E S S A Y

ON

SECONDARY MICROBIC INVASION OCCURRING IN THE COURSE OF THE COMMONER FEVERS.

By

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I.

INTRODUCTION

In light of the fact that cases of any given infectious disease have so many characteristics in common, the à priori assumption that there existed a specific materies morbi was reasonable, and, indeed, constitutes one of those early medical speculations which modern science has strikingly confirmed. The similarity in question is not always restricted to the essential features of specific affections, many of them being accompanied by a group of complications and sequelae marked by an individuality almost as strong as that of the primary diseases. Evidence has been accumulating during the last few years which indicates a separate origin for many of these morbid conditions, and it seems to me that the time has come for a general recognition in practice, as well as theory, of the fact that they are attributable to secondary invasion by micro-organisms differing in kind from the primary ones. Against the probable objection that the existence of an etiological connection between certain of the secondary bacteria and the lesions with which they are associated requires further proof I can only submit my conviction that the clinical and experimental facts (especially the former) already available are sufficiently conclusive, and that treatment founded on a recognition of a relationship gives better results than any other method. Premising, then, that certain micro-organisms infect patients in the

course of acute specific diseases, it is proposed to consider the causes and effects of such invasion and, subsequently, to induce from the facts collocated a rational system of treatment.

> That the question is one deserving attention is proved by the mortality consequent on such a disease as Measles. As a primary infection Measles - except when introduced into a community lacking hereditary protection - is seldom fatal; but a high mortality results from invasion of the bronchi and lungs by secondary cocci, by the supervention (often unrecognised) of Diphtheria, and, later, of Tuberculosis.

The local morbid conditions, being too diverse for general consideration, will be synopsized in an Appendix with a few additional therapeutic notes. Throughout, the question of secondary invasion (this term is used in the title in preference to infection as being wider and including putrefactive bacteria, especially intestinal) will be regarded chiefly from the clinical standpoint. Illustrative cases will be submitted, and such records, with other non-essential matter will be separated in order to preserve continuity.

The bacteriological facts, treated chiefly in the Appendix, have not been accepted without detailed experimental work, including all the ordinary methods except the inoculation of animals. Nevertheless, I am much indebted to Muir and Ritchie's Manual of Bacteriology and especially to the bibliography which it contains.

It will be found that many parts of the Thesis have a varying degree of relevance to primary as well as secondary infection. It has been impossible to exclude these, and, at the same time, to present a coherent view of the subject.

II.

THE ETIOLOGY OF SECONDARY MICROBIC INVASION.

The factors favourable and essential to secondary invasion are numerous, the nature of their influence is often obscure, and the majority of them are also related to primary infection.

Susceptibility is obviously necessary, and may be hereditary.

> Many examples of inherent susceptibility might be given. Reference may be made to the case of A.C. (page 63) two of whose brothers died at different times from secondary respiratory complications following Measles of a primarily mild type under conditions not adverse to recovery, while a sister barely recovered in similar circumstances.

In the majority of cases, there can be little doubt that susceptibility is the outcome of diminished resistence. Whether the latter be due to the bactericidal action of cells and fluids, to tissue-tolerance, or to both, its disappearance seems to be mainly dependent on the depressing effect of the primary infection. That one acute Zymotic disease predisposes to another is now generally accepted, notwithstanding the comparative infrequency of mixed cases of the primary fevers. This infrequency, which might be regarded as a proof of immunity, is explained by the fact that isolation, adopted for the benefit of others also protects the patient from addi-

tional infections. When isolation, in the latter sense, proves ineffective, as occasionally happens in hospital, the existence of susceptibility is speedily evidenced.

> In 1894 a case of Varicella was admitted, owing to mal-diagnosis, into a Scarlet Fever Ward for children at the Linacre Hospital. It was removed from the ward within two hours, but six of the Scarlet Fever patients contracted the disease, although not all from the primary source. Taking 15 days as the average incubation period, one of the patients was attacked during the scarlatinal fastigium, one during defervescence, and the remainder at a later stage.

As a general rule, the more profound the constitutional disturbance resulting from the primary disease the more likely is secondary infection to supervene.

> The incidence of secondary complications among 100 cases of Diphtheria treated in my wards has been calculated as 52 per cent for the "severe and very severe" and 19 per cent for the "mild and moderate" cases. The secondary complications of Enteric Fever, Small-pox, and Scarlatina are similarly related to the severity of the primary affections. In Scarlet Fever cases grouped as "severe and very severe" the percentage rises as high as 66.6 per cent. As regards Measles the relation under consideration is not very marked, but hospital data, which alone are reliable, are too restricted to

provide satisfactory returns.

Conditions which reduce resistence to primary infections will also favour the secondary forms. Among such inanition may be specially mentioned. Its importance is due to the fact that, for various reasons, patients primarily suffering from an acute Zymotic disease are apt to be in a condition of semi-starvation.

Starvation would appear to be a main factor in the development of so-called malignant, (+) but really secondarily-infected cases often sent late into hospital from the homes of the very poor. It is common to find that such patients have been insufficiently fed - often actually starved - owing to ignorance and want of nursing-skill on the part of their attendants. During the great privations from which the working classes of Liverpool suffered in 1895, I was struck by the increased prevalence of secondary complications among the patients admitted to my hospital and regarded this fact as throwing a new light on the high mortality which is a feature of famine epidemics.

Age-suspectibility is traceable in the case of certain secondary infections.

Diphtheria, when introduced into a Scarlet Fever ward appears to pick out the youngest patients

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(+) The term "malignant" is here restricted to those cases in which special susceptibility or excessive virulence induces grave toxic symptoms manifested at the outset.

while, under reversed conditions, Scarlet Fever, if the influence of acquired immunity be taken into consideration, evidences no such selective action. Again, susceptibility to infection by the pyogenic cocci seems to vary inversely with the age. This is well seen in Typhoid cases, for, although children usually have a mild form of Enteric Fever, abscesses containing pyogenic organisms are commoner among them than among adults. An interesting illustration of age-susceptibility to this group of bacteria has been noted in a large Scarlet Fever ward, one end of which is reserved for cot-cases, while the remainder is occupied by beds. The preponderance of "septic" complications among the cot-cases as compared with those in the beds caused a question to be raised as to whether the end of the ward might not be subject to some unrecognised insanitary influence. A consideration, however, of the age-incidence of similar complications among the total Scarlet Fever cases, treated in different wards over a considerable period, indicated only a slight excess for those in the suspected ward, This excess I interpreted as resulting from an aggregation of cot-cases which ensured the continuous presence of the secondary micro-organisms - a view which was strengthened by the fact that no sanitary defect could be discovered.

The influence of the primary pyrexia on secondary infection is clearly a question of clinical importance but is difficult to discern. The additional rise in

temperature which frequently precedes secondary infection is to be regarded as the fever of onset rather than a favouring circumstance. On the whole, experiments which I have carried out to determine by incubation the absolute optimum temperature of the Bacillus Diphtheriae and the Streptococcus Pyogenes point to the conclusion that, so far as these bacteria are concerned, a previously raised temperature, per se, is deterrent, and that, when it is associated with secondary infection by them, this is owing to the preponderating influence of other conditions which favour susceptibility.

> As a clinical fact bearing on this view it may be pointed out that Scarlet Fever patients, while in the febrile stage, seldom develop Diphtheria, but are extremely susceptible during early convalescence Many instances could be given of Diphtheria breaking out in Scarlet Fever wards and selecting only the convalescents.

It is probable that an abnormally low temperature, taken alone, discourages, although in a very minor degree, the occurrence of secondary infection. This is in accordance with cultivation experiments which indicate a much less restricted downward than upward thermic limit to bacterial growth. Moreover, the reduced temperature is accompanied by depression, which as a factor favouring secondary infection far outweighs its feeble protective effect.

