations, it has been found that this is more common than could be accounted for by coincidence. Further, that any suggestion of school or household spread among non-siblings is uncommon. Evidence to the contrary might be marshalled from the experience in the Armed Forces during recent years. There have been reported outbreaks of streptococcus hemolyticus pharyngitis amongst young recruits in Training Centres. Some of these have remained as such while others have been diagnosed as scarlet fever. A much smaller number have had definite arthritis or arthralgia and have been diagnosed as acute rheumatic fever. Of these a few undoubtedly presented or developed signs of cardiac damage such as a prolonged P.R. interval in the electrocardiogram, or signs of mitral stenosis. But it must be acknowledged, I think, that they were a very small minority. The picture, however, is confused as many of the cases with arthritic symptoms and signs had been inoculated against scarlet fever and the possibility that this could have played a role in producing an allergic response cannot be hastily discounted. I do not mean to infer that a certain number of cases of true rheumatic fever with carditis did not occur, but that it was in epidemic proportions is open to reasonable reservations.

But to return to familial aspects of this disease. Careful genetic and epidemiologic studies were published in 1943 by Wilson, Schweitzer and Lubschez<sup>2</sup> based upon 109 households comprising 113 families (including remarriages) selected from a children's cardiac clinic. Every household included at least one rheumatic child. The period of observation ranged from 6 to 20 years and all but 9 families were observed for more than 9 years. These studies indicate that a most important factor in the pathogenesis of rheumatic fever is the genetic susceptibility of the host. Further studies are necessary

before it can be stated whether every susceptible individual in the general population develops rheumatic fever. Final interpretation of the age expression of this disease should reveal the factors responsible for its onset. At the present time it may be concluded that heredity is primarily responsible for the familial incidence of the disease, the age risk determining the time of occurrence of cases in the family.

#### GEOGRAPHICAL DISTRIBUTION

It is now fairly well accepted that this disease is more prevalent in the North Eastern States, Eastern Canada, Great Britain and the Scandinavian countries. It may be taken as a general statement that rheumatic carditis is found throughout all countries except perhaps Central Africa. Also as a general rule it is least prevalent along the equator and as we pass North and South past Capricorn and Cancer there is a rapid rise in its incidence. This, however, can only be taken as a general rule, as there is apparently a considerable difference between the incidence in the North Eastern States of the Union and in Minnesota and Wisconsin. It would appear, therefore, that latitude were not an unadulterated factor.

A recent survey by Sampson et al.<sup>3</sup> in California, covering three communities with markedly different climates, revealed strikingly divergent results. In one with a warm, dry climate, the incidence was least and comparable to such climates in more northern districts. In a mountain community with average humidity and precipitation but with wide extremes of average summer and winter temperatures there was a high incidence comparable to the North Eastern United States and Great Britain. In the third community with a uniformly cool climate and high precipitation an unusually high incidence was found. It, therefore, seems clear that it is not temperature alone or humidity alone which may influence the frequency of this disease but a combination of wide temperature variations, a cool climate with heavy precipitation which seems to have a derogatory influence.

#### SEASONAL INCIDENCE

Geographical distributions cannot be considered independently of the season of the year. If a combination of wide temperature variations with heavy precipitation has an influence on the occurrence of this disease it might be expected that the incidence would vary locally in accordance with such meteorological conditions. This is found to be the case as the following peaks will show:—

Minneapolis: November & December, and March & April.

Scotland: October and November.

New York: Always high but particularly in April and May.

London: November, December and January.

Melbourne (Australia): June and July.

## AGE INCIDENCE

It is generally conceded, irrespective of geographic and seasonal variations, that rheumatic fever is a disease of childhood and adolescence. It is comparatively rare before five years of age but soon following this there is a rapid rise which reaches a high peak about the seventh to ninth year. The exact age at which the peak is reached varies slightly in the findings of different observers but the extremes may be taken to be six to ten. There is usually a secondary rise just before or during early adolescence.

There is an indeterminant variable in all these observations resting upon the fact that the onset and initial attack may be so insidious and mild as to escape the notice of the parents until a well established carditis is detected, so the exact time of onset is open to speculation. In spite of this, all children in a rheumatic family must be held suspect and considered potential victims of this disease until well into adult life.

## ECONOMIC AND SOCIAL FACTORS

It has been repeatedly found that the incidence of rheumatic fever is higher in low income groups. There are a number of factors which might enter into this finding.

It has been established that the average family is larger in the lower income brackets as compared with higher income groups. Three possible deleterious factors might be operative in such a familial state: (1) increased incidence of susceptibility; (2) over-crowding, and (3) low nutritional standards.

If the facts revealed by the study mentioned under "Familial Considerations" above are accepted it would be expected that large families with a rheumatic fever parent or parents would show a high incidence of this disease, which would be coincidental rather than aetiologic.

Over-crowding is a common condition in low income groups and it is now accepted that all of the common communicable diseases show an increased incidence under such conditions. This may apply to rheumatic fever but must be proven for the community as a whole, independent of the possibility that large rheumatic fever families may be included and make an artificial weighting of the final results.

Low nutritional standards run parallel to low incomes and with this there is more likely to be deficiencies in vitamin protective food-stuffs as compared to the caloric intake. There have been a number of studies along these lines but the findings have been inconclusive and often contradictory. For instance, Rinehart and Mettier<sup>1</sup> in 1934 and subsequently, presented evidence that rheumatic fever was a result of latent scurvy and superimposed infection. This was somewhat sup-

ported by the work of Stimson, Hedley and Rose,<sup>5</sup> while on the contrary Sendroy and Schultz<sup>6</sup> in 1936, and Perry<sup>7</sup> in 1935, failed to confirm any specific relation of vitamin C deficiency and this disease.

It is but natural under present conditions that investigations into a possible role of avitaminosis in influencing this illusive disease should be pursued. It is true that in the low economic groups the supply of vitamins would be lower than in the higher brackets. But this in itself should not be taken as of specific import unless the vitamin intake is consistently so low as to be a menace to health. It is the absolute rather than the relative lack that is of importance. In recent studies Coburn and Moore<sup>8</sup> in 1943 found that there was a relation between poor diets and susceptibility to rheumatic fever. Further, it appeared that there was no particular component but always there were many factors which were deficient so that the evaluation of the relative importance of one essential was precluded. These findings are in accord with considered opinion in regard to many other conditions such as tuberculosis, rheumatoid arthritis, communicable diseases of childhood, pneumonia, traumatic shock, retarded convalescence, etc. Simply stated it is that undernutrition renders a person more vulnerable or susceptible to trauma or insults of most qualities.

In a further small series of observations Coburn and co-workers<sup>9</sup> in 1944 confirmed some previous findings in regard to blood levels of vitamin A and carotene; (1) that other things being equal it is proportionate to the level of intake of Vitamin A; (2) that the onset of a pharyngitis is accompanied by a fall in Vitamin A blood levels but the carotene remains unchanged. It would seem to be a general rule that increased metabolic demand is accompanied by a decrease in plasma level of vitamin A. Whether it is destroyed in some abnormal manner or whether it is utilized in normal metabolic processes but with increased velocity must await further knowledge concerning its mode of action. (3) Following the subsidence of the pharyngitis the plasma level rose, but in those who developed rheumatic fever there was a secondary fall which was proportionate to the severity of the attack. The carotene in the plasma did not change materially.

It is difficult to assess the significance of these observations. It would not seem to be peculiar to rheumatic fever alone and might be equally expected in other diseases with a febrile reaction as there has been found a decrease in the concentration of this vitamin in the plasma when fever is produced artificially.

#### BACTERIA AND VIRUSES

For many decades persistent search has been made to find some bacterial agent to account for the cause of this disease. This was a natural aspiration as rheumatic fever has many features which would

suggest that it is an infectious disease. In the early nineteen hundreds the work of Poynton and Paine attracted much attention. They described the finding of a diplococcus or streptococcus in short chains which they claimed was the probable cause of this disease. This was never accepted by many workers in this field and now their work is practically forgotten. But the association of the streptococcus with the disease recurs periodically after one manner or another. The high incidence of an acute pharyngitis as a precursor of the original attack or of a recurrence and the associated rise in the streptococcal flora of the pharynx at these times has been repeatedly demonstrated. There are few, if any, who claim that the streptococcus is the cause of the disease, but that their presence plays some role in its initiation and recrudescence is impossible to deny or to dismiss as unlikely. It is also difficult to neglect the common—and claimed by some, constant—finding of the streptolysins in the blood of rheumatic fever victims during its active stages.

From time to time many other bacteria have been described but all have been discredited and soon forgotten. The same may be said about viruses. I merely mention these findings and failures as there have been perennial attempts to treat rheumatic fever by various vaccines and sera after the common manner which has been employed successfully in the prevention and cure of certain infectious diseases.

#### ANAPHYLACTIC HYPERSENSITIVITY

It is not my intention to deal extensively with the histo-pathology of this disease, but it is necessary if we are to consider its management on broad lines that it should be touched upon. The characteristic lesions of rheumatic fever in the heart consist in (1) focal alterations in the collagen of the connective tissue; (2) the presence of the Aschoff body; (3) focal and diffuse inflammatory lesions; (4) focal alterations in the cardiac muscle, and (5) verrucose valvular vegetations.

Some students of this disease, particularly in the United States (Swift and Coburn) and in Germany, have been active proponents of the view that whereas this disease might not be due to a direct action of a bacterial toxin it might represent the effects of a hypersensitive reaction to bacterial products.

Klinge<sup>10</sup> in 1933, and Vaubel<sup>11</sup> in 1932, and Junghans<sup>12</sup> in 1934 reported that they had produced lesions resembling those of rheumatic carditis by repeated injections of horse serum into rabbits. This concept was received with certain doubts not because lesions were produced but, as Gross<sup>13</sup> in 1929 stated, the experimental production of lesions of the Aschoff body type were "entirely unconvincing". The matter lay fallow for some years until in 1943 Rich and Gregory<sup>14</sup> published their findings of the production of the histological changes



outlined above in a series of rabbits sensitized to sterile horse serum. They do not claim to have solved the question of the cause of rheumatic fever but quite conservatively state that their experimental observations are "highly suggestive". In their opinion, in some cases, cardiac lesions so produced resemble closely in their basic characteristics those of rheumatic carditis. Further, they point out that a wide variety of lesions are common both to rheumatic fever and to the anaphylactic reaction of human and experimental serum sickness.

