OUR PRESENT CONCEPTION OF THE RELATIONSHIP OF YAWS TO SYPHILIS.

by

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Experimental evidence (Schoebl & Hasselmann) shows that the regional lymphatic glands in yaws-infected monkeys harbour viable treponemata only, while the frambesia lesion is still active. Once the yaws lesion is healed, either spontaneously or due to medicamental therapy, no further infestation could be detected. The lymph nodes transplanted into other monkeys ceased to produce yaws lesions. Thus, the ECTODERMOTROPISM of the Treponemata of yaws becomes clearly apparent. Though Treponema pertenue may be carried from a strong, active yaws lesion unto the regional lymphatic filter, it is not capable of multiplying or surviving for a long time in mesodermal tissue.

The treponemata of syphilis, on the other hand, are permanently and always demonstrable in the lymphatic glands of syphilis-infected animals (Brown & Pierce). Thus, treponema pallidum shows preference for mesodermal layers.

This experimentum crucis is of basic importance for the understanding of the two treponematous diseases. It clearly demonstrates the different organotropism of the two treponemata which, otherwise, are indistinguishable by morphological, staining and cultural methods. The evaluation of clinical data and facts as well as the interpretation of immunologic phenomena are possible only by the full appreciation of the behaviour of the respective treponemata in regard to the body tissue of the affected host. Keeping this in mind, we put yaws and syphilis in the group of treponematous diseases considering the resemblance.
of some of the cutaneous manifestations, the identical serological phenomena, the efficacy of certain drugs and the similarity of the respective causative agents.

The histo-pathology of any treponematous lesion consists of an inflammation. The initial, primary lesion, both in yaws as well as in syphilis, is a PAPULAE. Consequent to the ECTODERMO-TROPIC proclivity of Treponema pertenue, the treponemata of yaws are found mainly in the rete Malpighi. The histo-pathological changes of the framboesical, initial efflorescence show the characteristic acanthosis with enormous downgrowth of the rete pegs and, sometimes, spongiosis, parakeratosis and hyperkeratosis to a lesser degree. The cutis proper responds but slightly to the infection. The blood vessels themselves are never affected during the early as well as the generalized period of yaws. Their intima is intact and does not show any cellular infiltration nor hypertrophy or proliferation of endothelial cells to any appreciable extent. There is, however, a loose cellular infiltration in the stratum papillare and reticulare composed of mostly plasma cells with but few eosinophils, round cells and fibroblasts, respectively. Giant cells are generally not met with, and there is no sharp outline of the cellular infiltration.

This reaction on the part of the corium leads to extensive emigration of leucocytes into the epidermal layers, sometimes to the extent of forming minute, intradermal, miliary abscesses.

The dermatological, clinical appearance of these changes is a soft papilloma, slightly raised above the surface of the surrounding skin. The stratum corneum, stratum lucidum and stratum granulosum are soon lost, and oozing out of serum tends to the formation of a non-adherent, amber-coloured crust. There is lack of induration. No tendency towards the formation of an ulcer exists as there is no obliteration of the blood vessels.

One outstanding feature of the initial, framboesical lesion is its healing mechanism. The initial, primary papilloma may last until the appearance of a metastatic crop of generalized polypapillomata. Healing of the initial, papillomatosus lesion may begin in the centre, which flattens, and soon becomes covered with thin, dry scabs. At the same time, spreading of the lesion and progressing on the periphery may set in, simultaneously leading to a circinuted or semilunar configuration. At any time of this process, if stationary or migrating local initial yaws lesion, periodic exacerbations may occur, leading eventually to nodular and lupus-like efflorescences, very unlike the initial papillomatos lesions. Areas of scarred, thin, depigmented and hyperpigmented skin interrupted by nodules and ulcerations may result.
As in yaws, so in syphilis is the primary lesion a papule too. Consequent to the MESODERMOTROPISM of Treponema pallidum, the Treponema of syphilis are met with predominantly in the mesodermal layers, namely in the corium and subcutis. Here, they produce early changes of the capillary blood vessels in the form of cellular infiltration of the intima, hypertrophy, and proliferation of the endothelial cells to such an extent as to cause narrowing and even obliteration of the vessels' lumina. Consequently, the blood circulation in the affected area is greatly and early altered. Coagulation necrosis follows soon, and the clinical picture of a sharply-punched-out ulcer results, otherwise called chancre.

Other histopathological changes are not different enough to be of value for differential diagnosis, though in syphilis giant cells are generally present to a certain extent. The nodules of infiltration are more sharply outlined, and with lesser preponderance of plasma cells than usual in the primary framboesiac lesion.

The typical efflorescences of framboesia tropica during the metastatic generalisation period are both, histologically as well as clinically, identical with the primary lesion, namely a plasmaeytoma and soft papilloma. Though the typical crop of polypapillomata during the early metastatic generalisation stage shows an almost monotonous uniformity, other framboesides during the generalized, metastatic period may be of a quite different and multiform character. Experimental evidence in humans and monkeys, however, has established their framboesiac etiology. Due to the protean appearance of these framboesides, unlike typical polypapillomata, it seems feasible to apply such descriptive designations in regard to their morphology as are generally used in dermatological terminology, namely “ring-worm yaws,” “framboesiderma manu,” “psoriasis framboesica,” “lichen framboesicicus,” and “keratosis pilaris framboesica,” respectively.

Whereas the early polypapillomatous lesions of experimental yaws are evanescent, the atypical framboesides are more persistent, and occur somewhat later during the metastatic generalisation period. This is due, apparently, to the onset already of a partial immunity as shown by the resistance to superinfection soon after the onset of these protean framboesides.

It would be absurd to call this stage of metastatic, generalized yaws “secondary,” as this term in syphilology implies a certain sequence of lesions and successive stages. In yaws, however, the primary, framboesial lesion may last not only to the metastatic stage, but it may change even into a late, ulcerative form with none or only a modified metastatic crop of generalized framboesides having occurred or still being present. It is not yet clear, under what conditions this initial, primary yaws lesion shows, after a long persistence, this ten-
tendency to form late ulcerations. It seems that the development of a high homologous immunity is retarded in these cases. The com-}
parative frequency of such a condition is evidenced, however, by the numerous records of "Mother-Yaw," which, at least, shows the persistency of a primary, initial yaws lesion, and which is often accompanied by tendency to ulcer formation of the central "mother yaw" as well as the peripheral lesions. Again would it be absurd to call these late, framboesial ulcerations "tertiary," as it might be that the supposed to be "tertiary ulcer" is de facto still a "primary" one. Furthermore, supposed-to-be "secondary" papillomata, though slightly modified, are present at the same time besides this "primary-tertiary" ulcer. Which all shows that in yaws the successive stages are most liable to overlap each other without any clear-cut line of sequence, con-trary to syphilis.