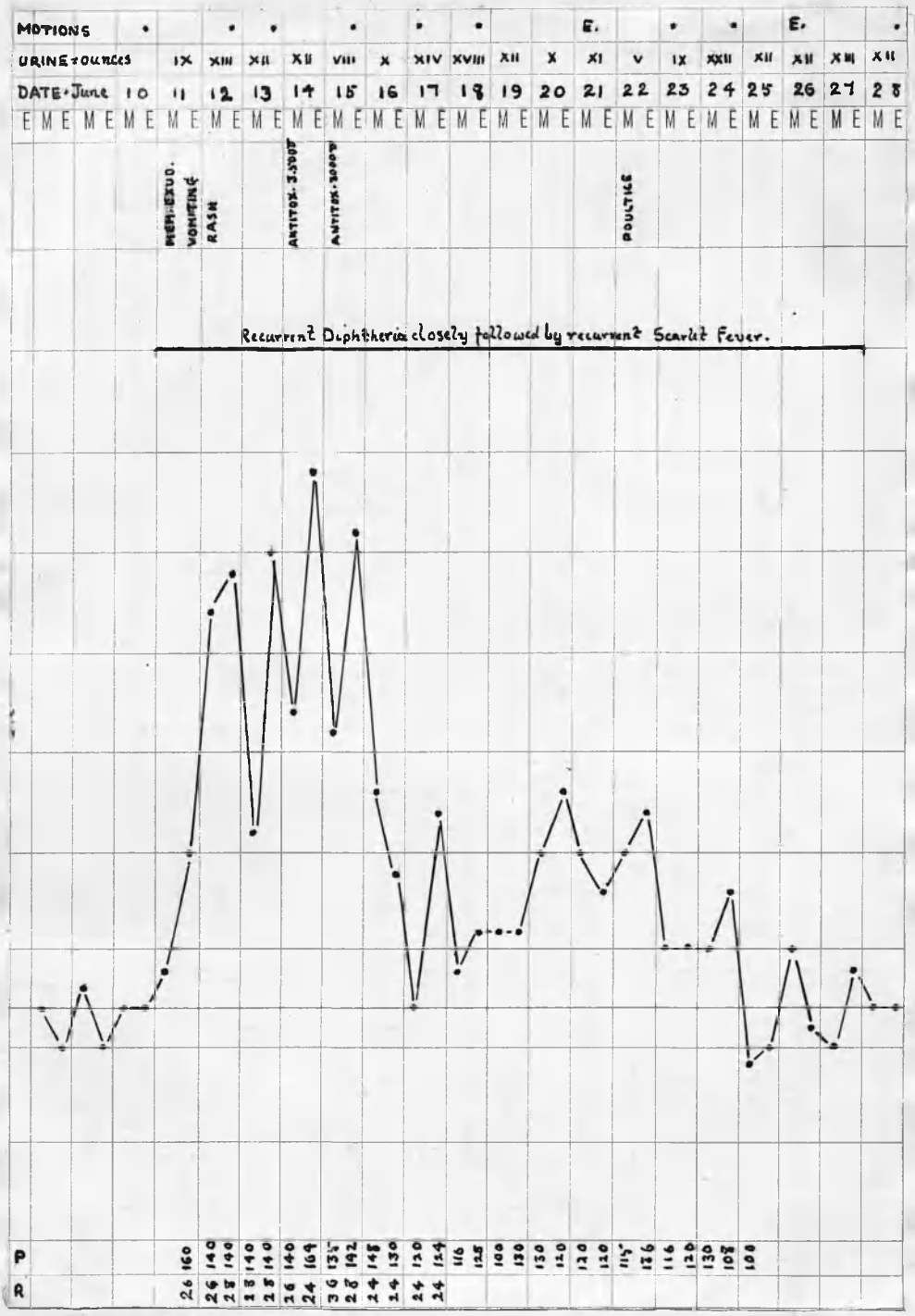
If susceptibility is essential, it is, à fortiori, ne-

cessary that acquired immunity to the secondary organism, when present, should be annulled. The question of the nature of acquired immunity need not be here discussed. What is of etiological consequence is the possibility of the predisposing conditions originating from the primary infection counteracting acquired immunity. There would be nothing incredible in the loss, under such conditions, of the transient and imperfect immunity which is a probable factor in recovery from infection by pyogenic bacteria. When, however, the virus is one which confers prolonged and thorough protection against a second attack - as, for instance, is generally the case with Scarlatina and Measles - its temporary disappearance, owing to the influence of another disease, cannot be accepted without weighty clinical proof. Nevertheless I accept this possibility, founding my belief on a study of so-called "mixed" cases, in which the infections, although concurrent for a portion of their course, have not been coincident as regards onset.

G.R., aet. 4, was admitted to Plaistow Hospital on December 7th, 1897, as a mixed case of Diphtheria and Scarlet Fever of six days' duration. His family history and past record were good. The initial symptoms, as detailed by his parents, were indicative of Scarlet Fever. All his organs were healthy. The pulse was 80, the respirations 20, and the temperature normal. There were faint traces of a scarlatinal rash about the neck and the "circumoral ring" could be distinguished. The tongue was typical

of Scarlet Fever. Both tonsils were slightly enlarged and upon each was a patch of diphtheritic membrane. The glands below the angles of his jaw were slightly inflamed. There was no discharge from the nose. The diagnosis (bacteriologically confirmed) was Scarlet Fever with Diphtheria. Treatment on the lines to be subsequently described was adopted. On December 9th there was a faint trace of albumen in the urine, but no clinical or microscopic evidence of nephritis. The other symptoms soon abated with the clearing of the throat, but the albuminuria increased to a maximum on December 15th, after which it rapidly disappeared. The patient was up for the first time on December 26th. He was then uncertain on his feet and his knee-jerks were diminished, while his voice was slightly nasal, He continued to improve until the first few days of January, when he contracted a mild bronchial catarrh, presumably specific, colds being at this time epidemic in the hospital. On the 7th the Sister noticed that he was somewhat apathetic. His temperature rose to 100° Fahr. on the 11th and he complained of sore throat. Both tonsils were again somewhat enlarged, and, within a few hours, showed traces of membrane. The same evening the pulse ran up to 160° and the patient vomited repeatedly. The temperature continued to rise during the night, reaching 102.4 Fahr. at 11 a.m. when a scarlatinal rash appeared on the chest, at first diffuse, but subsequently be-

ABBREVIATED CHART OF G.R.'S CASE COVERING THE PERIOD OF RECURRENT MIXED INFECTION.



coming punctate and spreading to the parts usually affected. By the 13th, the diphtheritic membrane had spread over both tonsils and the right side of the soft palate. There was a discharge from the nose and the glands on both sides of the neck were swollen. The urine was normal. Earlier injection having been prevented by delay in the delivery of a fresh consignment of antitoxin, 3,500 units were administered on the 14th inst. and 3,000 on the 15th. The urine now contained a distinct trace of albumen which, however, only persisted for a few days. On the 19th the membrane was clearing but the last trace had not disappeared until the 24th. The patient then gradually improved but had marked palatal paralysis, with paresis of the lower limbs. He desquamated a second time and was not discharged until March 16th.

Remarks: - This case might be classed with those in which there is apparently a lack of power to acquire a high degree of immunity even from a markedly protective affection. Be this as it may, interpreted in light of the average incubation periods of Scarlet Fever and Diphtheria, the following inferences suggest themselves: - The patient having recovered from the mixed infections acquired some degree of immunity to both, the protection against Scarlet Fever being, as is usual, more thorough than against Diphtheria. He remained during convalescence in a ward with two other patients

suffering from both affections. For a time he progressed satisfactorily, but having contracted a bronchial catarrh of a mild influenzal type, his power of resistence was sufficiently lowered to counteract the slight degree of immunity produced by the first attack of Diphtheria. Thereupon he contracted that disease. As a result resistence was still further weakened, so that even the immunity to Scarlet Fever was annulled and he developed that affection also. Those who accept the view of Goodall and Washbourn (the accuracy of which I am not prepared to admit) that the scarlatinaform rash sometimes occurring during convalescence is not a recurrence of the disease might maintain that the patient did not have a second attack of Scarlet Fever. The accompanying symptoms, however, negative such an objection, the authors in question founding their belief on the absence of constitutional disturbance. It is, of course, generally admitted that relapses and recrudescences do occur, the latter, however, being excessively rare. It may be finally pointed out that the rash was not due to serum as none was administered for the primary diphtheritic attack.