In a further publication they draw attention to the similarity of the peculiar lesion of rheumatic pneumonitis and that produced by sulphonamide hypersensitivity, in that they are basically identical and both exhibit the primary capillary damage characteristic of focal anaphylactic reactions.

But the matter cannot be allowed to rest at this point. There is a trend to link up a number of conditions which exhibit somewhat similar capillary and small artery necrotising processes such as rheumatoid arthritis, explosive phases of essential hypertension, lupus erythematosus (Libman-Sachs disease), periarteritis nodosum and malignant nephrosclerosis. It seems to me that we are on the threshold of a new concept applicable to a group of diseases, the aetiologies of which have been illusive. It would be rash even to suggest that they all stem from a common root any more than one could suggest that all malignant tumors do, or that the granulomata do or the pyogenic inflammations. But the diseases mentioned have certain attributes in common, namely the chronicity of some of the lesions, the tendency to recurrences, the evidence of capillary and small artery lesions, and their fragility. The similarity of these lesions to those produced in persons susceptible to certain drugs or chemicals such as sulphonamides and arsenic may carry the question a step further. It is granted that much of this is speculative and must not be taken for granted; but, if it even emphasizes that we know mighty little about these diseases and must explore all new avenues with a dispassionate objectivity it will have served a useful purpose. For instance, the work of Selye and his co-workers<sup>15</sup> in 1943, in producing arthritis, nephrosclerosis, hypertension, and lesions similar to periarteritis nodosa by the administration of large amounts of desoxycorticosterone acetate gives us food for thought. The whole landscape is confused but through the fog there may be a road still not clearly seen which may lead us to the truth.

I know you are impatient for me to get down to the management of rheumatic fever but I cannot do this until I can see even ever so dimly what we are to manage. This disease has through the ages been treated by nearly every drug in the pharmacopoeia and by every physical and biological mode of the moment. Through them all there

has been only one that has stood the test of time in even ameliorating the signs which have given the disease its name—arthritis and fever. This has been salicylates introduced in 1876 by MacLagan. But this compound in various preparations was an analgesic and antipyretic in diverse conditions, but in none so definitely and persistently as with rheumatic fever.

It has been known for many years that an increased sedimentation rate of erythrocytes was associated with infections, malignant diseases and certain other conditions. The one that concerns us at the moment is rheumatic fever. In the course of time it has become almost an accepted criterion of the progress or otherwise of this disease even after the fever and arthralgia had disappeared. It is important to mention that the sedimentation rate is seldom retarded but that it has been so reported in certain of the allergic states, although this is by no means a constant finding.

In 1932 Bendien, Neuberger and Snapper (*Biochem. Z.* 1932, 247, 306,) <sup>16</sup> noted that sodium salicylate added to human blood in vitro greatly reduced the erythrocyte sedimentation rate but the minimum effective concentration of sodium salicylate was about 90 to 120 mgms. per cent. This represents at least three times the value given by Hanzlik <sup>17</sup> in 1926 as an average blood level obtainable in rheumatic fever patients (*Med.* 1926, 5, 197).

In 1941 (*Proc. Soc. Exper. Biol. Med.* 1941, 48, 69) Lichty and Hooker <sup>18</sup> reported seven cases of acute rheumatic fever in which they followed the sedimentation rate during acetyl salicylic acid therapy. It was an accepted fact that salicylates lowered the temperature and leucocyte count of patients with this disease so they used the sedimentation rate of erythrocytes as the best index of disease activity. Acetyl salicylic acid was combined with sodium bicarbonate and was given in amounts of 2.6 to 4 grams per day and was continued from nine to forty-two days in different cases. The drug was administered by mouth; the sedimentation rate was followed daily until it returned to a normal level, when the drug was discontinued, assuming that the rheumatic activity has then ceased. In a number of cases the sedimentation rate became appreciably elevated during the first week after stopping the medication and this was occasionally associated with an elevation of temperature with or without a return of other symptoms. In a few of the cases receiving two or three courses of the drug the same course of events was observed.

Rich and Gregory <sup>14</sup> in their publication in 1943 (*Bull. Johns Hopkins Hospital*, 1943, 73, 239) raise the question of whether salicylates are of value in the arthralgia of serum sickness. They point out that while the majority recommend their use some writers believe they are of little value, although these opinions were based on very

little documented evidence. They drew attention to the fact that after studying 25 histories of patients who developed serum sickness with arthralgia on the medical wards of the Johns Hopkins Hospital, 13 of these were treated with salicylates and 12 were not. Of the 12 untreated cases the arthralgia persisted from 4 to 7 days in seven cases, for 3 days in one case, for 2 days in one case, and for 1 day in 3 cases. In the treated group salicylate therapy was begun on the day of onset of arthralgia in ten cases and in seven of these the joint pains were relieved within 24 hours. In three cases there was no appreciable effect of the drug upon the arthralgia and in the remaining three cases salicylate treatment was begun in two 1 day after the onset, and in both of these cases it was relieved within 24 hours after the first dose. In the remaining case this treatment was begun two days after the onset and the symptoms persisted for seven days.

In 1943, Coburn<sup>19</sup> (Bull. Johns Hopkins Hosp. 1943, 73, 435) published his article on salicylate therapy in rheumatic fever entitled "A Rational Technique". The principal feature in his course of procedure is the daily determination of the level of the salicyl radicle in oxalated blood and the intravenous and oral administration of sodium salicylate in order that a level of over 350 gamma per cc. might be obtained. His observations seem to indicate that there was a relation of the rheumatic activity to the plasma salicylate level; that if this level were maintained between 360 to 500 gamma per cc. (36 to 50 mgms. per 100 cc.) there was a prompt and progressive subsidence of the rheumatic inflammation, whereas patients with plasma levels below 250 gamma per cc. continued to manifest an active inflammatory process.

The symptoms and signs which were taken to represent the activity of the rheumatic fever process were the elevation of temperature and of the sedimentation rate. His results paralleled those of Lichty and Hooker in regard to the decline of the sedimentation rate on the continuance of salicylate therapy and a tendency in certain cases for it to rise again after this therapy had been suspended. He also states that after two years' experience with this technique none of 38 rheumatic fever patients so treated with 10 grams of the sodium salicylate daily developed valvular heart disease, while 21 of the 63 similar cases who received small doses of sodium salicylate developed physical signs which would indicate a rheumatic carditis. He suggests that these observations would indicate that a plasma salicylate level of at least 350 gamma per cc. may be required to suppress the rheumatic reaction while plasma levels below 200 gamma per cc. may be sufficient to relieve symptoms while masking a progressive rheumatic process.

Since the publication in 1943 of Coburn's "Rational Technique" I have been able to find no similar reports from other workers until

March 1945, where in the *Journal of Paediatrics*, Wegria and Smull<sup>20</sup> report on 17 patients treated with what they call "adequate salicylate therapy" which was a serum salicylate level between 350 and 500 gamma per cc. They used the intravenous route when necessary, dissolving 7 to 10 grams of sodium salicylate in 200 to 500 ccs. of normal saline. The drug was administered over a period of one to two hours every day for a few days. They found, however, that the optimum levels (350 to 500 gamma per cc.) were not maintained by the time of the next infusion. These fluctuations were avoided by using combined intravenous and oral routes of administration and most of their patients received the salicylate by mouth in enteric-coated tablets to prevent the vomiting which so frequently occurs after the ingestion of aspirin or sodium salicylate. The optimum levels were reached within the first twenty-four hours and the maintenance dose was given every four hours day and night. When these optimum levels were maintained throughout the course of the disease the regimen was referred to as "adequate salicylate therapy".

Seventeen patients were treated with "adequate salicylate therapy" and compared with nineteen patients who for various reasons were "inadequately" treated. The two groups were comparable as to age, number and previous attacks of rheumatic fever, and duration of the acute attack before hospitalization. The erythrocyte sedimentation rate was taken as the criterion of activity of the rheumatic process and there was no difference in the response of the two groups. At the end of two weeks of hospitalization the erythrocyte sedimentation rate was still above 20 in every case in both groups. At the end of three weeks it was still elevated in 16 cases of the control group and in all 17 patients of the "adequately" treated group. The response was similar in both cases after 4, 5 and 6 weeks of hospitalization. It is apparent, therefore, that in this series of cases the "adequate salicylate therapy" did not hasten the control of the disease. The authors state that "it is possible, however, that had 'adequate salicylate therapy' been instituted within a few days of the onset of rheumatic fever the course of the disease might have been shortened." They are frank to confess that most of their patients were treated sometimes several weeks after the onset of the rheumatic fever and only three patients were treated within one week of the onset, and that two of these three patients responded promptly, the erythrocyte sedimentation rate falling below 20 during the third week of "inadequate salicylate therapy"; but, these were the only two in which this happened, while in three patients of the control group the sedimentation rate had similarly fallen in the third week. So this verdict must stand as not proven if it were not for a report from one of the Armed Forces with concentrated experience of treating over 4,500 cases of

rheumatic fever with salicylates in one special Centre. The following summary was issued:

- (a) The optimum serum level of salicylate is 25-30 mgms. percent.;
- (b) ten grams of sodium salicylate per day in divided doses, day and night, is the effective amount;
- (c) the sedimentation rate is not affected by this drug in therapeutic doses;
- (d) there is no clinical proof that salicylate alters the course of the carditis in this disease;
- (e) intravenous therapy is not justified.

So that is that!

A word about the use of sulphonamides in the prophylaxis of the pharyngitis due to streptococci. This has been advocated during the past ten years and the same principle was used in the Armed Forces to prevent and control outbreaks of streptococcus sore throat which was a grave hazard in training camps and ships. The early reports from civilian workers and in the Armed Forces were at first favourable on the whole. But recent reports on larger numbers and over prolonged periods under strict control have raised some reasonable doubts as to the validity of the earlier conclusions as to the prophylactic efficiency. These do not take into consideration the possibility and probability of producing sensitization to the drug which also applies to salicylates, particularly aspirin, which is found in every household medicine cabinet and is taken along with sulpha drugs—and will soon be joined by penicillin—for every imaginable ailment, like the proverbial apple to keep the doctor away.