In syphilis, the variety of syphilides during the secondary stage is well known. All are distinctly differing from a metastatic luetic chancre. There is no phase in syphilis where a metastatic lesion is identical with the initial, primary lesion in regard to the morphological appearance and the healing tendency. The primary luetic lesion is running the well defined course: papule, sclerosis, chancre, healing with scar formation, though healing may commence at any of the stages. In Framboesia tropica, be it repeated, the initial lesion has a wide range of protean mutability.

The LATE SKIN MANIFESTATIONS IN YAWS as fungoid, ulcerative lesions may become impossible to differentiate from tuber-
serpiginous lesions and gummata of syphilis. On the legs, late yaws ulcerations may, clinically, be indistinguishable from so-called "tropical ulcer," and, doubtless, among these latter a number of framboesial gummata may be hidden. Other late framboetic ulcers resemble Mycetoma pedis (Madura foot). Paronychia of toes and fingers have been also observed. During this late stage of framboesia tropica episodical exacerbations are frequently occurring, apparently showing an acute stage of allergy. As it has been stated before, the initial primary lesion of experimental yaws in monkeys seldom heals, quite contrary to the regular healing of syphilitic chancre. But the "Mother-Yaw" has an outspoken tendency to persist, to wander and migrate, and to undergo various morphological changes—apparently caused by changes of allergic condition—as to result in lupus-like lesions with ulcerative and nodular appearance. As these latter forms of ulcerative yaws lesions are very common among natives, it is only logical to assume that they, too, have developed from persistent "mother yaw" as experimentally so frequently observed. It might be appropriate, however, in this connection to again recall that the initial, primary yaws lesion is rapidly and completely healing once a heavy crop of metastatic
polypapillomata takes place. This will produce such a high immunity that late, ulcerative lesions are never observed.

The presence of an allergic stage seems likewise to be necessary for the mutilating destruction of the soft parts of the nose, septum nasi and even parts of the palate, otherwise known as GANGOSA or RHINOPHARYNGITIS MUTILANS. In the course of his experiments, Schoebl succeeded in producing gangosa in monkeys thereby proving its framboesial etiology. He observed the initial, local yaws lesion descending from the eyebrows over the nose and down to the nostrils, where it lingered for some time after the original site of the lesion had healed. When, at this stage, superinfection was performed on the eyebrow, a deep, ulcerative lesion developed at the site of superinfection, and the residual lesion around the nostril exacerbated, spreading onto the mucous membrane proper, resulting in the vast destruction so characteristic for gangosa, as you will see later on, on the lantern slides. Whereas Treponema pertenue ordinarily does not gain a foothold on mucous membranes proper—contrary to the treponemata of syphilis—the close affiliation of the mucous membranes of the face orifices to the outer skin explains this condition in gangosa. The close relationship of outer skin and mucosa of mouth and nose is revealed by the embryonic genesis of the face contours with the upward growth of the mandibular arch, nasal and maxillar processes around the stomodeum, where the latter's ectodermal lining comes, temporarily, into contact with the ectoderm of the fore-gut pressing aside the intervening mesoderm.

KERATODERMA PLANTARE ET PALMARE which, dermatologically, should be better termed ECCEMA TYLOTICUM FRAMBOESICUM PLANTARE ET PALMARE, is another late manifestation typical of yaws infection and very common among natives. The framboesial pathogenesis rests not only on clinical grounds but on experimental evidence as well. Eccema typloticum framboesicum is a late manifestation, comparable as well with the obstinate papulosquamous syphiloderm on palms and soles as, perhaps, even with metasyphilitic conditions such as tabes and general paresis. Comparison with the former may be made regarding the appearance of eccema typloticum framboesicum at a time when metastatic framboesides on palms and soles are still present, though these latter, framboesiderma manu et plantae, do not constitute the forerunners of Keratoderma. On the other hand, Eccema typloticum framboesicum with the enormous hyperkeratosis, marked parakeratosis and acanthosis, respectively, and but slight inflammation in the corium, has more the characteristics of an allergic condition manifesting itself in a specific tissue site, wherefore, comparison with the phenomena in metasyphilitic conditions may be well drawn.
Bone affections, other than of the palate which takes place per continuatatem, as just described, have been mentioned by some observers. As experimental evidence has failed, so far, to show bone lesions in experimental yaws, it is highly probable that the described pictures are of a different etiology, e.g. leprosy. However, even though bone tissues are of mesodermal origin, periostitis and osteoporosis may have been caused by continuity only, when a local, initial mother-yaw was present. As long as experimental evidence is still lacking, the possibility of framboesial osteitis cannot be reasonably accepted.

The serology of yaws and syphilis are identical so far as the blood serum is concerned. The cerebrospinal fluid, on the other hand, never shows any pathology in yaws, proving again that the central nervous system is never affected.

Yaws, doubtless, is a contagious disease though the modus of infection is yet unknown. Contrary to syphilis, framboesia tropica is but very rarely transmitted through sexual intercourse.

If immunity is understood as that condition, where no disease symptoms of any kind develop after inoculation with a virus known otherwise to produce such disease in question as a matter of course, then immunity develops and exists in treponematous diseases. The mechanism of immunity in treponematous infections is that of any anti-aggressive immunity as found in certain bacteriological diseases (symptomatic anthrax caused by Bac. sarcocephylawos Kitt). This means that a scale of immunity exists ranging from full susceptibility with unlimited multiplication of treponemata, to low grade resistance with restriction of the propagation of treponemata, and, finally, to full immunity where the propagation of the parasites is completely suppressed and where they die out after their life-time expires. Thus, of course, immunity does not stipulate that the parasites are killed immediately after inoculation or superinfection, respectively. Just as in bacterial infections, as typhoid fever or diphtheria, immunity is not understood to mean that the respective bacilli have disappeared ipso facto from the body, once immunity has developed.

Whereas in syphilis immunity sets in very early, as well known, immunity in yaws does not develop before 6 months after infection. Likewise, cross immunity develops much later than the homologous immunity sets in. If yaws infected monkeys are tested about 9 to 10 months after the infection by (super-) inoculation with syphilis, no lesion develops nor is treponema pallidum encountered in the regional lymph glands. Cross-immunity, therefore, is fully developed at this time in all three embryonic layers.