Given the existence of susceptibility the necessity for the presence in sufficient numbers of a pathogenic form of the secondary micro-organism is apparent. Nevertheless, in practice it seems too often to be ignored.

> Taking measles as an example it is rare to find that definite means are employed to do away with the presence of adventitious organisms which produce respiratory and other complications or that the milk taken by the patient during the period of special susceptibility is boiled in order to obviate a recognised source of infantile tuberculosis.

Certain secondary micro-organisms may be found apparently living a saprophytic existence on the skin and mucous membranes of patients who subsequently succumb to the same infection. Apart from increased susceptibility this may result from the bacteria in question becoming pathogenic owing to association with other kinds, to numerical re-enforcement from extrinsic sources, or to the adventitious introduction of a fresh and more virulent strain. It is not always possible to distinguish between exalted virulence due to association (of which I take post-scarlatinal Diphtheria to be an example) and that resulting from successive passages. It is noteworthy that epidemics are at times marked by a specially high mortality due to secondary complications which develop early. I am of the opinion that, in these cases, the secondary as well as the primary organism is conveyed from patient to patient, and that the virulence of the former is the outcome of the process just mentioned.

With the existence of susceptibility and the presence of micro-organisms clinical evidence goes to prove that there is usually - if not always - associated in the genesis of secondary infection some form of local

lesion caused by the primary disease. This lesion, there can be little doubt, is due to the irritating effect of a primary specific toxine which induces local degenerative changes. The severity of the local lesion varies with the virulence of the toxine from a trivial inflammatory reaction to extensive destruction of the tissues. The tract affected by the secondary organisms depends partly on their nature, but more on the distribution of the primary lesion with which it tends to coincide.

> Thus the same bacteria may in one case appear as a surface invasion, while, in another, they penetrate deeply into the tissues. Streptococci, for instance, show a special tendency to spread along the mucous membrane of the respiratory tract in cases of Measles; but, in scarlatinal cases, are found more often in the substance of the pharyngeal mucous membrane and in the adjacent glands.

A spreading surface-invasion may become very extensive and is sometimes accompanied by the formation of false membrane. In the case of serous surfaces fibrinous exudation is the rule. As regards penetrating microorganisms, access may be gained to the lymphatics, and they may be arrested in the glands, or may, directly or in indirectly, enter the blood stream. In the latter case they do not remain long in the general blood current, but settle in certain organs for which they appear to have an affinity.

Thus the Bacillus Tuberculosis specially affects the spleen and the pyogenic cocci the kidneys.

In addition to this selective action almost all secondary organisms gaining access to the blood show a tendency to attack tissues which are primarily diseased.

As an extreme but pertinent example may be quoted the settlement of staphylococci, streptococci, pneumococci and the Bacillus Coli on non-organised endo-cardial vegetations, constituting Ulcerative Endocarditis - which has a place among the secondary sequelae of acute infectious diseases.

It is of clinical importance to distinguish the above two methods of settlement, rendered possible by the presence of bacteria in a free state in the blood from embolism in which they are attached to other matter and depend for their location on purely physical conditions.

As supplementing morbid changes in the tissues it has been suggested that chemical substances originated by the primary bacteria may favour the growth of secondary ones. It is possible that perverted secretions due to the general toxic disturbance have a similar effect. In particular, changes in the gastric juice by diminishing its anti-microbic qualities, probably allow prejudicial organisms to survive until they find, in the intestines, conditions favourable to multiplication. Again the excess of bronchial secretion which precedes broncho-pneumonia appears to encourage the growth of the bacteria in-

volved while suction-action mechanically aids their passage to the air cells.

Before passing from the subject of the etiology of secondary invasion reference may be made to the theory that many of the commoner fevers are only apparently primary, being preceded by some minor form of infection which prepares the ground for the more obvious secondary disease. Many of the points raised bear upon this theory, which, in the interests of prevention, is worthy of systematic examination.

III.

THE LOCAL AND GENERAL EFFECTS OF SECONDARY MICROBIC INVASION

The morbid consequences of secondary infection are local and general. The former vary in severity from mere disturbance of function to grave organic mischief. In conformity with the distribution of the invading bacteria, as described in the last section, the secondary lesions often appear to be, for a time at least, an aggravation or recrudescence of primary ones. Their extreme diversity renders them unsuitable for collective consideration and the main facts ascertained in regard to them will be found in the Appendix. As a matter of fact, although contrary to what might be expected, they are only of secondary importance to the physician, since they rarely endanger life. Exceptions, of course, exist, as in cerebral abscess following Scarlet Fever and occlusion of the larynx owing to secondary oedema; but, in the great majority of cases, it is in the less obvious secondary constitutional disturbances, fundamentally toxic, that danger lies, and it is to this aspect of the subject that attention will be almost entirely directed. It is one which hitherto appears to have attracted very little attention.

It will be necessary to a clear statement to deal in the first instance with the antecedent general pathological condition. One of the multiple toxines evolved by the primary organisms almost invariably induces py-

rexia, which, in its turn, originates a limited train of symptoms, mostly nervous, and possibly also determines qualitative and quantitative alterations in various secretions and excretions, while there is associated with it an augmentation of a group of poisonous substances normally present in the blood. The remaining toxines originate the specific symptoms upon which the identity of the disease depends. It is obvious that the resulting pathological state must be exceedingly complex. It is proposed first briefly to examine the pyrexial condition leaving for subsequent consideration the remaining - often preponderating - toxic element. To avoid periphrasis the subsidiary febrile state will be described as having an "indirect" and the specific symptoms a "direct" toxic origin, while the term "total" will be applied to the effects of intoxication as a whole. The views advanced in regard to the indirect toxic or febrile condition are, of course, not original, being in accord with the teaching of Professor Bouchard. This condition is one which approaches or actually attains the so-called uraemic state or, rather, an aggravated modification of uraemia. A few words as to the nature of non-febrile uraemia are therefore necessary. Bouchard, chiefly on experimental grounds, denies that its toxic phenomena are in any considerable degree due to the accumulation of urea and imperfectly oxidized nitrogenous matters. Seeking in the urine for the toxic substances to which uraemic symptoms are attributable he has distinguished a number of poisons and experimentally demonstrated their effects.

Of these poisons potass alone is absolutely identified. The others are organic and have been separated in impure form by various physical methods. One (probably pigmental) causes convulsions, like potass; a second, narcosis and coma; a third (present in very minute quantities) salivation; a fourth (possibly pigmental) myosis; and a fifth, apyrexia. Bouchard shows that the convulsive and narcotic poisons antagonise each other so that the clinical type varies with their relative proportions. It is impossible to give a sufficiently brief account of the experimental and clinical evidence by means of which the various poisons are traced to intestinal putrefaction, alimentation, biliary secretion (especially pigmental) and disassimilation. The general conclusion is that uraemia is a condition to which "all the poisons introduced into the organism or found therein, physiologically contribute when the quantity of poison formed or introduced can no longer be eliminated in the same time by the kidney." Passing to the febrile type of uraemia, Bouchard lays special stress on the increased quantity of toxic potass liberated from the tissues owing to excessive disassimilation. To its effect he is disposed to ascribe mainly the convulsive symptoms so often noted in fever cases. I question, however, whether such ataxic phenomena have not frequently a specific toxic origin. In some cases they appear to be co-existent with the condition of narcosis to which they are stated to be opposed. Toxic narcosis, however, is not easily differentiated from the stupor which is only one manifestation of reduced