I should apologize for this long introduction which has been like the unravelling of a tangled skein in order to get on with the knitting. I would summarize the management of rheumatic fever based upon the above as follows:

(1) As rheumatic fever is a familial disease, all children should be held suspect by the family physician.

(2) The tissues of such persons appear to be unusually vulnerable to several injurious agents, and especially to substances contained in or derived from streptococci. Therefore, protection from such exposures should be striven for by all means, and sulphonamides (sulphodiazine preferred) in small daily amounts during vulnerable periods may be used for this purpose. Penicillin by mouth may be the answer!

(3) The vulnerable periods are closely allied to meteorological disturbances due to either season or geography, namely wide variations of temperature with high precipitation.

(4) It is a disease of childhood and early adolescence. Therefore

at these periods the potential victims in rheumatic families should receive particular care—especially the avoidance of damp housing, unsuitable seasons and districts, and under-nutrition in all counts of calories and vitamins. In the upper economic groups this in normal times may be accomplished by money and travel. In other groups this is too unreliable and can best be met by colonies or sanatoria for rheumatic children where a sojourn of years may be guaranteed.

(5) Salicylate therapy at the first suspicion of a pharyngitis to be continued for three weeks or longer with the hope of forestalling the onset of a rheumatic recurrence and meet it with optimum serum level of this drug. The dose should be a gram per year of age, given in divided doses every four hours day and night. A maximum of 10 grams per day is sufficient.

(6) Bed rest. The duration of this is one of the most difficult questions to answer. Until the sedimentation rate returns to within normal limits? Perhaps! If its elevation persists over the weeks and months in spite of continued salicylate therapy a risk may be taken when warm, dry summer weather approaches. Suitable bed exercises, occupational therapy and education must be continued through this period. Bathroom privileges should always be permitted after the acute phase of fever has passed lest much worse befall the victim!

(7) The family physician must act as a family physician through the weeks, months, years and decades. He must watch the family not only individually but collectively, and all must appreciate thoroughly that there is no royal or easy way to contest with this enemy of childhood which reaps its victims or suffers defeat after years and decades of treacherous and repeated attacks.

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# Post-War Trend In Medicine\*

By J. C. MEAKINS, C.B.E., M.D., LL.D.

Mr. Chairman and Gentlemen:

WHEN I was asked to discuss this evening "Post-War Trends in Medicine" I immediately felt that I was being called upon to act the role of a prophet—and you know what is the destination of every prophet. Either by chance he hits the nail on the thumb, but usually he is discredited. I cannot speak from a colloquial point of view on the future trends of medicine because I am surrounded by an international group of young men. At the present time my resident, assistant residents and internes come all the way from California to Nova Scotia, and from Georgia to China, but perhaps for that reason I can milk from them first-hand information or knowledge from local tradition of what the medical profession has gone through in the past twenty years and looks forward to in the future.

If we are to consider post-war trends, first let us briefly consider what were the pre-war conditions in the hectic twenties and the doleful thirties. In the thirties the whole world was in chaos and it was out of this that there came a great deal of talk about health insurance. Naturally it would come at that time when there was a depression and people found it hard to meet the commitments of folly and extravagance which had preceded that period. As governments do, they began to play with these ideas of social security. This was their first flirtatious gesture, and the profession was naturally suspicious of these advances. I think it was a most important step when, at the meeting of the British Medical Association in Winnipeg, under the leadership of Harvey Smith, the Canadian Medical Association started a serious study of these health insurance plans. But the Provincial Medical Associations were suspicious, and I think rightly so. They were apprehensive that there was going to be eventually a medical dictatorship. The medical profession of all others is conservative. It is conservative because their traditions are very deep in the social soil of at least three thousand years. They view any drastic change as a menace to their security. As a result of the boom which affected the medical profession as well as other professions and industries, there was a division between the rural; the county and small-town group and the urban practitioners. The former were, on the whole, dissatisfied. I do not say venomously dissatisfied, but they compared themselves and the hard work they had to do to make a reasonable living to their colleagues in the large cities who were quite complacent and were making large incomes and not working very hard, and could have Wednesday afternoon, Saturday afternoon and all day Sunday

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off playing golf and two evenings a week playing bridge. There was, I think you will agree, an inequitable distribution of wealth and endeavour.

About the same time there was growing up a domination of the social agencies, which some people thought were perfectly fine. They were dissatisfied with the medical profession. The social disciples began to explain why. A large number of people were chronically incapacitated and they took it into their hands, rightly or wrongly, to rectify these things. They often made frightful blunders, but still with their failures they could still blame the medical profession because it had not assumed the responsibility of laying a basis for individual health and its maintenance. The social agencies began to educate the people as to the importance of health and its preservation, as compared to illness and its cure. I think that this is a very fundamental concept which we must accept. We must make a distinction between the prevention of communicable disease in the community and the maintenance of personal health and well-being. The medical profession takes a great deal of credit to itself for what has been done in preventing epidemics. But let us be honest—Pasteur was not a medical man; Lister was a medical man but he was discredited for many years by most of his colleagues. Donald Ross was a medical man and his heart was almost broken when his concept of the transmission of malaria was ridiculed. Almroth Wright was a medical man and he was laughed at when, in the South African War, he proposed vaccination against typhoid fever. We have been too apt to ridicule men with original ideas instead of being sympathetic and trying to understand what is new.

I speak frankly of the social agencies because I have sometimes disagreed with them. I do not hold that the medical profession is only interested when a person is ill. They have criticized us because of the indifference of most of our profession to health hazards in the way of bad housing, overcrowding, malnutrition, juvenile delinquency, and the control of chronic disease—especially tuberculosis. What have we, as a medical profession, done—not individually but collectively—to rise up and preach the gospel, preach that these things should not be and that ill health due to such conditions is preventable as far as the individual is concerned? We patted ourselves on the back that we have wiped out typhoid fever, but *we* did not do it. It was done by a few men in the Public Health Service and Sanitary Engineers. I remember well in Montreal when we always accepted with fatalism the fact that every April we would have an epidemic of typhoid fever. A few had to get up on their hind legs and fight as we now should preach against slums, preach against the emotional hazards of industry, of sweat shops, of poor employment, of slave labour and of the conditions which follow from the train of such accepted profit-making health hazards.



I think that a great deal could be done by technology without the loss or lack of humanism. The great majority of our medical students in North America aspire to be specialists at one time or another, and the minority aspire to really look after the people in rural and small communities.

What has 1939-1945 taught us? I will give you the lessons that they have taught me through bitter experience and chagrin, of a failure where I should have raised my voice in protest. I acknowledge that they are a cross section of the medical profession of the country. The profession was and is chiefly concerned with the gross manifestations of disease. It is a very interesting thing to make a pre-mortem diagnosis so that the pathologist cannot say "you made a mistake". With our technology we can tell in nine cases out of ten just why the patient died and in one case out of ten the pathologist cannot tell you. The medical officers in the Armed Forces were definitely put on the spot because they were chiefly concerned with the gross manifestations of disease and they were not equipped to assess the potential indices of minor degrees of disability on a functional level. That is why, at one time, we had more recruits refused for the Navy, Army and Air Force than we accepted, and we were known by the flippant as a C-4 nation. That was perfectly ridiculous because the medical officers had never been properly trained for this specific job. A systolic murmur was found and heart disease was recorded. Fifty per cent. of you in this room have systolic murmur and it means nothing. But they were brought up in that tradition—systolic murmur—heart disease. And the irony—if a man did not have a systolic murmur they did not realize that he might have heart disease. We have brought up our medical students on the end results as found in the department of pathological anatomy. We see the end of a perfect life:—cirrhosis of the liver, tuberculosis, nephrosclerosis, cancer, etc. The outdoor department is where you find the patients who should be the basis of our medical training. The patients with a pain in the back come with their trials and tribulations, the same as come to their family doctor. We impress upon our medical students, unconsciously perhaps, that the epitome of medical knowledge is to be found in the wards. But the place where they should really learn to handle and look after people is in the outdoor department. I think that we who teach in medical schools labour under a great handicap because for twenty-four hours a day, through say five, ten or fifteen years we see too many end results and not enough of the beginnings of disease.

The medical teaching profession are too apt to entirely neglect the psychological concepts of medical training and practice. The medical officers in the Armed Forces soon became appreciative of the importance of these things. After all they were looking after a million men who, taking them all in all, had been screened through a fine sieve and

were supposed to be perfectly fit anatomically. But the discharges from the Armed Forces were mounting day after day and they had never yet been in battle. This experience acquired in training centres has been of tremendous advantage to these young medical men and I would say that probably thirty per cent. acquired a knowledge and a concept of something which they had never thought existed before.

As I stated quite a few months ago, to my mind the reduction of mortality and morbidity from enemy action was due to:—(1) realistic forward front-line surgery; (2) blood and blood substitutes; and (3) the judicious use of sulphonamides—and I still believe that this is correct. Some people want to put blood and blood substitutes first, sulphonamides second, and realistic surgery third. I entirely disagree. The reduction in our death rate and amputation rate, in this war, will be entirely due to the efforts in that order. The thanks are due to the young men who within a few thousand yards of the firing line have done such wonderful surgery. Quite true, at first they made blunders; who has not? But they soon caught on to what was required. The resuscitation teams that worked with them used physiological therapy with the utmost critical judgment and these combined efforts are the secret of these triumphs which reduced to an all-time low the maiming and deaths from battle injuries.

Medical practice in the future, as I see it, must face changing times. Not only changing times for the profession, but changing times for the people who come to seek advice from us. I think that the future must be viewed from two aspects by both, namely: health and health maintenance, and diagnostic and therapeutic measures. The second naturally arises when the first has failed. These again can be divided horizontally into the psychological and psychiatric groups, and into the physiological and the structural groups. The psychological and physiological are the disturbances of spiritual and of functional orientation. These probably account in the way of illness for two-thirds of the total; in other words the structural or anatomical group accounts for only one-third of all disabilities. If you find gold at the outlet of the river you know there has been gold somewhere in the water-shed. When we find the end result we must try to work backwards step by step and find out what had been the initial disturbance which eventually lead to the death of the individual. About forty years ago the chief problems of life expectancy were with the paediatrician. The death rate among children was enormous. The mortality rate in the older decades is less important than the morbidity rate. Why are people sick is just as important as why they die. The economic wastage from so-called minor illness is enormous, and that from chronic diseases which may even promote longevity is even more so.