In testing experimentally the phenomena of immunity in treponematous diseases it has been brought to light that the lack of response of any clinical lesion, i.e. resistance to infection, is indepen-
sent of the healing of lesions and vice versa. This explains why in one instance all lesions may completely disappear and yet super-infection will be followed by the appearance of new lesions, or, on the other hand, superinfection will not produce any lesion at all, though the old lesion may persist.

The experimental proof that cross-immunity exists between syphilis and yaws, may enlighten certain problems of the epidemiology of the two treponematoses. It is well known, that in yaws endemic countries of the tropics syphilis is not very common. A certain stage of cross immunity against syphilis may well have been developed among the natives, who mostly had framboesia in childhood. On the other hand, be it noted, syphilis may well occur in natives. However, the notorious infrequency with which syphilis is found in natives of tropical countries, where otherwise gonorrhoea and yaws are rampant, would be inexplicable except by the existence of cross immunity as shown by experimental evidence. Yaws, affecting the majority of natives in early childhood, may convey such a heterologous immunity against syphilis as to account for the arbitrary low records of primary luetic chancre, visceral lues, syphilis of the central nervous system and congenital syphilis, respectively.

Framboesia tropica is limited to countries with a tropical climate, contrary to syphilis. This may be due to the inability of Treponema pertenue to survive at low temperature outside of the body for any considerable time, whereas Treponema pallidum is far more resistant. It accounts probably, for the peculiar retreat of yaws to the warm and moist mucocutaneous junctions (anus and genitalia) in higher altitudes (Northern Luzon, Assam). Like Leprosy, so has yaws a rather spotty distribution. It is difficult to understand why in villages with identical conditions in regard to geology, climate, sociology, and food habits, respectively, such arbitrary incidence of yaws still exists.

The assertion has been made by some physicians working for a short time in Haiti that, over there, framboesia tropica affects the viscera as well as the central nervous system. The results of the subsequent investigations by such an authority as Howard Fox, however, represent an utter negation of that assertion, confirming that yaws in Haiti does not differ from yaws in any other part of the world.

Experimental evidence shows that the Philippine monkey (CYNOMOLHUS PHILIPPINESIS) responds in 100% with the appearance of typical initial yaws lesion, whereas rabbits do not seem to give uniform results. On the other hand, syphilitic infection of the Philippine monkey results mostly in a feeble syphilitic lesion, though positive seroreaction follows, and viable Treponema pallidum is found in the regional lymphatic glands. For studying framboesia tropica and
for differential diagnosis of questionable lesions by transplanting them into suitable animals, thereby reducing them to an initial, easy recognizable lesion, the monkey rather than the rabbit is of greater value.

There remain, still, many unsolved problems in regard to the two maladies and even in regard to their clinical differential diagnosis in obscure cases of late, ulcerative forms aside from the easy recognizable differentiation. But we humbly hope that our experimental evidence supplemented by clinical research will definitely do away with the difficulty that some have in admitting yaws to be a disease sui generis. This difficulty does not exist for the tropical practitioner, whose daily experience of framboesia tropica lets him readily differentiate it from syphilis, the late, ulcerative lesions excepted. The majority of those who claim that the two diseases are the same, must have been either mislead by descriptions only, or at most seen few, isolated cases of yaws without the possibility of careful observation and thorough study. Furthermore, those holding that yaws and syphilis are identical cannot reasonably specify what stage or what form of syphilis they claim yaws to be, nor under what conditions or why syphilis and yaws occur not only among the natives of one and the same tropical country but are even coexistent in the same individual.

The notorious differences in regard to morphology of the lesions, histo-pathology, general pathology, and immunology—all of which are explained by the different ORGANOTROPISM of the respective treponemata, together with epidemiological phenomena, demand at once to consider Yaws and Syphilis as fundamentally different, clear-cut disease entities, though both belong to the group of Treponematoses, —just as Tuberculosis and Leprosy belong to one group, too.
**THE ANTIGENIC RELATIONSHIP BETWEEN BACILLUS TYPHOSUS AND BACILLUS DYSENTERIAE FLEXNER.**

by

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It must be a common observation that B. dysenteriae Flexner is often agglutinated by B. typhosus agglutinating serum. In fact many commercial agglutinating sera prepared against B. typhosus are stated by the manufacturers to have an action on B. dysenteriae Flexner. For example, several samples of Burroughs Wellcome typhosus agglutinating sera which have recently been examined are stated to agglutinate their specific organism (B. typhosus) to a titre of 1 in 3,200 and to agglutinate the Flexner bacillus at 1 in 400.

Formerly such a phenomenon would have been described as co-agglutination and left at that. In these days however, when it is sought to explain such relationship between different bacterial species according to their antigenic structure, it is desirable to analyse the question in greater detail. Moreover, in the light of recent knowledge, the subject presents an aspect of practical importance in connection with the identification of organisms. The sugar reactions of B. typhosus and of B. dysenteriae Flexner are of course similar, i.e. they both produce acid in glucose, maltose and mannite. The Flexner bacillus is non-motile, whereas the typhoid bacillus is normally motile, and in the old text-books is so described. Now however, that it is recognised that non-motile "O" forms of B. typhosis exist, the distinction between the two organisms cannot so readily be made. Isolating an organism from a stool, the investigator may be deceived into labelling a dysentery organism as a non-motile typhoid bacillus unless he bears in mind the necessity of its agglutinating to a relative high titre with its homologous agglutinating serum. The type of agglutination furthermore can afford him no help. For while the normal typhoid bacillus agglutinates in a floccular manner, its "O" variant agglutinates in small granules just as the dysentery bacilli do.

Reference to the available literature yields but a scanty information on this point. Bruce White (1926 and 1928) refers to the non-specific agglutination of rough races of the Flexner groups, and suggests that there may be a phylogenetic relationship between B. typhosus and the Flexner races. Andrews and Inman (1919) state that sera prepared against the various Flexner races failed to agglutinate formalinized broth suspensions of B. typhosus.

Lentz (1913) states that the sera of patients with Flexner-Y dysentery agglutinate B. typhosus and B. paratyphosus. Lowenthal

* The experiments described in this paper were performed in the Public Health Laboratories, Cairo.
and Bertkan refer to the non specific agglutination of B. Flexner—Y by the sera of pregnant women.