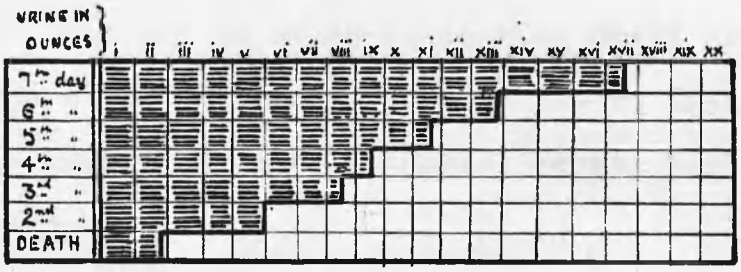
metabolism depending on the establishment of a partial equilibrium between the blood and the tissues as a result of the retention of imperfectly oxidized nitrogenous substances. In febrile uraemia, it is important to note, not only is the potass augmented, but increased - and, often, anomalous- intestinal putrefaction provides additional toxic material. Moreover, constipation is common, at least during the evolution of the uraemia, so that stagnation favours bacterial activity in the intestine while absorption of deleterious substances is facilitated. Apart from putrefaction, perverted digestion no doubt also produces toxic substances. With excess of toxic matter in the blood an equivalent increase in renal excretion is obviously necessary to prevent accumulation. Pyrexia, however, is usually accompanied by a reduction in the quantity of urine passed - a reduction which is most marked at the time when the blood has attained its maximum toxicity, - namely, at the end of the acute stage. If the patient survives the intoxication, in the majority of fevers (Diphtheria being a striking exception) a "critical polyuria" sets in and has been empirically recognised as of highly favourable significance. So long, however, as the reduction is maintained, uraemic poisons are accumulating. Indeed, I am convinced that some degree of accumulation occurs in all pyrexial cases even when the urine is not markedly diminished and its specific gravity is high. If the rate of accumulation is slow, or the febrile attack short, the toxic effects never become distinctly recognisable. This is also true

in regard to prolonged cases of intermittent pyrexia (such as the hectic fever of phthisis) in which there is a recurrent polyuria coincident with defervescence. Otherwise, the appearance of toxic symptoms is only a matter of time. The supervention of nephritis - so common in the latter part of the acute stage - greatly hastens their occurrence, while uraemic vomiting, by preventing the absorption of fluids, brings about an additional reduction in the flow of urine, and is often the factor which determines suppression.

It is unnecessary to enter in greater detail into the genesis of the febrile type of uraemia. As previously stated, it is only one element in the morbid condition induced by acute infections and its symptoms (cardiac debility, muscular spasms and tremor, dyspnoea, convulsions, coma, headache, drowsiness, amaurosis, urticaria, vomiting, hiccough, diarrhoea, salivation, transient trismus, etc.) even when fairly severe may be outweighed by those having a direct toxic origin. The specific toxaemia, of course, varies with the disease, but there is one fact which has a general application. THE SPECIFIC POISONS, LIKE THE URAEMIC ONES, ARE ELIMINATED BY THE KIDNEYS AND THE INADEQUATE EXCRETION WHICH HAS BEEN INDICATED AS MAINLY PRODUCING THE URAEMIC STATE IS EQUALLY EFFECTIVE IN INTENSIFYING DIRECT SPECIFIC INTOXICATION. Thus, the total toxicity of the blood varies inversely with the rate of renal excretion.

If the above interpretation of the pathogenesis of the toxaemia manifested as a result of acute specific

ANALYSIS OF FORTY FATAL CASES OF DIPHTHERIA SHOWING GRAPHICALLY THE DIMINUTION OF URINE DURING THE LAST WEEK.



The darkened squares in the above diagram indicate the ounces of urine passed daily on the average during the last week, viz: 16.6 ounces on the 7th day; 12.9 ounces on the 6th; 10.6 ounces on the 5th; 8.5 ounces on the 4th; 7.5 ounces on the 3rd; 5 ounces on the second; & 1.8 ounces on the day of death.

When, among the practically consecutive cases used, the quantity of urine passed has been doubtful, it has not been allowed to enter into the calculation and, consequently, has not affected the average either way.

It has, of course, been necessary to include urine passed in bed; but in such instances the estimation has been made by a Sister whose accuracy of judgment has been proved by experiment.

infection be correct, oliguria in the course of fevers should be of grave significance. Of this I am satisfied and regard the quantity of urine passed as the most valuable general prognostic sign. In every acute case in my wards the quantity of urine is charted daily and my observations cover Small-pox, Enteric Fever, Typhus (a considerable number of cases), Scarlet Fever, Diphtheria and Measles.

> The appended table of 40 fatal cases of Diphtheria, showing the average quantities of urine passed during the last week is specially striking, the disease in question being the one in which oliguria is most marked and has the gravest consequences.

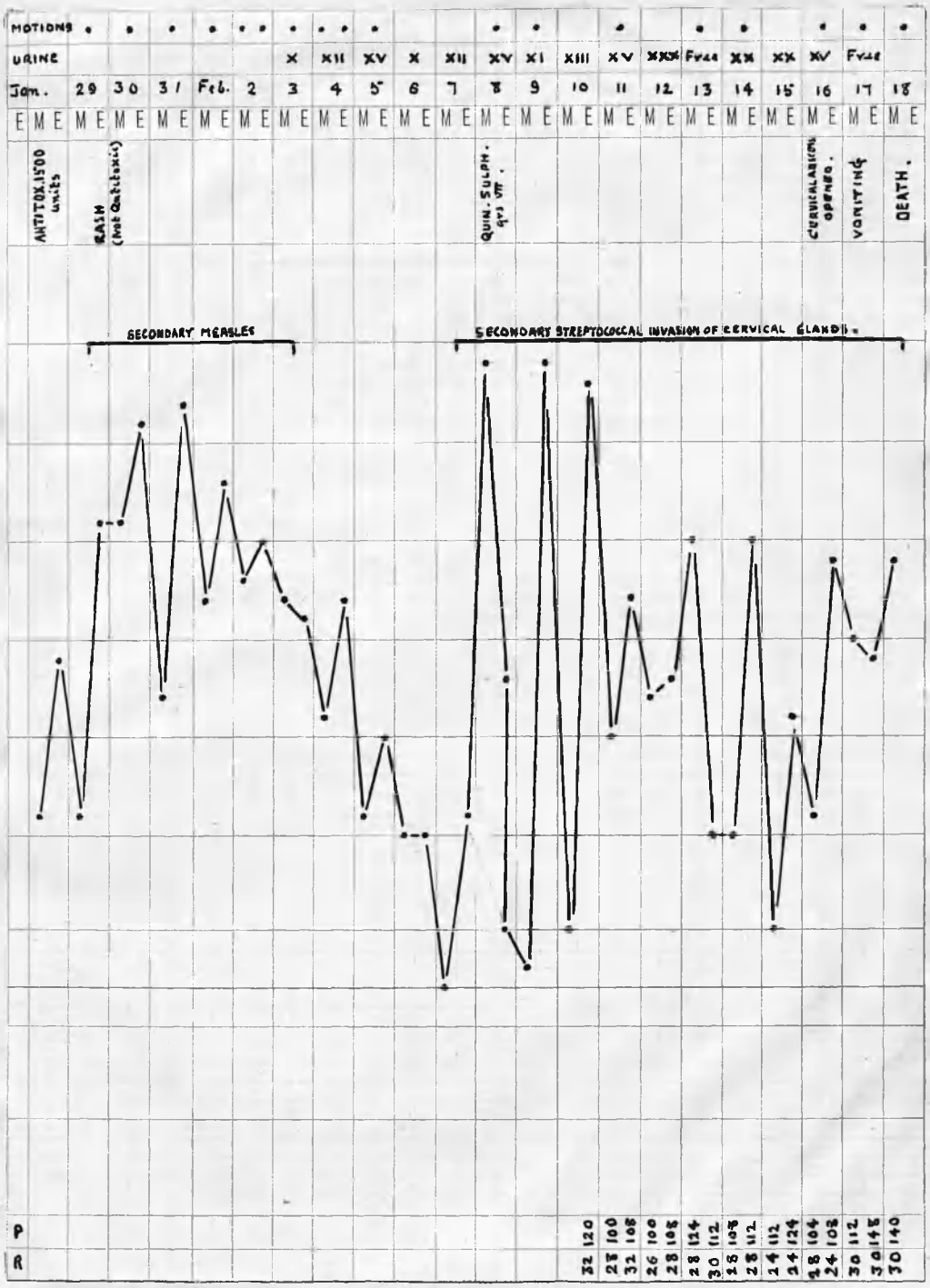
So far only the primary general toxic condition has been under consideration. It remains to deal with the relation of secondary infection to the facts discussed. Although it is possible to sum up this - the main - question much more briefly than has been the case with the preliminary matters just reviewed, the part which even trivial forms of secondary infection almost invariably play in the occurrence of fatal cases entitles it to the gravest attention on the part of the physician. This relation may be summed up in the statement that secondary infection adversely modifies the primary intoxication by introducing an additional toxic element, often at a critical time, with all the possible consequences, direct and indirect, which have been traced in connection with