We, the medical profession, are only about 10,000 in a population of 10,000,000. We are their servants. What they want is simple and sensible. They want good guidance to health and the maintenance of health. They want us to help them towards this end. They are tired of being cured. Any of you who have had a chronic illness know how tired you get of people trying to cure you. They expect expert guidance from the medical profession both as to the family and the individual. When they become unavoidably ill they expect expert diagnosis and therapeutic facilities reasonably near at hand and at a reasonable price. They are anxious and willing to pay in advance for this in some form of insurance and trust the profession. I know how deeply they do trust the profession, and far more than they trust any government to provide this service from a human, personal point of view. What does the profession think? What is our point of view in this matter? This may be divided into two groups. One group would devote their time and thought to the diagnosis and cure of disease. These are chiefly found in the hospital wards. They look after those already ill. On the other hand, the people—while deeply appreciating this—want their families kept healthy and free from illness. At first there was a minority in the Armed Forces who appreciated the point of view that they were responsible for a group of men who had to be kept mentally and physically healthy. All should know that this is an important part of our mission. I grant that in the ordinary run of the mine we of the medical profession get very little remuneration for keeping people well. Unfortunately we gain our livelihood from people who are ill. But after this war I think that there will be a large group of young men who will see this objective and be ready and equipped to follow the lessons they have learned in the Armed Forces.

I think the trend will be away from the specialist and will be towards the family physician, provided that he can have the facilities with which to practise his profession. We know full well that our profession is badly distributed. In the big centres there are many specialists of one kind and another with the services of large hospitals at their disposal. The men in the country have not the facilities to practise as they were trained to do. We hear it said—why not train our graduates to meet this state of affairs? In other words, go into practice without the training and the advantages of the modern medical science. They are trained and equipped to use scientific methods. But where is the health centre? Where is the x-ray department? Where is the technician to do blood sugars or basal metabolisms for them? They pass over the patient to some clinic which must charge rather high fees but cannot continue to carry the patient to health and its maintenance. The charges and other expenses to the patient are out of reason for the simple tests which should be available to all. This

further applies to the relative fees paid to physicians, surgeons, general practitioners and specialists. Our whole system is out of proportion to what it should be. You may say that I am wrong, but I am in a position to judge these things without fear or favour. It is not fair. It is not just that the rural doctor has not got the facilities with which to work properly. So he may go to the city where he can make money more easily and he does not have to worry about his family and his own future. But where is the man who is going to prevent individual diseases and look after the chronically ill, which is the greatest cause of social insecurity? To this end we have to look into the future. If we do not, the people as represented by the government are going to bring it about, whether we like it or not. It is in our hands to improve and meet the demands for the better care of the people. It is our problem to prevent disease in the individual. Public health officers, sanitary engineers will see to the wholesale business that we do not get dysentery, typhoid, paratyphoid, etc. The schools will see that we do not have epidemics of diphtheria. For the care of those with the chronic diseases and those of the aged in the population we must demand the tools with which to practise our profession, not only for our own gain but for the gain and the happiness of the people. We will always be reasonably rewarded. Along with this we must also demand that every practitioner, without financial detriment to himself, has one month off at least every two years, apart from ordinary holidays, in which to visit clinics for the good of the people he is looking after. Many doctors keep on saying—"I will go next year, next month, tomorrow." Then he says it is too late. "I have forgotten everything, it is too late to go now. Why should I bother? I'll just carry on!" But this professional resuscitation must be insisted upon.

Do not let us be misled by the bogey of socialized medicine. I think we can solve the question ourselves. A few months ago I spent a very profitable evening listening to the results of a survey of a medical health service. The speaker said the people are behind the profession, but we do not advertise! We do not plead your cause. We are not nearly as good as those behind Jergen's Lotion or Hinds honey and almond cream! There is no glamour in your campaign.

The profession want tools with which to carry on their profession. They need public health facilities and small or large hospitals serviced by technicians. They want a modicum of financial security for their wives and education for their children. They will want to be away for an average of six months every five years. We must get away from complacency and I think there is a great future for the medical profession as a whole to take the lead. I think that the time has come for the medical profession to gird up their loins and without any suggestion of fear or favour tell the people what they need and how

best to provide for it. State medicine cannot solve it. We must be given the tools of our trade throughout the country so that men at the crossroads can give as good service as the men in the city, which is not perfect by a long way. I have a great admiration for the country practitioner. He is doing a job. We do not help him. He has not the facilities, amenities or security he should have.

Present day medical practice is the progeny of many thousands of generations. This has been determined by the strict personal relation of doctor and patient designed to diagnosis and treatment of a specific disease. Where this may have come from or where the patient may be going from the immediate recovery is of secondary importance, if at all seriously considered. This may be a rather extreme statement but within it there is a great deal of truth. Medical education is based on this premise. It has been forced to do so not only by tradition which is perpetuated by the requirements of licensing examinations but also by the custom of specific anatomical diagnosis.

If one stops to consider the matter, the choice of doctor by patient is a happen chance determined by many extraneous factors. It is true that a family tradition may determine the choice in certain instances when family doctor is handed on through several generations. But this is mostly so in settled rural districts, villages and towns, but relatively seldom now in large urban communities. In the first three it is usually "Hobson's" choice, as an unpopular doctor soon moves to other pastures; but, if there is only one doctor in a district he must be acceptable and usually is. There is naturally a close tie between patient and doctor, as the latter is the repository of many intimate matters; but, it would be more realistic to view this as between the patient and the profession, as many patients have a series of doctors in more or less rapid succession. It can be quite appreciated that these intimate relations should be respected but that it is absolute and perpetual as between man and wife is theoretical rather than real. The cynic might see a close relation in these days of rapid divorce and re-marriage

But when we come to consider those who are not blessed with a steady family physician, the choice of a new one depends on diverse and often unreliable tips. The virtues and shortcomings of doctors are discussed over teacups, cocktails (when there are any), dinner plates and back fences. One who has cured the husband's varicose veins or haemorrhoids is lauded as the only one to care for another's wife's constipation or headache, or the daughter's dysmenorrhoea, or the son's pimples. All of this may be quite true, but the advice is not based on reason but rather on the "bedside manner" and an assurance of infallibility dominates while scientific knowledge goes by the board unless it has a long-term chance to prove its worth. How else can

a person judge the merits of a doctor except by gossip which has ruined the professional career of many a scientifically honest physician or surgeon? Few people welcome the truth but would rather believe what is most convenient. Most of us are "ostriches", particularly in matters we do not understand or do not want to understand, as over fifty per cent. of illness is a protective or escape mechanism to camouflage frustration, disappointment, jealousy, economic worry and a host of other psychological insults. So one can see where the bedside manner and the sympathetic ear gives such solace, but in the end little permanent relief. It would be unfair to pursue this thesis farther, but there is more truth than fiction in it, although you may protest. It is left to them to give a better answer as to why patients choose their doctors except for the few who are of the craft.

It is interesting to note that most protests concerning the free choice of doctors come from the medical profession. There are a number of reasons for this. In the first place, the best Medicine can be practised for the good of the patient when the sequence of events can be followed, not as to a specific disease necessarily, but through the decades of life and the vicissitudes of time with the percussions and repercussions which make up the life of an individual and so influence his general well-being. It is really an unrecognized branch of Psychological Medicine. Unfortunately unrecognized, because if the modern importance of Psychology and the concepts of Psycho-Somatic Medicine had been known to our grandfathers and their grandfathers, there would have been built up an understanding of human behaviour which would have brought comfort and understanding to countless unfortunates, particularly through the Victorian era and the aftermath of succeeding generations.

What other reasons are there for the doctor to be so insistent on this matter of free choice? Doctors are human and have the human privilege of disliking some people even as patients whether they are good "pay" or not, and those who demand the most do not necessarily appreciate the fairness of the bill when presented. Also as a corollary it cannot be denied that the profit motive enters into the picture. Medical practice in urban and in some semi-urban communities is highly competitive. The race is not always to the knowledgeable nor the income to the impeccable. But within limits of a thoroughly good method of practising our profession this matter of doctor-patient relation should not arise as one of much importance. It is rather a shibboleth handed down from a past when the sanctity of the priest-physician was part confessional, part sanctuary, and part therapeusis, and all were mingled into an amorphous mass of superstition and magic.

There is little doubt that the present confusion and criticism of medical care and health security is a combination of economics and

professional maladjustment. The great trend towards specialism is to be found in all walks of life. The more skilled the artisan the higher the pay and the shorter the hours. So it is with the practice of medicine. Specialists in Obstetrics are comparatively few because the life is hard and the hours uncertain. Eye, Ear, Nose and Throat specialists are relatively common and they seldom have much to worry about. The modern numerical predominance of surgeons is hard to explain. If they would stick to their scalpels there would not be so many of them and there would be more frank general practitioners and better surgery done. Many so-called surgeons are such, but pose as specialists and do neither well. When surgeons practise Medicine by treating diabetes, pneumonia, pernicious anaemia, Addison's disease, rheumatic fever, heart disease, obesity, emaciation, painful menstruation, hyperacidity, etc., without a background except that of an undergraduate who has forgotten most of what he knew, it is just too bad for the clientele. It is quite acknowledged that our system of practice has made this necessary in rural communities, but here the practitioner knows his limitations and usually restricts the use of the knife to dire emergencies. It is in the towns and small cities that the pseudo-surgeon has a year-round open season.

The time has come for the profession to put its house in order and to discipline its own members as to what they are trained for and capable of doing well. This latter means that there should be a certain control over therapeutics. Treatment too often may help the immediate disability but leave in its train secondary conditions which are worse than the original. An inestimable amount of good is done by the medical profession but at the same time much more happiness could be afforded to many poor unfortunates if our methods of treatment were not of such a routine and haphazard character. Rational treatment rests upon accurate and painstaking diagnosis. Therefore, we should be sure before we leap. This is the key-note of the present deficiency of adequate medical care. The requirements for diagnosis today have become complicated and expensive. Most laboratory examinations can be carried out by well-trained technicians who under a co-operative plan can give a relatively cheap service to many practitioners, and these facilities should be made available after a co-operative system sponsored and underwritten by the community.