The present small series of experiments represent a preliminary attempt to explain the reason of this agglutinogenic relationship between the two species of organisms. The results are summarised in the accompanying tables. The agglutination reactions were in all cases observed in Dreyer's tubules, after four hours in the water-bath.
The dilutions made by the drop method, commencing at 1 in 25; dilutions lower than this were not observed. In some cases the bacterial suspensions were formalinized (0.1%) broth cultures, in others they were made by emulsifying agar slope cultures in 0.5% carbol-saline. The titre and character of the agglutination—floccular or granular—is indicated in the usual manner.

Table I indicates the action on various dysentery strains of typhoid agglutinating sera prepared against normal motile organisms and against the smooth "o 901" strain of Felix. This strain was procured from the National Collection of Type Cultures. It is apparent that the Flexner Y strains are readily agglutinated by the typhoid sera to a titre of about one tenth of that for their homologous somatic agglutinogens.

The other strains of Flexner bacilli were not agglutinated so readily. Flexner—Y was therefore used for the remaining experiments. It will be seen that a saline suspension of the Hiss and Russel strain was prepared from growths that had been extracted with chloroform and alcohol according to Bruce White's technique (1928). Such treatment according to him eliminates any tendency to non-specific agglutination. It may be stated that this suspension remained stable after boiling, thereby demonstrating its freedom from "roughness." All the strains of typhoid and dysentery bacilli used in these experiments were subjected to this test, and none of them appeared to be "rough."

**TABLE II.**

<table>
<thead>
<tr>
<th>Bacteria agglutinated</th>
<th>B. dys. Flexner Y—Agglutinating serum</th>
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<tbody>
<tr>
<td></td>
<td>Hiss and Russell</td>
</tr>
<tr>
<td>B. dysenteriae Flexner Y</td>
<td></td>
</tr>
<tr>
<td>(Oxford)</td>
<td>12,500 G</td>
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<tr>
<td>B. dysenteriae Flexner Y</td>
<td></td>
</tr>
<tr>
<td>(Hiss and Russell)</td>
<td>2,500 G</td>
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<tr>
<td>B. typhosus Rawlings</td>
<td></td>
</tr>
<tr>
<td>(carbol-saline)</td>
<td>250 G</td>
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<tr>
<td>B. typhosus Rawlings</td>
<td></td>
</tr>
<tr>
<td>(formalinized broth)</td>
<td>500 G</td>
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<tr>
<td>B. typhosus o 901</td>
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<td></td>
<td>500 G</td>
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<tr>
<td>Bacteria Agglutinated</td>
<td>B. typhosus serum (Burroughs and Wellcome) absorbed with:</td>
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<td>-----------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>unabsorbed</td>
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<tr>
<td>B. typhosus Rawlings (carbol-saline suspension)</td>
<td>5,000 F</td>
</tr>
<tr>
<td>B. typhosus o 901 (carbol-saline suspension)</td>
<td>2,500 G</td>
</tr>
<tr>
<td>B. dysenteriae Flexner (Hiss and Russell)</td>
<td>250 G</td>
</tr>
<tr>
<td>B. dysenteriae Flexner (Oxford)</td>
<td>250 G</td>
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</tbody>
</table>
Table II shows the effect of agglutinating serum prepared against this strain of Flexner—Y on suspensions of B. typhisus. Standard Oxford Y serum which was of a much lower titre for its own organism failed to agglutinate the typhoid suspensions at 1 in 25.

Table III gives the results of absorption experiments, in each case total absorption was aimed at. heavy doses of absorbing organisms were used, equivalent to thirty agar plates for each cubic centimetre of agglutinating serum.

The result of absorbing typhosus serum with somatic typhosus antigen (o 901) proves that the relationship between Flexner and typhoid organisations is concerned solely with the somatic antigen.

The remaining experiments demonstrate that Flexner (somatic) antigen is incapable of absorbing typhosus agglutinin, and that typhosus somatic antigen cannot absorb Flexner agglutinin.

In the case of B. dysenteric Flexner it presupposes that the factor is additional to the normal specific combination of elements which enter into its antigenic spectrum.

SUMMARY.

(1) It has been shown that typhoid agglutinating serum agglutinates B. dysentery Flexner Y to about one tenth of its titre, and that high titre Flexner Y agglutinating serum will similarly bring about a granular agglutination of B. typhosus.

(2) The agglutinin in typhoid serum for B. dysenteric Flexner has been shown to be associated with the somatic or "O" factor.

(3) Cross absorption experiments demonstrated that this agglutinogenic factor common to B. typhosus and B. dysenteric Flexner Y is additional to and separate from the specific homologous agglutinogens.

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Schematic representation of probable relationship between B. typhosus and B. dysenteriae Flexner.
A DISCUSSION ON ACUTE EMPYEMA THORACIS AND ITS TREATMENT.

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I believe that the common complaint of the profession is that far too many papers have been written, read and printed but quite a number of them contain very little in the way of facts. As a result, when one desires to study a certain subject he has to go through large numbers of papers before he could get any clear idea of it. The reading of this paper with nothing original to claim, therefore, has very little justification except, perhaps, that students of medicine who, owing to the pressure of their examinations, cannot afford to plunge themselves into the vast literature of the medical science, might like to hear the summary of a certain subject in order to give themselves a little stimulation. Personally, I owe the Professor of Surgery of the Hong Kong University an apology for reading this paper in his absence. As you know, although working single-handed at most of the times, it is he who has not spared any energy to bring the standard of the Surgical Unit of this University in line with other leading teaching centres. It is plain that whatever comments I might make, the credible side goes to him and blemishes are due to my misapprehensions of facts.

Empyema thoracis is a very complicated subject, owing to the many different factors which come to play in its etiology, the great variations in its clinical aspects and the differences of opinion in its treatment. As this is meant to be a short lecture I would endeavour to discuss the most important types only. Instead of calling "Empyema" a disease it is perhaps better to consider the condition as a complication accompanying or following some other diseases. The disease which most commonly causes the presence of pus in the pleural cavity is found to be pneumonia either of the lobular or of the lobar type. Others which I do not wish to discuss much in this paper include lung affections due to injury and aspiration of foreign bodies, extension of affection of the neighbouring organs, septicamic conditions and tuberculous disease.

On the bacteriological side Fraser and Heuer have pointed out that pneumococcus, streptococcus, influenza bacillus and staphylococcus can cause pneumonia and empyema, whilst bacillus tuberculosis, bacillus coli communis and even anaerobes are found sometimes in empyemas following other affections. With the exception of cases due to pneumococcal and streptococcal infections, very little data has been worked out, this being due to the rarity of cases caused by the other organisms mentioned above. The tuberculous type of empyema either pure or mixed belongs to another category, but empyemas following other
diseases have little surgical interest and they can be treated on the same lines as those following pneumonias. Encysted and Interlobar empyemas are more or less like lung abscess and they are omitted here.