primary infection.

(1) Secondary infection, by rendering more acute or prolonging the febrile condition, may increase the uraemic poisons in the blood without materially affecting the rate of excretion.

V,H., aged 5, was warded on January 27th,1898, suffering from very severe uncomplicated Scarlet Fever, stated to be of 6 days' duration. The patient had been a weakling from birth, and there was a past history of rickets and bronchitis. He was fairly well nourished. There was a typical fading Scarlatinal rash. Both tonsils were enlarged, and, seen after syringing, there was no exudation upon their surface. Both sides of the neck were generally swollen. There was a discharge from the nose and also lachrymation. Further enquiry elicited the fact from his parents that there were un-isolated cases of Measles in the house from which he was admitted. Antiseptic treatment was adopted with 5 minims of spirit of camphor every 4 hours, and, in accordance with the recommendation of Fournier, 1,500 units of Diphtheria antitoxin were administered on the ground that the patient was probably developing the anginous type of Scarlet Fever. On the 28th the discharge from the nose was much increased, and on the 29th a macular rash appeared on the face, body and limbs. This rapidly faded. The discharge from the nose continued, conjunctivitis became mark-

OUTLINE-CHART OF V.H.S CASE.



ed, and the patient developed slight bronchial catarrh. Nevertheless the throat symptoms improved and there was a steady fall in the temperature from January 31st until February 7th. The patient's general condition, during the earlier part of this period, although not immediately dangerous, caused considerable anxiety as to the ultimate result. His pulse was poor and averaged 130. His respirations were occasionally shallow and sighing - a common feature of severe scarlatinal cases which I believe to be directly toxic. Between January 30th and February 3rd there was slight Mind-wandering, but from the latter date this symptom disappeared and there was marked general improvement. No uraemic element could be detected. His temperature being normal on the 7th and, in spite of slight bronchial catarrh, his general state satisfactory he was regarded as out of danger. On the same evening, however, he had recrudescence of the sore throat and his temperature began to rise, being 103.8° Fahr. on the following day. The glands at the angle of his jaw became rapidly swollen and it was considered that the secondary invasion by pyogenic organisms was taking place. The pyrexia was of the oscillatory type. Up to this point it had been a feature of the case that the patient passed sufficient urine of average specific gravity to render the incidence of dangerous uraemic symptoms unlikely - and also, perhaps, to account for his having survived the severe direct scarlatinal

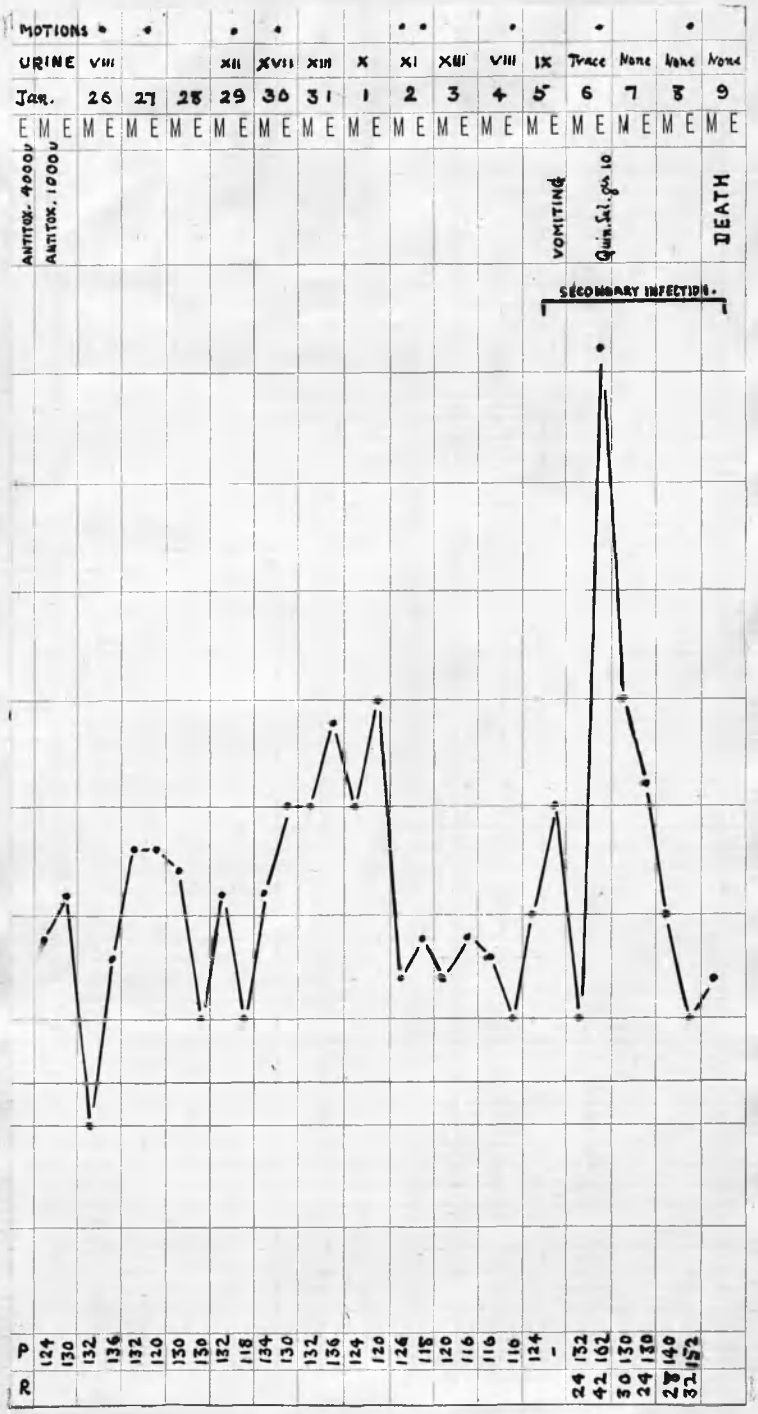
intoxication. Curiously, during the progress of the secondary infection the urine, on the whole, increased in quantity, reaching 30 ounces on the 12th and this comparatively free excretion continued until the end, although, during the last few days, the amount could not be measured. In spite of vigorous antiseptic treatment the glandular inflammation increased, pus formed, and was liberated on the 16th. It contained the streptococcus pyogenes. On the 12th - the fourth day of the secondary infection the patient was noted to be drowsy, and from this time onward, stupor, which I regarded as uraemic, gradually became intensified. On the 17th the pupils were contracted, sickness set in, and the patient died on the evening of the 18th. For the last two days his breathing was semi-stertorous.

Remarks: - According to my view of this case, death resulted from the febrile type of uraemia overshadowing the mixed specific intoxication. The uraemia was determined by the secondary invasion by the streptococcus pyogenes. If this be correct, the uraemia was engendered notwithstanding the fairly free excretion of urine. The patient's chart is appended and will help to eke out the few details which have been given.