Being a physician, I do not want my surgical colleagues to think that I am particularly hard upon them. I do not exonerate physicians from some of the same faults which I have mentioned about the surgeons. The fault in the practice of Medicine as compared to Surgery is the reverse. Practitioners who devote themselves entirely to Medicine are comparatively few and those who make a careful study of this subject and keep abreast of the times are fewer still. As a result the advances in medical diagnosis and therapeutics are just as apt to be

unreasonably enthusiastic, uncritical and haphazard or are entirely neglected as being too academic and requiring an unprofitable analytical judgment. Examples may be cited in the use of insulin in diabetes, liver extract and allied substances in pernicious anaemia, Digitalis in heart disease, vitamins in dietary deficiencies—in fact, the whole realm of nutrition—gold and vitamin "D" in arthritis, and finally the uncritical and unknowledgeable use of hormones. Medical therapeutics has become simpler and more direct but requires a careful and thoughtful analysis of its indications, and the indiscriminate use by the trial and error method leads but to confusion doubly confounded.

The habit of giving a bottle of medicine before a diagnosis is arrived at and a placebo when no organic disease can be found is pernicious and harmful. Both are a cloak of ignorance or neglect with the hope that a cure may occur by the spontaneous bodily defences. But if it does not and the act be repeated so as to become a habit, valuable time is lost which cannot be regained if the disease is dangerous and progressive. If the complaints are the result of a psychogenic disturbance, the conviction or defence mechanism is confirmed and hardened and the foundations for a prolonged disability are firmly laid.

So let no one cast the first stone whether it be at the surgeon who operates to cure a pain of which the origin is not known or on the off chance that the knife is a good psycho-therapeutic agent, or at the physician who uses placebos or speculative therapy without a diagnosis or at least reasonably substantial indications. Both may be the result either of harassment, hurry or self-deception, none of which is justifiable or likely to succeed except by happen chance, and will most probably start a succession of effects which are difficult to put into reverse. The net total lesson to be learned from this is that the good and intelligent doctors become too busy to have enough time, and others are too lazy to use the time they have. This brings us back to the question of the distribution of the medical profession, the lack of the facilities to practise medicine according to modern standards and certain leisure to keep in touch with the times by reading and periods of study in suitable surroundings amongst their fellows. No man can practise his profession for twelve to sixteen hours a day and keep up with modern progress, especially when the eight to twelve hours he has off are not his but are merely borrowed in bits and pieces as unpredictable chance may allow.



# Medical Responsibilities in Practice\*

By J. C. MEAKINS, C.B.E., M.D., LL.D.

**I** FEEL a heavy responsibility in addressing you today. I seem to sense that what I say may in some way influence you for the better or the worse of Canadian Medicine, as you are part and parcel of Canadian Medicine of the future!

You will soon face a new world in more ways than one. In the first place you will pass from the sheltered tutelage of a Medical School into the responsibilities of life and death—of health and happiness with that intimate dependency of those who are often afraid of the present and the future!

In the second place, you will be launched into a period when the traditional tenets of Medical Practice will be put to the test of a changing order. To meet this we must be faithful to our trust but withal understanding of what is required of us to meet the demands of this changing order and still preserve the basic articles of faith of the medical profession.

It is held by many that science and technology have outstripped the humanities. If this be true—it is most true in Medicine. We of the profession have made little attempt to bring the former to the people but rather to bring the people to them, to the detriment of both the people and the practitioner who is far removed from technology in his everyday life.

I know many of you are thinking of these matters. I know it from your discussions in C.A.M.S.I. and the many talks I have had both privately and in classes with our own students. Don't be too critical of past generations. They have given you much with which to help the present and the future. Even though technology ruled and the humanities were submerged—this is but a passing phase of imbalance and the social sense of responsibility with which to weight the pendulum to a more even march of time.

Some weeks ago at one of our seminars we had for the subject of discussion "Social Medicine". The two students who were allotted to lead were given this task more or less at random. These seminars are friendly open forums with no favours asked or punches pulled but are conducted within the reasonable limits of the Queensbury Rules.

One might rightly ask what a seminar on "Social Medicine" has to do with the diagnosis and cure of disease. I grant but little for anatomical lesions, but a lot to do with the present and future practice of Medicine. Seminars on this particular subject have ranged over

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wide spaces. The notes of these two students, Arthur J. McInerney, and John A. Lockhart, I will use in part and as the text of what I have to say to-day, as I think they carry a message to all of us, and I almost entirely agree with their concept.

As I see it in its simplest form a physician has three main responsibilities. These are:—

1. To his patient;
2. To his profession;
3. To himself.

In examining these individually we will run across the following trends:—

A patient comes to us seeking relief from some maladjustment of his constitution which prevents him from being efficient at his work and enjoying his usual recreations. In other words, his routine of life is upset and he is to a varying degree uncomfortable, worried and unhappy. Our immediate responsibility is to restore him to his own mode of life as quickly and economically as possible. That is what he wants, and to do this we must strike a balance between the aids of science, their probable value and their relative cost. We must not restore his physical well-being at the cost of wrecking the social structure of his life.

If a patient is ill it is granted that all the aids science has given us should be used without hesitation *when indicated*, but certainly not to the extent of doing expensive tests to satisfy our own curiosity regarding some obscure condition with which he has been apparently happy and well adjusted when he is complaining of some far graver ill.

All this boils down to one simple thing, and that is to have a genuine human interest in the welfare and happiness of our patients. Remember, a doctor makes his living from the misfortunes of others; don't add to them unnecessarily. Look beyond the pathological condition, weigh each decision carefully. I hope I have not given the impression that I am discounting technical aid. Without it there would be no science of Medicine, and one of our main responsibilities to our patient is to be as competent as possible in our field of the profession. We must keep up with the times, but not employ necessarily new and spectacular procedures of unproven value. Certainly one should be well up on those things which have proven to be of value and always on the lookout for some means of improvement. "Be not the first to try the new nor yet the last to discard the old." To his patient a doctor should be able to offer:—

- (1) a friendly, genuine interest in his well-being,
- (2) adequate technical knowledge to cope with the situation and enough sense to refer him elsewhere if he can't.

Few, if any, professions can look back along its ranks with as much justifiable pride as we can. The older generations were men who worked hard and well, often with little knowledge but limitless curiosity and energy, always working to beat some problem of disease and then spreading their new-found knowledge to their fellows that all people could benefit from their discovery. They were leaders of men, ready to accept responsibility in any form that worked towards the advancement of their community. And that is what we should be planning to do. We owe it to them to enter practice—it does not matter where—in such a way which shows we have benefited from their teachings and example.

It is our duty to keep the general public's faith in the profession intact and nothing will be gained by running down the work of our colleagues other than a series of lawsuits in which we will probably come out second best. Remember, no one is infallible, everyone at one time or another will have results which are far from perfect.

On the other hand, it is our duty to ruthlessly expose a doctor who is guilty of malpractice providing you are sure you have enough evidence to bring the case to a favourable judgment. One cannot afford to have a man in his community who consistently brings dishonor and shame to one's own profession without taking vigorous action against him.

Our final responsibility to our profession will be that of teaching. We in Medical School get hundreds of hours of instruction in different subjects, all highly technical and devoted to the scientific basis of medical practice, but the art of medical practice—equally important—we must learn from older members and from experience. It is something we must learn through experience alone. In Medical School we learn the basis or fundamentals of knowledge. The internship is the first step in practice and responsibility. The manner of handling patients must be acquired from this stage onwards. It will be our duty to pass along our knowledge to those who will follow us so that they may profit from our experience and not from their own mistakes, and in so doing they will be able to carry the achievements of the Medical World to a new high. Our fellow doctors can reasonably expect us to carry on their work, maintain their prestige and accept responsibility; to be apt pupils and later still better teachers. It will mean a lot when we are starting out to have an older man to lean on. We must be prepared to help others get started when we are the experienced ones.

First and foremost we owe it to ourselves to enjoy our work. No one, no matter how highly trained, can put that extra something into his practice which marks him as a successful practitioner without deriving a lot of pleasure from his work. In order to do this we must

keep up with it. We owe it to ourselves and our patients to see to it that we don't get rusty. If possible one whole month each year should be spent at some recognized Medical Centre where one can keep abreast of the most recent advances in one's own field, appraise their value, learn them and go home and put them into practice.

Finally, we owe to ourselves a reasonable period for reading and recreation. We must keep up with the world politically and culturally. We must have at least one, and preferably two or more, hobbies in which to lose ourselves and in so doing achieve physical and mental relaxation. We must know people, not only sick ones but well ones; see how they live; learn their views; enjoy their company; learn to laugh with them and how to make them laugh. An active sense of humor will often handle a situation which would otherwise be disastrous.

While this list of responsibilities is certainly not complete, and there are probably many of you who do not agree with them, I hope that when you enter practice you will realize it is no light undertaking. We have a job to do, with certain standards to live up to. What these are is largely a matter of individual make-up, but the mere realization that we have responsibilities will, I hope, make us better doctors and better citizens.

During the past few months, and indeed for the past couple of years, there has been a great deal of discussion as to the meaning, purpose, and prospects of "social medicine". The term "social medicine" is frequently being misused not only by the public but by members of the medical profession itself, thus there must be some basically wrong ideas bringing this about. The chief misconception may be divided into two: (1) the idea that social medicine is just another name for preventive medicine as we know it today, and (2) that social medicine and State or socialized medicine are synonymous. From the above statement then it would seem that it may be advantageous to give a brief account of just what the true meaning and objectives of social medicine are.

The great majority of the profession of today are well aware, or should be well aware, of the fact that Medicine of the past 20-30 years has become much more technical and more specialized, and in this transformation one notices that the old-time type of physician has become outmoded and appears out-dated—it would seem that the old humanism of our predecessors has been relegated to a secondary position. So it should be quite obvious that some revolutionary changes are presently needed in our basic medical philosophy.