Historically speaking, I would advise those interested to read Schochet's paper published in 1923, which gave a vivid account of this disease. I shall content myself with stating that modern work on empyema was heralded by two discoveries near the end of the last century. The first is due to the work of Arbuthnot Lane in 1882. He practised primary resection of a rib to drain empyema. The second is due to the work of Bulau in 1890, who practised insertion of a catheter into the pleural cavity through an intercostal space and established continuous closed drainage. It was only towards the end of the Great War that the first piece of great work on this disease along modern lines was conducted by Evert Graham and his colleagues in the empyema commission in the camps of Lee Va. It was by them that empyemas caused by streptococcal infection and pneumococcal infection were seriously separated. The physiology of the pleural cavity and the chest was then better understood and definite data as regards pneumothorax especially its effects on vital capacity was established. It was found that the previous belief of the dangers of an open pneumothorax was exaggerated, whereas closed pneumothorax had little to do with patient's respiratory function and intrapleural pressure. Stress was laid on the result of late operation in all streptococcal cases as the developement of empyema occurred generally before the resolution of the pneumonic process and the reduction of mortality treated thus was found to be considerable. I would call your attention that in those days empyemas were commonly treated by the practice of thoracotomy with or without rib resection as a routine. Further, a general anaesthetic was usually administered and open drainage was the timely favoured procedure. The drawback of this line of treatment for streptococcal empyema is obvious as the reduction of vital capacity and shock produced does more harm than good that is gained by letting out pus. Hence it was then unanimously favoured that operations for streptococcal empyema should not be performed until frank pus and adhesions had formed. This led Graham to the conclusion that "practically the decision as to when to operate is not difficult and in all probability a difference of few days on one side or the other is not of very great importance. A convenient criterion is the presence of frank pus, for almost by the time the exudate has changed from its initial serofibrinous nature to a distinct purulent quality, the pneumonic involvement has practically cleared up, the vital capacity is probably increased, the patient's resistance is better, abscess is walled off and the general condition has improved as shown by diminishing of fever, absence of delirium and a decrease in the rate of the pulse and respirations." However, a fair criticism of the above statement was
ACUTE EMPYEMA THORACIS.

PNEUMOCOCAL.
FROM LATE CHILDHOOD TO ADULT LIFE.
META-PNEUMONIC FORM.
FOLLOW LOBAR PNEUMONIA.
MUCH ADHESION.
EFFUSIONS:
FIBRINOUS
PURULENT.
MAY BE (1) DIFFUSE.
(2) ENCRYPTED.
(3) INTERLOBULAR.
PNEUMONIA APPARENTLY RESOLVED, THEN BECOMES WORSE AGAIN.
CHEST SIGNS.
MORE MARKED.
SECONDARY AFFECTION OF OTHER ORGANS—RARE.
DEATH RATE LOW.

STREPTOCOCAL.
EARLY CHILDHOOD.
SYN-PNEUMONIC FORM.
ACCOMPANIES LOBAR PNEUMONIA.
LITTLE ADHESION.
EFFUSIONS:
IN CHILDHOOD PURULENT.
PNEUMONIC CONDITION GRADUALLY BECOMES WORSE. NO SIGN OF INTERMITTENCY.
CHEST SIGNS.
DISTURBED BY TOXICITY (ESPECIALLY IN CHILDHOOD).
SECONDARY AFFECTION OF OTHER ORGANS—COMMON.
1. MENINGES.
2. PERICARDIUM.
3. PERITONEUM.
4. JOINTS.
5. MIDDLE EAR.
DEATH RATE.
IN ADULTS—HIGH.

STAPHYLOCOCCAL.
B. INFLUENZAE.
B. COLICOMMUN.
ANAEROBES.
ALL AGES.
VERY LITTLE DATA IS AVAILABLE.

PNEUMOCOCAL.
B. INFLUENZAE.
B. COLICOMMUN.
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made by Morriston Davies in an article which appeared in the British Medical Journal, 1931, in which the author said "if however, the intensely toxic fluid swarming with streptococi is left pent up in the chest there is the probability that the patient will die from toxæmia, at least he will suffer from the compression effect of the fluid." It has to be mentioned that Graham too, realised this point and he practised partial removal of the fluid in the early stages by repeated aspirations.

In 1923, Cameron and Osman of Guy's Hospital had put a second instalment to our knowledge of Acute Empyema Thoracis, especially in early childhood. The terms "meta-pneumonic empyema" and "syn-pneumonic empyema" were introduced by them. These give quite different clinical pictures and prognosis. The first type is usually found in older children and it usually develops after the pneumonic process has resolved itself. Here the child is found to have apparently recovered from pneumonia but he becomes ill again with gradual rise of temperature and appearance of chest signs. In the latter type, the empyema develops as soon as pneumonic affection sets in or soon after pneumonia has developed. In this case, the convalescence of pneumonia seems to be prolonged and the child gets gradually worse with the disease showing no signs of intermittency. The part revealed by the postmortem findings is rather interesting. It shows that the meta-pneumonic empyema is usually associated with the lobar type of pneumonia, whereas the syn-pneumonic type is usually associated with the lobular type of pneumonia. The more acute affection is the lobular type, in which the lung changes are intensely acute and toxic, producing extensive patchy consolidation and even necrosis of the lining of the bronchi. Quite often coexisting meningitis, pericarditis, arthritis and peritonitis may be demonstrated which seldom happen in the lobar type. The age of the child has a very definite bearing on the disease. It is found that pneumonia caused by any organism in the first 2 years of life is mostly of the lobular type and the infants usually die of the affection if empyema has developed. After the age of three, a distinct pathological change takes place. The pneumonia of children is then usually of the lobar type and if followed by empyema at all, the process is usually found to be meta-pneumonia. The prognosis of the latter type was found to be very much better. A drop of mortality from the average of 65% in the first two years of life to less than 6% hereafter was noticed. Their statement was found to be true by subsequent observers and confirmed by statistics from various leading clinics, including Johns Hopkins University.
The work of Fraser on the intrapleural tension in syn-pneumonic and meta-pneumonic cases is worth mentioning. He found, as you will see in one of the accompanying pictures, that in syn-pneumonic cases the intrapleural tension varies greatly from a positive to a negative phase in each respiratory cycle which shows that the respiatory effort is greatly taxed. That the mediastinum is not fixed by any adhesion is also revealed by the positive and negative excursions during respiration. In meta-pneumonic cases, the intrapleural tension is always above zero instead of being always below zero, as in normal cases. In this case, it can only be assumed that strong adhesions must have formed, otherwise respiration would be impossible.