(2) In addition to increasing the total toxaemic elements, direct and indirect, secondary infection may, owing to superadded pyrexia, vomiting or diarrhoea, produce a reduction in the quantity of urine passed.

L.W., 6 years of age, was admitted to Plaistow Hospital on January 24th, 1896, suffering from Diphtheria. There was nothing noteworthy in the family record or past history. Pallor was marked and the patient was very restless but not delirious. The pulse was 124, small and feeble, The heart and lungs were normal. There was marked albuminuria. Both tonsils were covered with thick white membrane which was also present upon the palate on the right side. There was slight cervical adenitis on the same side. Antiseptic treatment was adopted and 4,000 units of antitoxin injected, with another 1,000 on the following day. On the 27th, the condition of the pharynx was unchanged and the membrane persisted until the 31st when it rapidly became diffluent. The albuminuria varied, as is usual, from day to day, but on the whole, there was an increase until January 31st when the urine is described as "loaded". From this time onward there was a decrease. On February 2nd, the quantity was still "marked", but had fallen to a "faint trace" on the 4th. As regards the amount of urine passed daily, a reference to the chart will show that the average was about half a pint between January 25 and February 5th - sufficient to permit a hopeful but very guarded prognosis. The average of the temperature reached its lowest point on the 4th. The pulse was then stronger and slower than it had been, although still variable. At the time of admission the patient was fairly alert, but during the succeeding week she became gradually

OUTLINE - CHART OF L.W'S CASE.



duller. From January 31st there was improvement in this respect also, and by the 3rd of February she was much brighter and took an interest in her surroundings. Although still pale, she had lost the earthy tinge which was noted at the outset. On the 4th of February, therefore, she was in every way at her best and apparently on a fair way to recovery. On that day she passed eight ounces of urine. In the evening she complained of pain and tenderness on each side of her neck. Slight swelling was found, due to inflammation of the glands and apparently also of the adjacent tissues. Soon there was great enlargement. A thin purulent exudation covered the fauces and the breath was very foetid. On the 6th, within a few hours the temperature reached 105.2°Fahr. Although the patient had previously to be fed very carefully with over-Zyminised milk, there had been no actual sickness. She now vomited frequently, this being the "early sickness" associated with the onset of the secondary infection and not at the outset, at least, uraemic in origin - although its effect on the renal excretion would be the same as that of the latter form of sickness. On the 6th she had a motion with only a trace of urine, on the 7th and 8th she passed none at all, and died at 7.40 a.m. on the 9th. During the last two days there was stupor, almost amounting to coma, with distinct muscular tremors.

Remarks: - Oliguria is, of course, specially

common and dangerous, in Diphtheria cases, and not uncommonly supervenes after the pharyngeal lesion shows signs of improvement. Such oliguria often - probably more frequently than is generally recognised - eventuates in suppression, and it might be held that the above case was to be explained in this way, the secondary infection having no part, or a very minor one, in the fatal result. As shown in the table on page 22A , however, Diphtheritic oliguria does not supervene abruptly. In my opinion death was brought about by the accumulation of direct and indirect poisons in the blood, there being increased production on the one hand and entire cessation of excretion on the other - the adverse change in the case being wholly due to the secondary infection.

(3) Secondary infection may, in virtue of its own direct toxic effect, and apart from the patient's previous state, cause death; or its toxic influence may determine a fatal issue when, owing to the primary disease, a critical condition already exists.

Innumerable examples of direct secondary intoxication might be given. The best is afforded by Diphtheria complication Scarlet Fever - a very common and fatal combination.

The general prejudicial effects of secondary infection then, are mainly in the nature of an aggravation of the

primary toxaemia and of the conditions which tend to maintain it. The importance of such infections depends upon the fact that they are secondary. As primary ones they would, in the majority of cases, be trivial affections; but, as an additional weight against recovery from other acute zymotic diseases they frequently strike the balance in favour of death.

THE GENERAL TREATMENT OF SECONDARY INFECTION, PREVENTIVE AND CURATIVE.

It is difficult to overestimate the value of prophylaxis in relation to secondary infection and when the consequences involved receive wider recognition, no doubt a more thorough system of prevention will result. Without suggesting a strict parallel it may be pointed out that the elaborate precautions taken against the infection of surgical wounds has had only a slight influence on the treatment of acute infectious diseases in which predisposition to secondary infection is often associated with the presence of a suitable lesion.

In seeking for a rational prophylactic system of treatment it is necessary to keep in mind the various factors favouring and inducing secondary infection. These will now be dealt with in the order in which they have been already considered.

As natural and age susceptibility cannot be influenced their existence should call special attention to the means available for preventing the advent of secondary micro-organisms.

In so far as depression due to the primary disease is a main predisposing factor, its treatment bears on the prevention of secondary infection. The point of chief importance in this relation is the feeding of the patient. Observations which I have made before and after the adoption of an improved hospital dietary show beyond

doubt that under-feeding is highly favourable to secondary infection. If Enteric Fever be excepted, I am of the opinion that liberal and often over-feeding is indicated in fever cases. It is not possible to deal here at length with the question of dieting and feeding fever patients. I should like, however, to emphasize the great value of the nasal tube, In almost every severe case of fever there is a period when feeding is difficult or impossible, owing to refusal or dysphagia. In such circumstances the nasal tube provides an easy method of administration which is too often - even in hospital - adopted only as a last resource. From the history and condition of a large number of "late" cases sent into hospital, I have no hesitation in expressing a conviction that the mortality due to zymotic diseases, especially among young children, would be materially diminished if nasal feeding were generally adopted in private practice. The nasal tube also provides the means for the forced administration of water in cases of oliguria. "Early"vomiting which almost invariably disappears when the acute stage is reached is only of slight prognostic significance and its dietetic treatment is therefore not so important as that of the "late" form, which is a uraemic symptom. The latter may well be regarded with apprehension since, as previously explained, it aggravates the very condition of intoxication to which it owes its origin. The method of treatment adopted in my wards is as follows: When a patient has rejected a feed of over-zyminised milk, the next one is replaced by water given by mouth or nasal

tube according to circumstances. The following feed also consists of water with two drachms of the pre-digested milk added, and this quantity is doubled in each successive feed until the patient is once more taking pure milk. It is encouraging to find that in a large proportion of cases the over zyminised milk continues to be tolerated. In others, however, a degree of concentration is attained beyond which it is not safe to go. Very rarely even water is not retained, and enemas, given by the gravitation method, have to be substituted. The principle underlying this treatment is to maintain the water-supply to the kidneys even at the expense of nourishment. When, however, the quantity of milk taken by the mouth falls below a certain minimum (usually five ounces every two hours for an adult) a hard zyminised meat suppositary is given six hourly. This suppositary, in my opinion, provides by far the best means of rectal feeding, so long as a sufficient quantity of water is taken.

From the statement already made as to the probable deterrent effect of pyrexia on infection, it might be expected that the antipyretic method would be associated with an increased incidence of secondary complications. Reliable evidence on this point is wanting.

> The antipyretic treatment is seldom so effective as to deserve its name. As the result of the bath treatment in 6,000 cases of Enteric Fever the average reduction in temperature has been given as half a degree, Cent. (Bouchard). Nevertheless, the frequency of secondary complications is stated to

be diminished. If such be the case, it is possible that the improved general condition of the patients has greater protective potency than the higher temperature.

The advantage of protecting patients against chill, especially in the case of fevers which predispose to secondary respiratory complications, is beyond question.

So far as secondary infections are concerned the prophylactic use of bactericidal serum cannot be regarded as more than a possibility of the future.

To secure the patient, when possible, against the advent of secondary micro-organisms is clearly a point of greater practical weight than to combat susceptibility. It is a method which, in spite of its limitations, deserves wider acceptance. It has to be admitted that some of the micro-organisms are commonly found to be present in health. Clinical experience, however, shows that secondary infection rarely occurs until they are re-enforced from an adventitious source. Possibly, as elsewhere suggested, they are of an attenuated strain or present in insufficient numbers.