In the teaching hospitals in general the need for a change cannot be denied. There we see laboratory investigation extensively carried out, mostly on the objective side, whereas there is usually little or

nothing said to, or done for, the patient as a person during or even after this tiring process. This is especially noticeable in the chronic or more obscure varieties of disease—we often walk through a Ward and hear the Doctor ask the Interne, "Well, what are you doing for this man?"—and hear the Interne's not too brilliant reply: "Well, Sir, we're putting him through the mill—flat plate showed nothing, but we are going to run right through." Is this what the practice of Medicine has come to with all its modern advances? The helpless patient must lie there while all these laboratory investigations are being carried out—and often his faith in the medical profession is going down, although in the end they may diagnose and cure him. Still the patient has the thought that he has been treated as some laboratory animal for about a week or more—due mostly to the simple fact that nobody has treated him as a human being, no one has really taken the time to talk to him.

More and more accurate assessments of disease and pathology are being made, with the help of more and more instruments and colleagues, and less and less intimate understanding of the patient as a whole man or woman with a home, economic problems, anxieties, with a job to hold, and with a past and a future. Everyone should appreciate that as our students of today are taught and trained so is the pattern of our next generation of doctors.

In the medical profession of today we see too much reliance on specific objective tests, too great a belief in the potency of certain treatments or too deep a despair at the apparent helplessness of other treatments. On the other hand, too little knowledge of morbidity and mortality figures, of the relative incidence of diseases in the community, or of the vast incidence or the prevalence of illness or debility, and very often with too little or even no appreciation of the fact that these illnesses, and indeed many organic diseases, have their basic origin in social, domestic or industrial maladjustment, in economic insecurity, dietary insufficiency, or even fatigue. The clinical teachers of today quite often have very little, if any, close acquaintance with home or working conditions of their public patients, and this is the example our medical students of today are getting. Of course, it is true there are notable exceptions. Indeed, science and techniques have come to dominate medicine to the exclusion of that most important science of all, the science of men, and the most important technique of all—the technique of understanding the patient. It has been said that "science without humanism may work with atoms, but it will not work with humans."

Of course you will say that modern medicine is truly scientific and thus it requires a high degree of specialization if it is to reap the advantage of the new discoveries. We will readily admit that there is

much truth in this contention, but even today we see new remedies being put on the market with but little, if indeed any, scientific justification. We see remedies grasped at by physicians to try to cure some of the incurable diseases in the hope that the patient might be helped. We see around us specialists whose outlook is so cramped that they tend too often to attribute their patient's ailments to some unusual condition in their own restricted sphere. The only sure defence against over-specialization is, I believe, to give the general practitioner a dominant share in the care of the patient, and to fit him for this all-important position in the State we must see to it that he is properly educated along these lines. All medical students know the fascination of the study of fully-developed diseases, the care of dangerous illness, and the dramatic appeal of difficult operations. But the prevention of disease and the achievement and preservation of perfect health, both physical and mental, also have a compelling appeal if presented by teachers who have the right outlook on health and disease.

We often see the specialist and houseman who are responsible for the special investigation into a man's illness having to call in an outside practitioner to establish a suitable relationship with the patient, a relationship which they with all their techniques have failed to establish. With the aid of the trained social worker and with much closer collaboration with the Departments of Public Health, the inter-relation of clinical, social and environmental studies, and the contribution which each makes to a better appreciation of the prognosis, cause and convalescence, are now being taught to students in some Medical Schools. In these Schools also we see the students encouraged to make personal visits to the homes and working places of the patients. Today we see syphilis and tuberculosis being considered as human, educational and social problems, and not merely as medical and surgical problems with set routines for diagnosis and treatment. The neuroses and psychoneuroses are often better helped by these new alliances rather than by calling other specialists to the bedside; while the physician or surgeon who has "excluded organic disease" retires from the scene with a sigh of relief for something accomplished—even though it was a negative something as far as the patient was concerned.

What we need most of all today is to improve the environmental conditions, good food and habits of feeding, good houses, better facilities for open-air activities and cleanliness, better education and cultural opportunity, holidays and social security.

We must bear in mind the fact that social medicine has no immediate concern with medical or other politics, but we feel sure that it will in the near future influence our Governments and prompt reforms, and indeed already we can see that some steps have been taken in this direction. A great many seem to believe that both social

and individual medicine will progress better under a comprehensive and reorganized medical health service with no economic barriers or class distinction. It is only too apparent that many of the social evils manifested by disease call not for medical action but for drastic social and economic reform. For these our elected representatives—and not the doctors (as doctors) must become responsible. However, the factual evidence, the socio-medical experience, the statistical data must continue to be provided by our doctors and their scientific associates and field social workers. Thus we have reached the time when “the physician must assume leadership in the struggle for the improvement of conditions”. Without research and teaching in social medicine to guide him he cannot faithfully fulfill his mission. So we see that social medicine implies not only the practice of medicine as applied to the service of man as an individual, but also to the community.

It is quite often said that the general practitioner should concern himself solely with so-called “clinical medicine”—by which is meant the treatment of developed disease; surely this is contradictory to all the traditions of the profession and, indeed, even to common sense. No one expects the general practitioner to be an expert on environmental hygiene, although he should have a workable understanding of its principles; or to be an epidemiologist in the truer sense of the word. However, he should certainly be familiar with the ways in which infectious diseases are transmitted.

But if he is to fulfill his responsibility as the guardian of the patient's health he must have a knowledge of at least three essential points:—(1) his patient's heredity and environment, including his home circumstances and conditions of employment, in short all the factors which may result in a deviation from perfect mental and physical health; (2) his medical history and present condition, and (3) — but by no means least, all the agents—including not merely methods of treatment, but also all the public and private organizations which can be invoked to restore him to his normal or even better condition.

Thus, we not only must re-establish the Doctor as the trusted confidant and guardian of the patient and the family, but we must strengthen his position in every way possible, placing all the scientific weapons in his hands along with the advantage of the various State organizations—in reality making the private practitioner into a general practitioner.

I sincerely believe in these tenets and firmly hold that a proper conception of health and its maintenance should be taught to all the profession whether graduate or under-graduate. In fact, these disciplines should take a position of equality with those of diagnosis and therapy. To bring this about, Health and Human Relations or Social

Medicine with all the necessary associated techniques, whether physiologic, psychologic, economic or social, should form an integral section of the curriculum second to none. It is only through this approach that the *Medical Responsibilities in Practice* can be studied, training acquired and eventually followed through for the good of Mankind.

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### PEDIATRIC ANTIQUES ON TOUR

It has been well said that more progress has been made in pediatrics during the past three or four decades than in all the time before that.

As applied to the feeding part of pediatrics, the Mead Johnson Collection of Pediatric Antiques bears eloquent witness to the great strides made. Without such evidence, it would be difficult, indeed, to imagine our own grandparents being fed from some of these odd-shaped utensils that defied thorough cleansing. To be sure, sterilization and pasteurization were not then in vogue. Not all babies received breast milk in abundance. In the days when wet nurses were common, some of these enterprising women literally did a wholesale business, managing to nurse three or four infants.

The baby's cereal of a century ago was simply stale bread lightly boiled in water, wine or beer. Butter or sugar might be added but the use of milk was regarded as fraught with danger. It was thought, according to Dr. T. G. H. Drake, "Milk might bring on the watery gripes, or the infant might imbibe with the milk the evil passions and frisky habits of the animal supplying the milk."

From a personal hobby enjoyed by the late E. Mead Johnson, Jr., the Collection of Pediatric Antiques, illustrated in the pages of a catalogue just issued, has evolved into one of considerable historical importance, depicting as it does the progression of infants' feeding vessels from the Greece of twenty-five centuries ago down to time within our own memory.

The Collection has been steadily growing in size and scope and is of increasing interest for teaching purposes via the historical route. The destruction of original sources caused by the war tends to add to the value of these objects.

Hence it is that, by request, the Collection now goes on an annual pilgrimage to colleges, hospitals, museums, libraries and other institutions of learning. Arrangements may be made for "stop-overs" upon application to the curator, Mead Johnson & Company, Evansville 21, Indiana, U.S.A.



# Abstracts

## RH INCOMPATIBILITY AS A CAUSE OF MENTAL DEFICIENCY

*British Medical Journal*, p. 188,  
August 11, 1945

In a small proportion of infants dying of Erythroblastosis Foetalis, damage to the cerebral cortex and especially the basal ganglia was found. Children who survived showed mental defects associated particularly with extrapyramidal rigidity and athetosis. Thus, among the occasional Rh positive mental defectives with evidence of basal ganglion involvement, a history of extreme jaundice at birth may be obtained. This is, however, a very rare finding. In other cases, there is severe mental retardation without involvement of the extrapyramidal system. Of 56 idiots, 11 were Rh positive with Rh negative mothers. This is definitely above the 15 percent normal incidence of Rh negative mothers. These findings are the first indications that a portion of low grade defectives owe their condition to Rh incompatibility. Rh incompatibility, therefore, raises a problem in eugenics. The author states, however, that there is need for co-operative research on a wider scale in order to obtain more data from clinical investigations of this problem.

ROBERT TEASDALL

## PRIMARY CARCINOMA OF THE GALLBLADDER

By J. M. T. FINNEY AND

LT. MURRAY L. JOHNSON, M.C., U.S.N.R.  
*Annals of Surgery*, v. 121, No. 4, 1945

Carcinoma of the gallbladder is a much more common entity than is generally supposed by most practitioners and internists. Because of the extremely poor prognosis offered in this condition, the authors determined to

find if there is anything that can or should be done to prevent its occurrence.

A long standing history of chronic cholecystitis and cholelithiasis, in a vast majority of the cases, precedes carcinoma of the gallbladder. This fact advocates the early removal of diseased gallbladders. There are other excellent reasons for early cholecystectomy. Lahey remarks that if cholecystectomy is performed before a patient has suffered repeated attacks of biliary colic, the end results are better and the mortality lower. Chronic cholecystitis and cholelithiasis are definitely related to myocardial weakening and angina pectoris. Other conditions related to calculus and infected gallbladders are functional gastro-intestinal symptoms, intestinal obstructions due to calculus, arthritis and asthma.