Since the annual meeting of the British Medical Association at Bath in 1925, the prevalent views as regards the etiology and pathology of empyemas have been greatly consolidated and compromised. But
it is rather surprising to find that of the various authorities present who expressed their views none was advocating closed suction drainage with great zeal. The work of the later years however has shown a tendency to the general adoption of this line of treatment (viz.:—Simple Closed Suction Drainage) at least as a preliminary measure. Of the various writers who recommended this line of treatment during the last six years, great differences in opinion as regards apparatus and technical details were noticed. However, there appeared in the British Medical Journal of 1931, a classical and open-minded paper written by H. Morrison Davies entitled "Remarks on Empyema Thoracis." In his paper, aspiration and perhaps with oxygen replacement was laid down as the first line of treatment. Closed suction drainage without rib resection should be tried if the above does not cure the disease. Failing both he would consider open operation by rib resection to be followed by closed suction drainage. Carrel Dakinisation was mentioned and was highly advocated. Diet of high calorific value was put down as essential. Although we cannot work ourselves into total agreement with him in this cline, I personally would say that his paper represents the consummation of a task which compromises the great differences of opinion as regards the treatment of acute empyemas on the modern lines.

It is not within my competency to discuss chest signs as it is often said that the carpenter or surgeon cannot recognise oegophony by stethoscope and skodnic resonance by percussion. However, it is easy to diagnose an empyema case which is well formed but in early cases, persons of such prominence as Hector Cameron and others do admit that the diagnosis is extremely difficult, owing to the fact that in the early stage, fluid cannot be differentiated from consolidation by physical examinations or by X-ray films with ease. Besides, as in the case of infants, the small size of the chest adds to the difficulty of physical examinations and paracentesis. Some time ago, it was reported in Johns Hopkins Hospital that 50% of their cases of empyema had been either not recognised early or improperly treated before admission. (Heuer) Rienhoff and Davison recorded incidences of as high as 25% of undiagnosed early cases, not to say the infants who died of fulminating pneumonia and empyema. The presence of co-existing complications such as meningitis, pericarditis, arthritis and peritonitis, has a great deal to do in increasing the difficulty of making an early diagnosis.

From the treatment point of view, it must be admitted that a number of infants contracting pneumonia and empyema must die not that the treatment is in any way defective, but because the disease tends to be generalised and also infants do not react well to any infective disease. The high death rate of empyema caused by streptococcus is really due to the virulence of the organism. In those cases that have survived, the medical man should not attribute too much credit to him-
self whilst the public should be made to realise that some of the diseases will prove fatal in spite of treatment. It is interesting and important to note that in these favourable cases treated, no matter whether aspiration or rib resection or continuous closed suction drainage is applied, the temperature comes right down. This dramatic happening has often led the medical attendant to think that the particular form of treatment he applies has been responsible for it. I only wish to emphasize that the criterion by which the value of any form of treatment is judged lies really, in the shortened period required for lung expansion and convalescence, as well as the decrease and disappearance of residual empyemas as afforded by that form of treatment. I have already mentioned that Arbuthnot Lane has devised and practised the operation of rib resection and open drainage for empyema. His method soon gained universal favour but the incidence of residual empyemas after this form of treatment has led people to doubt its value. Further, the danger of an open pneumothorax which reduces the vital capacity in an already distressed patient so seriously as to cause fatal results at times, has made people think that operative interference delayed till adhesions have well formed, would ultimately be better. The other method of closed suction drainage introduced by Bulau in 1890 has its initial drawbacks of not giving adequate drainage, especially in pneumococcal cases; hence though ideal, it has not gained much ground to induce people to adopt this method even as the first line of treating empyema. By the improvement of technique and apparatus and by the introduction of Carrel Dakinisation, this method has however gradually gained recognition and is now almost universally adopted. There are still authorities such as Hansen and Graham who repudiate the method of closed suction drainage, but argument can only go one way. If there are people who can treat a large series of cases with the simple closed suction drainage method without having to resort to open operation ultimately, the reason why others fail to do so cannot but be one of two causes. The first, which is not likely, may be that the cases they are treating belong to a different category, and the second is that they have not taken enough pains to follow up the simple method which sometimes is tedious.

In order to go into the question of treatment in detail, a few principles must necessarily be remembered. Empyema differs in no way from ordinary septic infection with abscess formation more than the fact that the site of the disease has very important bearings anatomically. Owing to the proximity of the pleural cavity to the heart, embarrassment of this organ readily follows if the pleural cavity is distended with fluid. As regards the function of the lung, it has to be remembered that a person must breathe in a minimum of 500 c.c. of air during each respiration and the vital capacity is about 3,700 c.c. In pneumonia, a large number of the alveoli of the lung are thrown out of
action, as a result of that the vital capacity is greatly reduced, especially so when the infection is streptococcal. Withal, the presence of pus if under tension will certainly cause toxæmia and the vicious circle thus established will cause death of the patient if treatment is not promptly applied. Hence, we maintain that empyema of any form should be regarded as a surgical emergency with due attention to the question of vital capacity and that operative procedure which may add to the gravity of the disease should be reduced to a minimum.

Graham has shown that the presence of a fairly large opening (even as much as 8 square inches) in the chest wall is compatible with life. This is due to the fact that though working against a large opening, the glottis of the person is still capable of allowing the inspiring of the 500 c.c. of tidal air required to preserve life, provided that the whole of the vital effort is brought into play. He has also shown that the respiratory distress caused by the presence of an opening in the chest wall can be removed almost entirely if the opening is now closed even if a certain amount of air has been left imprisoned in the pleural cavity. Hence, while it is possible to make a suitable hole for draining the pus from the pleural cavity without causing much distress to the patient, it would actually be better if the hole could be led to a closed space. Further work has shown that if a negative pressure can be created within the closed space the draining would be freer and at the same time the lung will expand much more readily than leaving the hole open. The negative pressure created has the further effect of decreasing the extra effort necessary to bring about the required respiratory function. It will thus be seen that if the above mentioned lines can be worked out in practice, this form of treatment would be the ideal one.

Let us first of all turn our attention to the consideration of the treatment of empyema by the simple closed suction drainage method in detail.