Thus, streptococci may be found in the ordinary sore throat of Scarlet Fever, but the case remains simple until the patient is brought in contact with another suffering from the anginous type of the disease.

Isolation, employed to protect others from the primary protection also safeguards the patient in some degree against localised infections, and, in particular,against other diseases which are usually primary. Nevertheless, hospital practice indicates that "mixed" cases must be exceedingly common, especially among the poor. This will no doubt become increasingly apparent as diagnostic methods improve, and it will be found that many of the secondary rashes now regarded as anomalous manifestations of the primary disease are really the outcome of fresh infection. The frequent occurrence of mixed cases among the poor is partly explained by the fact that isolation at home cannot be more than nominal. The value of isolation to the patient depends on a recognition of its necessity. So long as the only end in view is to prevent the spread of infection from him, there will always be the danger of its spreading to him.

In addition to general isolation the patient should be protected against dirt-borne bacteria - especially pyogenic. In surgery the important influence of absolute cleanliness in this regard underlies all treatment. There is still room, however, for its more thorough application as a therapeutic - as against a mere hygienic - medical method. In the homes of the richer classes, no doubt, the hygienic conditions often approach therapeutic requirements, but among the poor the surroundings are commonly such as to provoke secondary infection. It is by no means uncommon for the children of the latter to use, as additional bed-clothes, garments which, from being

worn in dirty surroundings, are impregnated with organic filth. Can it be wondered that children lying ill of measles in such circumstances die in large numbers from broncho-pneumonic complications? Counsel of perfection, would, of course, be absurd where the obstacles are so great; but, in addition to the removal of all unnecessary fabrics from the sick room it would surely not be too much to insist that the patient's bed-clothes (including the blankets which are not usually treated in this way) should not only be washed, but boiled, before being used by him and that the attendant should pay special regard to personal and general cleanliness.

In hospital the source of infection lies in another direction. A considerable proportion of the cases admitted - especially from poor neighbourhoods - have been kept at home until serious secondary symptoms have arisen. The removal of these "late" cases is deprecated by hospital managers on the grounds that the patient's condition is often already beyond treatment so that he is uselessly subjected to a journey which must be trying under the most favourable conditions while the hospital death-rate is adversely affected. It is argued - and the contention is in keeping with the views I am advocating - that by earlier removal the grave secondary features of such cases would be obviated.

There is an aspect of the question, however, which I believe not to be generally apprehended, although the weightiest objection to indiscriminate removals turns upon it - and that is the danger of secondary infection to

which cases already in hospital are subjected. When a patient is suffering from mixed infection of two primary diseases, such as Scarlet Fever and Diphtheria, previous notice is sometimes given and special arrangements are accordingly made for isolation; or, failing such notice, the diagnosis is made on admission. In many late cases, however, the stage when a certain diagnosis might have been possible has passed and the patient is placed among those to whom he is infectious as regards one of the diseases from which he is suffering. Again, slight secondary febrile attacks are often not genuine recrudescences but superadded affections. In these two ways foreign infections are frequently introduced into fever wards by late cases,and herein, no doubt, lies the explanation of the outbreaks of Diphtheria among Scarlet Fever patients,which in certain large hospitals, was the cause of considerable mortality before ~~the~~ bacteriological diagnosis and seropathy came into vogue. The forms of secondary infection, however, to which I would like to draw special attention are those due to pyogenic organisms, because their infectious nature is rarely accepted in practice. In say, an acute Scarlet Fever ward there are almost invariably a number of so-called "septic" cases, admitted as such or resulting from secondary infection acquired in hospital. It must be within the experience of the medical staff of most large fever hospitals that a considerable proportion of mild scarlatinal cases, admitted in a condition which should make uninterrupted recovery a matter of reasonable certainty, develop an anginous type of the disease or

such complications as otitis conjunctivitis, adenitis, abscesses, and ulcers - and this under favourable conditions as regards ventilation, diet and nursing. These results of indiscriminate segregation explain, in part, the reason why the average period of isolation is so much longer in hospital than at home. The vexed question of what their friends regard as the excessively prolonged detention of Scarlet Fever patients in hospital is one which has received much attention during the last few years, and there is little doubt that the clinical facts connected with many cases in which parents holding the "six weeks' theory" assume a critical attitude are of a kind militating against the present system of isolation. As before explained, removal to hospital before secondary complications have time to develop is the fundamental remedy. When, however, a secondarily infected case has to be admitted or occurs in the wards I am of opinion that it should be segregated with other similar ones. I fully appreciate that such a system involves greater administrative complexity and an increased cost in hospital construction; but, so far as expense is concerned it appears highly probable that the public will sanction it, if, indeed, public opinion is not the means of forcing the question to the front.

In regard to prophylaxis it remains to note that antiseptics, when applied to the primary local lesion, have a distinct value. Lennox Browne maintains that an antiseptic gargle protects against diphtheria and experience

shows that similar treatment discourages secondary infections generally. For this reason local antiseptics should not be discontinued when the primary condition no longer indicates their use, but should be applied at less frequent intervals until the possibility of secondary invasion has passed. When the primary lesion is within reach of a stream of water, as is the case with the mucous membrane of the nose and pharynx, frequent syringing with an antiseptic solution such as Boracic Lotion not only fulfils the above mentioned requirement, but forcibly dislodges micro-organisms and thus hinders infection. The administration of intestinal antiseptics, in so far as it discourages secondary invasion by way of the ulcers of Enteric Fever falls within the preventive method. It has, however, a more general utility as will be presently noted. I have no faith in the so-called saturation of the system by antiseptics (excepting creasote in Phthisis), and have found that it has no influence in the prevention of secondary infection.

Once secondary infection has become established the preventive method is narrowed down to the continued local use of antiseptic solutions. In some cases it is possible in this way partly to control the process of infection. To others special local methods of treatment are applicable. The next indication is to neutralise the toxic substances resulting from secondary infection. The injection of diphtheritic and streptococcal antitoxins are examples of this method, the utility of which is at present very restricted. When it does not apply

the direct toxic effects can only be treated symptomatically and the excretion of the toxins encouraged. In the case of the indirect toxic effects, classed as uraemic, the therapeutic possibilities are greater, but the means which I systematically employ cannot be more than outlined here as they are more pertinent to primary infection and are never delayed until the occurrence of secondary complications unless the latter supervenes in a case previously regarded as too mild for more than expectant treatment. The system in question is the logical outcome of Bouchard's teaching as to the nature of the febrile toxaemic condition, and, indeed, some of its main features belong to his method of treating Enteric Fever. Its objects are to diminish the production of the various indirect toxic substances, and to prevent the accumulation in the blood both of them and of the specific toxines. The formation of toxic matter originating from perverted digestion is met by careful dieting with zyminised foods. Undue bacterial activity in the alimentary canal is combated by means of intestinal antiseptics which I regard as of the greatest value in the treatment of the toxaemia of all the acute Zymotic diseases. After careful experiment with all the commoner intestinal antiseptics, not excluding naphthol, I have formed the opinion that Yeo's chlorine solution stands alone in its all-round utility. Its efficacy has been doubted on the ground that it is absorbed early in its course along the intestine. The post-mortem of a case reported by my predecessor at Linacre Hospital, Dr Edwardes, and quoted by Yeo, disposes