Over a large series of cases, gallbladder carcinoma is found in one of all autopsies or about five percent of the total of all cancers thus disclosed. About 75 to 80 percent of all carcinomatus gallbladders were found, at autopsy, to have co-existing cholelithiasis and four to five percent of all calculous gallbladders may eventually be associated with malignancy of that organ.

The authors review a series of 18 cases of which two were males and 16 were females. The average age was 67.4 years. The presence of stones was proved in 11 cases; in 7 it was impossible to say due to the extent of the growth. Several points can be emphasized from this series. In nearly every case, the symptoms presented were due to inoperable growth with or without pre-existing symptoms of cholelithiasis. The result of surgery, once malignancy is established, is most discouraging as shown by the fact that 15 out of the 18

patients of this series died in less than one year. The mere removal of stones is not enough; the gallbladder should be removed when possible.

JOHN HARPER

### OPTIMUM DOSE OF SULPHADIAZINE IN TREATMENT OF PNEUMOCOCCIC PNEUMONIA

By MORRIS F. COLLEN, M.D. AND  
EDWARD PHILLIPS, M.D.,

OAKLAND, CALIF.

*Archives of Int. Med.*, July, 1945

In a twenty month period, 1,465 patients with pneumococcic pneumonia were treated at the Permanente Foundation Hospital. In the first half of this period, 618 consecutive patients were treated with usual doses of Sulphadiazine, namely, 5 gm. initially and 2 gm. every six hours thereafter, maintaining an average blood level of 8 to 10 mg. per 100 cc. In the second half of the period, 748 consecutive patients with pneumococcic pneumonia were treated with double doses of Sulphadiazine. The majority of the patients receiving the double dose received 5 gm. of sodium sulfadiazine in 500 cc. of sixth molar Sodium Lactate solution intravenously, and 5 gm. of Sulphadiazine orally, followed by 4 gm. orally every six hours, maintaining an average blood level of 12 to 20 mg. per 100 cc. Adjuvant therapy, including the use of specific pneumococcus serum was the same in both groups.

A comparative analysis of the various important factors influencing the mortality rate was made with specific reference to age, specific pneumococcic types, incidence of bacteremia, leukopenia, severity of associated diseases, extent of pneumococcal involvement, number of days illness, etc. It was found that the two groups of patients had pneumonia of comparable severity.

The treatment of patients with pneumococcic pneumonia with double doses of sulphadiazine resulted in:

(1) a decrease in gross mortality from 10.7 to 6.2%;

(2) a decrease in the incidence of sterile pleural effusion from 5.2 to 2.7%;

(3) a decrease in average period of hospitalization.

There was no greater incidence of drug toxicity in patients treated with double doses of Sulphadiazine.

CAMPBELL LAMONT

### TREATMENT OF CIRRHOSIS OF THE LIVER BY NUTRITIONAL MEANS

By NORMAN JOLLIFFE, M.D., AND  
ELMER ALPERT, M. D.,

*Medical Clinics of North America*,  
New York, p. 655-662, May, 1945

The difficulty in the treatment of cirrhosis of the liver is that the cause is not known. However, it seems probable on the basis of experimental and clinical experience, that the liver, made more vulnerable by an unfavourable nutritional environment, reacts to a variety of toxins which cause parenchymal damage by the deposition of excessive amounts of neutral fat, which may go on to progressive fibrosis and atrophy.

Experimental evidence showed that fatty infiltration and cirrhosis have been produced by diets low in protein and high in fat. There is clinical evidence of other signs of nutritional deficiency in a high percentage of cases of cirrhosis of the liver: polyneuritis, smooth tongue, encephalopathy, ascites, low serum albumin, reversed albumin: globulin ratio, and anaemia usually of a hyperchromic macrocytic type. There are a variety of hepatotoxic substances such as chemical poisons, hyperthyroidism, infectious processes and toxæmia of pregnancy.

Substances which prevent the deposition of fat or accelerate the rate of removal of fat from the liver are called lipotropic factors. In the depancreatized dog, maintained on a mixed diet and insulin, large fatty livers develop. This can be prevented by the addition to the diet of one of the following:

(a) Lecithin of which the active principle is choline;

(b) Fresh beef pancreas, the active principle being choline;

(c) Casein, the active principle being methionine.

It has been shown that there is a definite impairment of the liver function in protein depleted animals, and conversely, that dietary protein may protect the liver against the effects of exogenous toxins.

Favourable results in treatment have been obtained by the use of a diet rich in protein and carbohydrate, moderate to low in fat and supplemented by casein, dried brewer's yeast, liver extract and the administration of specific vitamins when indicated. In one study with 54 cases, 20 showed signs of "clinical recovery". In two years, 45% of the treated series were living compared to 22% of the controls.

The lipotropic factors—casein, choline and methionine—either alone or in combination may be used experimentally.

NORMA COOK

#### THE TREATMENT OF EARLY SYPHILLIS WITH PENICILLIN

By JOSEPH EARL MOORE, M.D., J. F. MAHONEY, M.D., COMMANDER WALTER SCHWARTZ, LIEUTENANT COLONEL STERNBURG, AND W. BARRY WOOD, M.D.

*Jour. Amer. Med. Assoc.*, v. 126,  
p. 67-73, September, 1944

This article is a preliminary report of 1,418 cases of early syphilis treated with penicillin by the Penicillin Panel, a group of American doctors in association with the American Government. Of these cases, 177 had sero-negative primary, 379 sero-positive primary, 698 uncomplicated early syphilis, and 97 various types of recurrent secondary syphilis. Of the patients, 461 were whites, 950 negroes and 7 of other races; 791 were males and 627 females (58 pregnant at time of treatment).

With the aid of tables and charts, the effect of the various time-dose-

route relationships are shown. Since most of the cases had been observed for only three to four months, only the immediate results and some information on the incidence of relapse were available. The report shows that penicillin has a profound immediate effect in early syphilis in causing:

(a) The disappearance of organisms from lesions in six to sixty hours;

(b) The rapid healing of lesions;

(c) A trend towards serologic reversal (within twenty days).

The same immediate effects were apparent within a dosage range of 300,000 to 1,200,000 units intramuscularly q.3.h.—60 injections in 7½ days.

The optimum time-dose relationship could not be determined by these immediate effects, but by the incidence of relapse. Relapse with the use of penicillin alone varied directly as the total dosage intramuscularly; greatest with 60,000 units and least with 1,200,000 units. Relapse was more frequent after intravenous than after intramuscular administration. The lowest incidence of relapse was found in some patients treated with penicillin plus a sub-curative dose of mapharsen.

The optimum time-dose relationship was not established absolutely, but the minimum dose, especially in secondary syphilis should not be less than 1,200,000 units (q.3.h. in 7½ days). Herxheimer reactions (mild fever and skin lesions) after the penicillin treatment of early syphilis were frequent but not serious.

The report also shows that penicillin had a favourable effect in early asymptomatic neurosyphilis, acute syphilitic meningitis, early syphilis treatment resistant to arsenic and bismuth, and in infantile congenital syphilis.

The same committee, with Stokes, also present an article about the action of penicillin on late syphilis and have planned to report at three-to-six month intervals further information on the progress of the patients with early syphilis treated with penicillin.

HARRY BOWER.

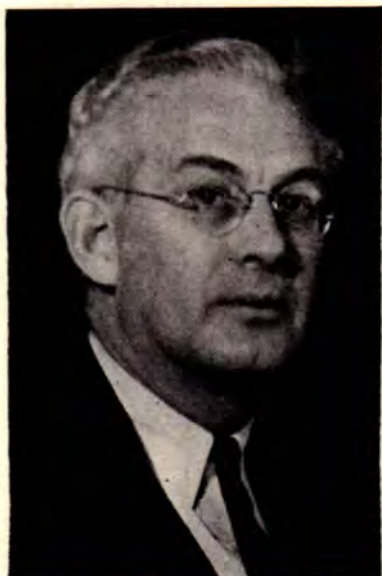
# Editorial

## THE MEDICAL ALUMNI LECTURESHIPS

**T**HE strength of a University is influenced to a large degree by the interest, good-will and support of its graduates. It was therefore in keeping with this principle that the University Alumni Committee made available to the Faculty of Medicine the life membership fees of medical members of the Alumni Association on their decease, as announced in March, 1945.

So that the moneys might be used to best advantage in the general interest of the student body, the active Faculty, and the Medical Alumni, the disposition of the money was left to the discretion of the President of the Hippocratic Society, the Director of the University Alumni Association, and the Dean of the Faculty of Medicine. Although there were many undertakings which were worthy of such support, it was considered that the greatest number would benefit through the establishment of a semi-annual Medical Alumni Lectureship, the lecturer to be appointed by the above-mentioned Committee. The Committee, in making this recommendation, took into consideration the many ways of influencing the medical thought of the students, staff and practising physicians and felt that, by making it possible to bring to the University outstanding men in the medical profession from other University centres, it would be fulfilling a specific need.

The first lecturer to be selected was Professor Jonathan C. Meakins, C.B.E., M.D., LL.D., Professor of Medicine, Director of the University Clinic, Physician-in-chief of the Royal Victoria Hospital, and Dean of the Faculty of Medicine, McGill University. The Lectureship was held during the third week of April.



J. C. MEAKINS, C.B.E., M.D., LL.D.

The London Academy of Medicine, ever working in close cooperation with the Faculty of Medicine, arranged their "Academy Day" in conjunction with the "Lectureship". Thus it was that Dr. Meakins took an active part in the Academy Day proceedings, discussing "Present Day Management of Acute Rheumatic Fever", and as guest speaker at the Academy dinner considered in a timely address the subject "Post-War Trends in Medicine".

As part of the "Lectureship", the students of the two final years, many internes and staff members were privileged to attend amphitheatre clinics at St. Joseph's and Victoria Hospitals, where Dr. Meakins discussed selected medical cases. Continuing his programme, Dr. Meakins spoke to the students, staff and visiting physicians on the rather contentious subject of "Penicillin, its Uses and Abuses". On the final day Dr. Meakins addressed specifically the medical students, speaking on "Medical Responsibilities in Practice".