This consists of introducing a small rubber tube or preferably a size 8 or 10 self-retaining catheter into the pleural cavity usually at the level of the 7th intercostal space in the posterior axillary line through a trocar and cannula. Local anaesthetic is used as a routine measure. The open end of the catheter can be joined in the simplest form to a rubber tube which leads to a bottle containing mild antiseptic such as Dakin solution, placed below the patient's bed. On the other hand, the open end of the catheter can be joined to any suction apparatus designed. Negative pressure can be created by raising a column of water to the desired height.

It has been found by experience that in pneumococcal empyema there exists in the pleural cavity fibrinous clots before pus-formation takes place. Hence, thick masses of clots are usually found in such cases during treatment. This presents the greatest drawback to the
treatment by simple insertion of catheter as the clots frequently block the lumen of the catheter and thus render drainage ineffective. It is by the use of Dakin's solution which possesses a fibrolytic power as well as an antiseptic but non-irritant character, that this drawback of the simple method of treatment has been largely overcome. Nowadays, practically all the authorities treating empyemas in one way or another, especially those who treat empyema by simple closed method, have found this solution to be of the utmost value to them. With its fibrolytic effect, it thus has the effect of decorticating the imprisoned lung by the thick layer of fibrinous clot present and favours early expansion if adequate drainage is applied. Frequently the application of this solution demonstrates the presence of bronchial fistula which would otherwise be obscured by the formation of a fibrinous plug at its fistulous opening.

Another objection which has been raised against the simple closed method is that whilst the tissue reaction tends to work the inserted tube loose after a few days, leakage of air into the pleural cavity by inspiratory effort will take place. This apparent objection has been found in reality to be of not much importance. By sealing the tube to the chest wall with certain agents such as collodion, tincture benzion co., or rubber solution to be supplemented by adhesive plaster strips, the exclusion of air leakage can be effected practically without any trouble. Further, even if air should have leaked into the pleural cavity provided negative pressure can be maintained by an efficient apparatus the air would be either sucked out or absorbed in due time. As already mentioned before, a closed pneumothorax has very little evil effect but certainly beneficial at times to the general condition of the patient.

Another practical difficulty is to maintain a continuous negative pressure owing to the fact that the multiple connections which are required for this form of treatment have rendered gradual leakage of air through the connections possible especially during the times of irrigation by the nursing staff. However, the introduction of a reinforcing type of suction apparatus which enables the leak of air to be counteracted by the loss of water from the high bottles to the lower one has enabled a continuous negative pressure to be maintained. An apparatus based on the same principle has been designed by me which I have here to show you. The only advantage that can be claimed in my apparatus is mechanical efficiency and devices for prevention of accidents. I shall have to explain this to you at the end of the lecture.

The amount of negative pressure to be used has unfortunately not been standardised as no definite data can be obtained from any of the papers I have come across so far. I would attribute this to two reasons. One is perhaps that this form of treatment is just on its way
showing principle of reinforcing suction drainage

Reproduced from Diseases of Lung & Pleurae
Morriston Davis

... to development. I believe that a lot of the workers treating this disease shared the difficulties we have had for years as the apparatus quite often went out of order in the suction aspect of it, hence no definite data could be worked out. The second reason, which is of practical importance is that in case of pneumococcal empyema, the viscosity of the pus has made it desirable to have high negative pressure. On the other hand a streptococcal empyema requires just a little bit more than the negative pressure present in the pleural cavity during laboured respiration i.e. about 30 mm. of mercury. I would therefore, venture to make a practical suggestion that negative pressure applied should be at least corresponding to 30 mm. of mercury and if we express this in terms of water it should be just 40 cms. high but if drainage is found not to be free a higher negative pressure should be given. If
the apparatus as you see, is used the increase of negative pressure can be easily obtained by simply altering the relative height of the relaying bottles. No data so far has been given by anybody as regards the maximum negative pressure that can be used with safety. Here I would advise the application of high negative pressure with some precaution although personally I cannot see what harmful effect it could produce. If, for instance all the pus has been drained away, the tissue will simply fall in thereby blocking the drainage tube. Further it is quite obvious that when the pleural cavity is well evacuated of its pus, the suction required should not be much more than that just above the normal negative pressure in the chest. To prevent regurgitation of pus into the pleural cavity during coughing it is desirable to put the negative pressure just about 40 cms. of water. The recent advocacy of a method of tidal drainage by D. Hart of Baltimore, has the disadvantage of not being able to use high negative pressure and at the same time we are not quite convinced that the idea of tidal drainage could have actually taken place since it is noticed that during each inspiration very little perhaps just neglectful amount of fluid could actually be sucked into the pleural cavity through the inserted tube.

I would like to point out that administration of general anaesthetic through still used, has now fallen into general disfavour. It has been argued that in children the administration of general anaesthetic lessens the amount of struggling which sometimes happens in an ill-tempered child. But this little advantage cannot counterbalance the amount of ill-effect which follows the administration of general anaesthesia, such as its toxicity to the overtaxed heart and its effect of reducing vital capacity. Besides, in ill-tempered children the use of anaesthetic in the induction period may cause the same amount of struggle, if not more, as when local anaesthetic is used in the short procedure. The sitting position which we generally use has to a certain extent relieved the heart and lungs of strain during the operation, and is practically impossible if a general anaesthetic has to be administered.

It is plain that if empyema is treated along the above lines, no differentiation is really necessary as regards the age of the patient and the type of the infection present, streptococcal or pneumococcal. The disadvantages of open operations with rib resection and open drainage have been largely eliminated, general anaesthetic is unnecessary, and the procedure involved is not much more than an aspiration.

With the improvement of technique so far, it is more than satisfying to find that many people can treat a large series of cases of empyema by the simple closed suction drainage alone, though there are great variations in the technical details. The number of cases treated in the University Surgical Clinic is so small that we cannot give statistics in any form, but there has been no failure since this method was adopted.
I would just wish to discuss the other forms of treatment briefly.

(1) Aspiration with a Trocar and Cannula.—The disadvantage of aspiration is that the lumen of the small cannula used will not allow thick pus to go through and that it has to be repeated. Besides, a good number, perhaps the majority of the cases treated by simple repeated aspiration will have to end in a drainage of certain nature. It should not be forgotten, however, that in case of emergency, with no proper equipment available, a preliminary aspiration will often turn the table of prognosis.

(2) Open drainage is in general disfavour now so we need scarcely spend any more time over it.

(3) Thoracotomy with primary suture is perhaps abandoned generally as the wound in most of the cases will not heal.

(4) Fraser advocated a method of rib resection at a high level to clear out the pus in the pleural cavity together with introduction of a rubber tube through a separate stab wound below to establish closed suction drainage, whilst the upper wound is then entirely closed. This should be used as a reserve as a small portion of the empyema cases with bronchial fistula or encystment requires more than the simple closed suction method of treatment.

(5) Rib resection with specially designed apparatus for closed suction drainage through the incised wound has the practical difficulty of ensuring air-tightness, and at the same time necrosis of rib and cellulitis sometimes follow that operation. The drawback of rib resection is that it involves operative procedure and it is found to be scarcely necessary in most of the cases. In streptococcal cases of course none of the above methods is favoured by any authority as the first line of treatment.

Instead of Dakin Solution, substances, such as pepsin, gentian violet, etc., have been used to some extent but we have had no experience to enable us to comment upon them. The use of lipiodol to try to clear off the residual tract is to our mind, justifiable. Lately, I had a case of empyema with bronchial fistula. We injected some lipiodol near the end of the convalescence to demonstrate the extent of the bronchial fistula, and this case recovered without eventuality. Of course we cannot attribute too much of the case’s recovery to the effect of lipiodol but certainly it has done no harm. As regards the general treatment you know only too well that fresh air, sunshine and liberal diet should be given. In empyema especially the metabolic rate is so much increased that diet of very high calorific value is considered essential.

We agree with most of the authorities that the convalescence of cases of empyema treated by the closed suction method takes about three weeks, but some cases may take longer.
**OUTLINE OF TREATMENT OF ACUTE EMPYEMA THORACIS.**

<table>
<thead>
<tr>
<th>Closed Suction Drainage by Introduction of a Catheter</th>
<th>Aspiration</th>
<th>Open Drainage</th>
<th>Thoracotomy with Primary Suture</th>
<th>Rib Resection and Closed Suction Drainage</th>
<th>Resection at High Level Combined with Closed Suction Drainage Through Another Stab Wound</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADVANTAGES.</strong></td>
<td>(A) Simple and easy to apply.</td>
<td>(A) For diagnosis.</td>
<td>Affords adequate drainage.</td>
<td>No tedious process necessary.</td>
<td>Adequate drainage.</td>
</tr>
<tr>
<td></td>
<td>(B) Period for lung expansion and convalescence is short.</td>
<td>(B) For immemrent relief.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DISADVANTAGES.</strong></td>
<td>Requires careful attention of attendants.</td>
<td>(A) Requires repetition.</td>
<td>(A) Incidence of residual empyema is high.</td>
<td>Wound in most cases would not heal.</td>
<td>(A) Difficult to get tight drainage.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(B) Does not cure.</td>
<td>(B) Involves operative procedure.</td>
<td></td>
<td>(B) Involves operative procedure.</td>
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<td></td>
<td></td>
<td>(C) Too much reduction of vital capacity.</td>
<td>(C) Necrosis of rib and cellulitis may occur.</td>
<td></td>
<td>(C) Necrosis of rib and cellulitis may occur.</td>
</tr>
</tbody>
</table>

Suitable for streptococcal and pneumococcal cases. Suitable for pneumococcal cases and only after frank pus and adhesions have formed in streptococcal cases.
I am indebted to Mr. F. C. Weller of the Ho Tung Engineering Workshop for his kind help in connection with the construction of the suction apparatus and also to Mr. Harold C. Leong for his help with the drawings and other things.

REFERENCES.


Notes and Comments

BRITISH MEDICAL ASSOCIATION.

PRIZES FOR CLINICAL PAPERS BY STUDENTS AND NEWLY QUALIFIED PRACTITIONERS.

[The following notification has been received from the Offices of the British Medical Association, London. It is hoped that it will be read with interest by our graduates and senior students and that it may be the means of enabling some of them to prove their worth in the Medical world at large.]

We feel sure that the members of the Clinical Staff of the Faculty will be only too pleased to give advice to any students desiring to avail themselves of this opportunity.]

The Council of the British Medical Association has decided to offer prizes for short clinical papers by fourth and subsequent year medical students and newly qualified practitioners, under the heading “Describe three cases of medical interest which have been under your care and, for each case, discuss differential diagnosis, aetiology, methods of prevention (where available), treatment, and prognosis.” For this purpose the medical schools of the British Empire have been grouped by the Council as follows:—

Group 1.—University of Aberdeen; University of St. Andrews.

Group 2.—Queen’s University of Belfast; University of Dublin (Trinity College); National University of Ireland (University College, Cork; University College, Dublin; University College, Galway); Royal College of Surgeons in Ireland (Schools of Surgery).

Group 3.—University of Birmingham; University of Bristol; University of Wales.

Group 4.—University of Durham; University of Leeds; University of Sheffield.

Group 5.—University of Edinburgh; School of Medicine of the Royal Colleges, Edinburgh.

Group 6.—University of Glasgow; Anderson College of Medicine; Queen Margaret College (School of Medicine for Women); St. Mungo’s College.

Group 7.—University of Liverpool; Victoria University of Manchester.

Group 8.—London: Charing Cross Hospital Medical School; King’s College Hospital Medical School.

Group 9.—London: Guy’s Hospital Medical School; London Hospital Medical College.
GROUP 10.—London: London (Royal Free Hospital) School of Medicine for Women; University College Hospital Medical School.

GROUP 11.—London: Middlesex Hospital Medical School; St. Mary's Hospital Medical School.

GROUP 12.—London: St. Bartholomew's Hospital Medical College; St. George's Hospital Medical School.

GROUP 13.—London: St. Thomas's Hospital Medical School; Westminster Hospital Medical School.

GROUP 14.—The medical schools of the Empire other than those of the British Isles.

For each group a prize consisting of a certificate signed by the President of the Association, together with a cheque for £10, will be available. Each clinical paper, which must not exceed 3,500 words (equivalent to about 2½ pages of the British Medical Journal), will be adjudicated upon by examiners appointed by the Council from among members of the Association not resident in the area of the group in question. If in the case of any group no clinical paper received is considered by the examiners to be deserving of a prize, no prize will be awarded in that group. Each paper must be plainly written or typed on foolscap (one side only), and reach the Medical Secretary, British Medical Association House, Tavistock Square, London, W.C.1, not later than April 15th, 1933. Each paper must be signed by a pseudonym only, and be accompanied by a signed statement that it has been the bona fide work of the competitor, and in what capacity he or she comes within the definition (as above) of those eligible to compete, together with particulars of his or her full name, pseudonym, address, medical school, and (if on Medical Register) month and year in which the examination qualifying for registration was passed.
Acknowledgements

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