Those who attended all or part of the "Lectureship" programme were stimulated by Dr. Meakins' presence, his knowledge and his words. To those who were denied the privilege of hearing him, and to those who did hear him and wish to reflect again on what he said, has now been given the privilege of reading the addresses which the first Medical Alumni Lecturer presented on that occasion.

The University of Western Ontario Medical Journal is an under-

graduate publication, operated and controlled by the Hippocratic Society through the undergraduate editor. The Society, realizing that a medium of publication was needed for the addresses given as part of the Medical Alumni Lectureship, has opened its journal for this purpose.

The interested action of the student body in revising their editorial policy to provide for the publication of the addresses of outstanding guest speakers at the Medical School is greatly appreciated.

—G. E. Hall, M.D., Ph.D., F.R.S.C.  
Dean of the Faculty of Medicine.



## THE MARCH OF MEDICINE IN WESTERN ONTARIO

*By*

E. SEABORN, M.D., F.A.S.C., LL.D.,  
UNIVERSITY OF WESTERN ONTARIO.

RYERSON PRESS, TORONTO, 1944, 386 pp. Illust. \$6.00.

Dr. Seaborn's book is exclusive in its field. This is understood when one considers the immense amount of energy, time and effort the author has put into the work. He has not only accumulated material from innumerable sources (as is shown by the extensive bibliography) and reorganized it into a living story but he has also preserved information which, but for him, would have been ultimately lost.

The history is opened by a brief yet thorough discussion of Indian Medicine which, we learn, was really an organized science and a classification of the known diseases—contrary to the popular conception of the old witch doctor. From here we are taken through the period of French Medicine, beginning with Cartier, up to the fall of Montcalm, which ushers in the English period in 1759.

The Practice of Medicine in those days was a haphazard organization as may be appreciated from the following advertisement:

"April 1, 1847.

Wanted—Student for Medical Profession, suitable young man, will meet with peculiar advantages and liberal terms. Apply to Dr. Turquand, Woodstock."

The history of Medicine in Western Ontario tells of the beginning of the Victoria Hospital and the Medical School in London. The Medical School has had a trying career, beginning with a staff composed of only a few general practitioners, none of whom was a specialist in any one field, and a totally inadequate building. It was this school which turned out the Honourable W. J. Roche.

The "Cuttin'-Up Place," as it was called, was a disreputable little cottage from which the passers-by often heard strange noises and groans. From here the school moved to the corner of York and Waterloo streets. This old building, which still stands, was the scene of many riotous student initiations. They are best described in Dr. Seaborn's own words, "that no one became a maniac was providential."

The medical school as it now stands was the next step. But this is not the last. The March of Medicine in Western Ontario has not been stopped and there are newer and greater things in store for the future.

For anyone interested in medicine or history, and especially for graduates of the University of Western Ontario, this book should be a "must".

—JOHN COLES

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### BABY DOCTOR

*By* ISAAC ABT

MCGRAW-HILL BOOK COMPANY, INC., 1944, 310 pp., \$2.50

One of the most interesting of the lighter books on medical history to come off the press recently is "Baby Doctor." This volume contains not only a well rounded summary of the development of one of medicine's relatively newer sciences, but also an autobiography of the life of the author. Dr. Abt, one of America's foremost paediatricians and recipient of many honours in medicine, has presented a book written in a most enjoyable manner. It is not too technical for the laity and yet not too simple and uninteresting for the physician and student.

Dr. Abt has been associated with paediatrics for over fifty years, being one of the pioneers in the specialty. Throughout this period of devotion to science, Dr. Abt has had many experiences from which he has tapped freely in the writing of his book. When reading the book, one cannot help but be impressed with the kindness and sincere interest which Dr. Abt has for the welfare of children.

Not only has he had many experiences but he has a keen sense of humor and the happy faculty of being able to express this in writing. The book is full of anecdotes. The following is an example:

"'Doctor', she said. 'I am afraid Milton has something wrong with his spine.'

'What makes you think that?' I asked.

A woman in the park told me so.'

At this point, I escorted her firmly to the door. 'Well, Mother,' I



said, 'if a woman in the park told you there was something wrong with his spine, there is certainly something the matter with it.'"

The reader will enjoy this book very much and it is recommended to anyone interested in lighter reading. Time will not be wasted and, what is more important, it will be spent in a pleasing way.

JOHN R. BARBER.

### CLINICAL PRACTICE IN INFECTIOUS DISEASES

By E. H. R. HARRIES, M.D., F.R.C.P., D.P.H.

and

M. MITMAN, M.D., M.R.C.P., D.P.H., D.M.R.E.

(555 pp., \$6.00. Second Edition. E. & S. Livingstone, Edinburgh, 1944.)

During recent years great advances in the knowledge of the prevention and treatment of disease have been made.

In this concise book, the authors have accumulated not only their own broad observations as clinicians, teachers and examiners, but also modern conceptions of "fever practice" as reflected by the work of others.

Preliminary chapters dealing with such topics as sources and modes of infection, resistance, allergy, general management, diet, rashes, laboratory aids and clinical tests provide an effective basis for the whole subject. The tabular method of outline is a proved popular method of presentation. A synopsis at the head of each chapter broadly introduces the subject matter.

The study of the diseases incorporates not only recent advances but covers the whole field without wearying the reader by a description of methods now discarded. First principles are emphasized and present theory and practice fully described.

To bring the practising physician up-to-date on this always important subject and as a foundation for the study of infectious diseases for the medical student, this book should prove invaluable.

—R. TRELEAVEN

### MARIHUANA PROBLEMS

By THE MAYOR'S COMMITTEE ON MARIHUANA, LANCASTER, PENN.,

(220 pp., \$2.50. Jacques Catell Press, 1944.)

"Marihuana Problems" is the report of a specially appointed group of scientific investigators who, at the request of the Mayor of New York and on the recommendation of the New York Academy of Medicine, set out to survey in a systematic manner all the aspects of marihuana smoking in New York City.

It is an important report, first of its kind to appear dealing with this particular subject. For that reason it would be presumptuous for any one critic to say whether or not the actual facts presented and the conclusions drawn therefrom are accurate and warranted. However, the association of the authors with such a distinguished body as the New York Academy of Medicine ensures that the report is authoritative.

In its 220 pages, the book deals thoroughly with all aspects of the marihuana problem,—sociological, clinical and pharmacological. Each chapter presents at its beginning the specific questions to be answered under the chapter heading. For example under "Sociological Aspects":

- “1. To what extent is marihuana used?
2. What is the method of retail distribution?
3. What is the general attitude of the marihuana smoker toward society and the use of the drug?
4. What is the relationship between marihuana and crime?
5. What is the relationship between marihuana and eroticism?
6. What is the relationship between marihuana and juvenile delinquency?”

Then the method of investigation is outlined, the results are presented, conclusions drawn and finally the chapter is summarized briefly. Where necessary or convenient, results are also arranged in tabular form.

Some of the conclusions regarding the clinical and sociological aspects are very startling and place the drug and its users in an entirely new light. The section on pharmacology is particularly scientific and parts of it would be understood only by those whose work concerns pharmacology and biochemistry. This latter section is the result of collaborative work of three laboratories—the pharmacological laboratory at Cornell Medical School, the Noyes Laboratory at University of Illinois, and the Laboratory of the Bureau of Narcotics, Washington, D.C.

The report may be of some interest to the general practitioner, but it will be of real value to sociologists, criminologists and others who have any contact with marihuana smokers. The pharmacological study will, of course, be a full reference for anyone desiring information about the drug.

—STEWART LOTT

**ATLAS OF THE BLOOD IN CHILDREN***By* K. D. BLACKFARR, L. K. DIAMOND,

and

C. M. LEISTER, NEW YORK.

(320 pp., \$12.00. The Commonwealth Fund, 1944.)

To understand the processes and the secondary changes of blood diseases, it is necessary to form a mental image, first of the normal, and then of the pathological pictures of the blood cells. To endeavour to transpose these pictures from verbal descriptions is not only laborious but misleading. Hence a book such as this Atlas is an essential part of a medical library.

The text of the Atlas begins with a thorough and adequate description of the normal cells and a discussion of their origin and morphology. Special attention is paid to the essential differences between the early and adult blood.

Each type of anaemia is described and discussed with regard to etiology, symptoms and signs, laboratory data, diagnosis, course and prognosis, and treatment. To further drive home the essentials of every condition, a typical case record is given for each disease.

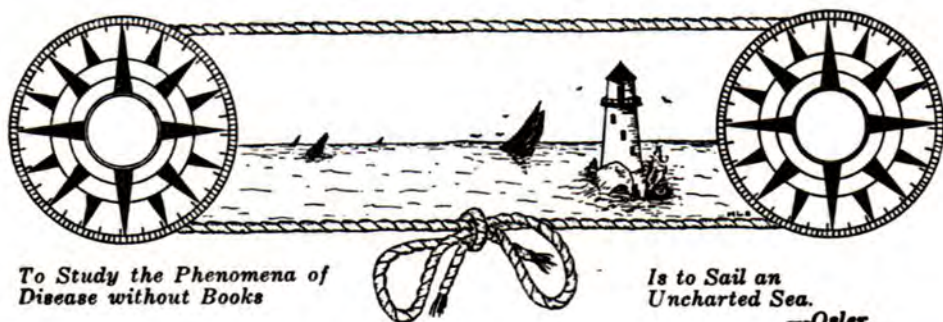
The leukocytes in disease are dealt with in a similar manner. Under this heading we find descriptions of leukocytosis, leukopenia, neutrophilic leukocytosis, neutropenia, etc.

The leukemias and variations in the platelets are dealt with in separate chapters.

In addition to all the above descriptions, the book contains seventy coloured plates of the blood pictures in the various diseases. The Atlas is written in a style easily read and is organized in such a manner that the plates and descriptions are easily correlated with the text.

The value of this book is not limited to paediatricians since there are essentially no blood disorders found in adults which are not found in children with the exception perhaps of Addisonian Pernicious Anaemia. Hence this Atlas should not be regarded as being of interest only to those specializing in the care of children; on the contrary, it is of vital importance to every physician who practises the art of medicine.

—C. A. WOOLEVER.



*To Study the Phenomena of  
Disease without Books*

*Is to Sail an  
Uncharted Sea.  
—Osler.*

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- Ashton: Doctor Serocold. 1930.
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