of this allegation. Moreover the effect of the preparation on intestinal putrefaction, as indicated by the stools, outweighs any theoretical objection. Excessive absorption from stagnating intestinal matters is prevented by the use of laxatives and large simple enemas. Purgation, especially by hydrogogue salines, is, on the other hand, avoided, except at the very outset. It is true that purgation produces an improvement in the uraemic condition, when present, but it is only temporary, and is followed by aggravation owing to reduction in the quantity of urine passed. For the same reason the prevention of vomiting and symptomatic diarrhoea is regarded as important. In the earlier febrile stage salts of potass are freely given in the form of imperial drink, with other saline substances; but when uraemic symptoms are evidenced precautions are taken against their excessive introduction into the blood, such substances as bromide of potassium being withheld. Chlorate of potassium is regarded as specially objectionable on account of its unfavourable effect on renal excretion. It is a substance which, of course, is widely prescribed, often in practically unlimited doses and also as strong douches and gargles, for the angina of Scarlet Fever, and I am satisfied that it may, in such circumstances, seriously prejudice the chances of recovery. It is a question as to how far the accumulation of imperfectly oxidized proteid substances can be checked. I generally exclude from my fever-dietary meat-extracts of the beef-tea type as likely to contribute to the condition to which Jaccoud has applied the generic

term "creatinaemia." At the same time, it is necessary to admit the "proteid-sparing" value of gelatine. When the concentration of the substances in question becomes so great as to interfere with the process of nutritive exchange and diminished metabolic activity is indicated by a falling temperature and general vital depression, Bouchard recommends the inhalation of oxygen. My experience of this treatment is small but favourable. In regard to the antipyretic method, it must be admitted that a high temperature is often accompanied by a group of symptoms closely resembling some of those which are ascribed to direct toxic influences. It is possible that the pyrexia produces these morbid phenomena by altering the blood distribution. In any case, a marked temporary reduction in temperature, such as that brought about by a cold bath, is frequently accompanied by a proportionate mitigation of the symptoms in question and this relation can be traced throughout the ebb and flow of the febrile stage. It is a matter which has only a slight bearing on the treatment of secondary infection as a consistent reduction of temperature by this method is not at present attainable, and, in my opinion, it has only a restricted value. The total toxicity of the blood can be reduced by depletion. In non-febrile uraemia, such as that resulting from post-scarlatinal nephritis (often occurring without pyrexia) this method may be serviceable and I have seen life saved by its adoption. Bleeding in febrile uraemia, however, is never likely to be re-established as more than a heroic and extreme resource. We

are able, nevertheless, to study its effect in certain cases of Enteric Fever with intestinal haemorrhage. It is impossible to overlook the great improvement - frequently sustained - which follows such adventitious haemorrhage.

The last and most important point in the treatment of febrile toxaemia, direct and indirect, is to maintain, and, if possible, increase the excretion of urine. The value of vicarious excretion I believe to be clinically disproved and statements already made indicate the danger of seeking to promote an intestinal action of this kind by means of purgatives. Again, I have been unable to satisfy myself that in cases in which uraemia is of the febrile type pilocarpine is otherwise than harmful. Digitalis as a diuretic, in such cases, cannot be given even in small doses with safety, caffeine being the best drug. The only effective method of augmenting the urine, however, is the liberal administration - forced, if necessary - of water, and the early and continued application of very large poultices over the kidneys. Cupping cannot compare with poulticing as means of treating oliguria or even suppression. Chilling of the surface of the body and especially of the extremities, is usually followed by a reduced flow of urine, so that keeping ~~of~~ the patient warm may be mentioned as a last cardinal point in the treatment of toxaemia.

The results obtained by the above system of treatment, to which, for convenience, I apply the term antitoxaemic, have been highly satisfactory, more particular-

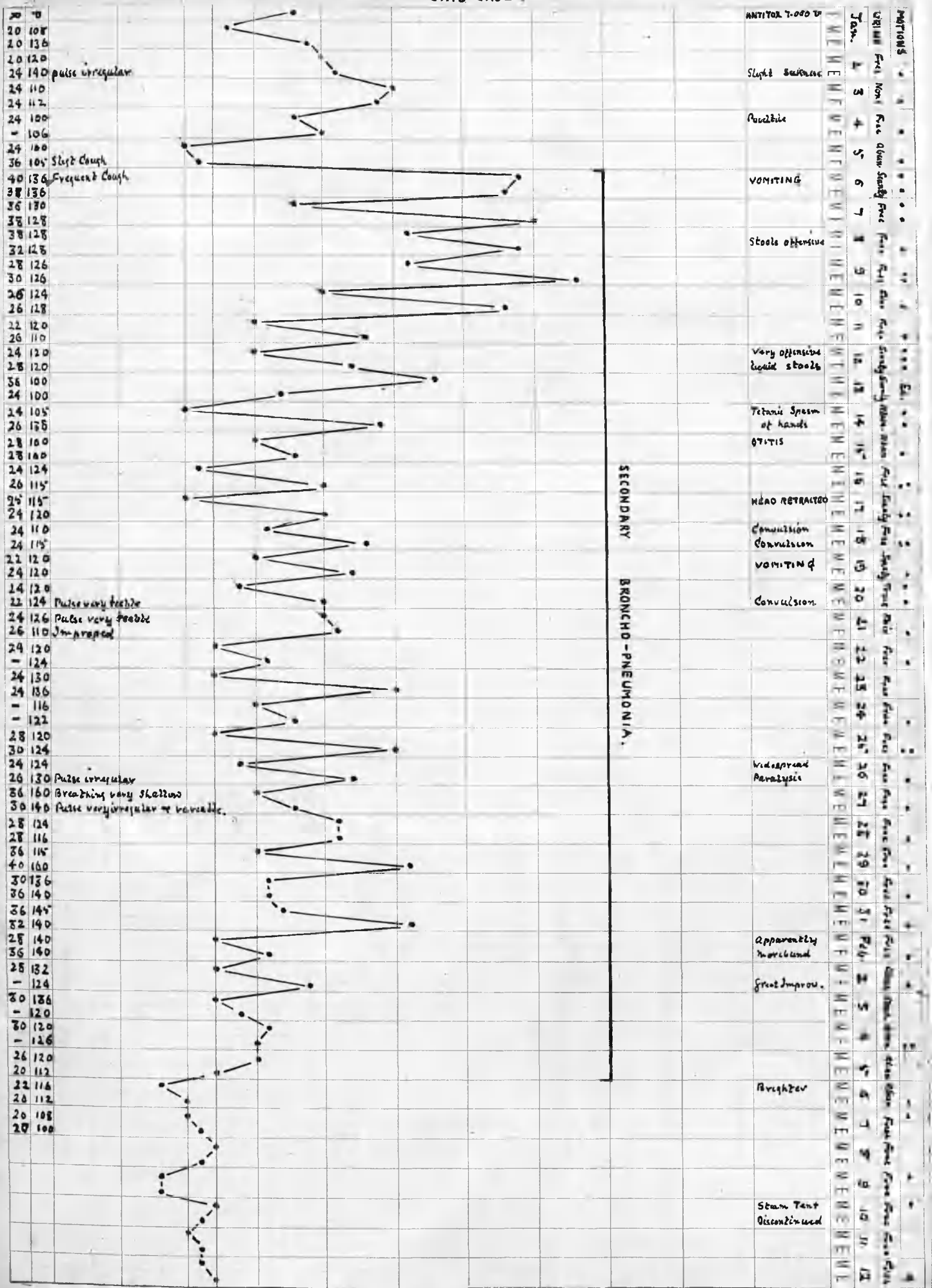
ly in cases rendered critical by the additional toxic effects of secondary infection. At Linacre Hospital, among exceptionally severe cases of Enteric Fever with a high percentage of secondary complications, especially pulmonary, the death-rate was reduced from 17 to 12 per cent. In Small-pox cases, during a severe epidemic, it was difficult to trace the result, owing to the perturbing effect of previous vaccination. In the unmodified type of the disease, however, the treatment seemed to have a controlling influence over the eruptive fever (which is partly, if not wholly, due to superadded secondary infection by pyogenic organisms located in the pox). This is important, because there is no condition in which the course of the pyrexia is of more reliable prognostic significance than the secondary fever of Variola. Scarlet Fever hospital returns, again, are apt to be misleading, as the patients admitted are divisible into a large group of "early" cases which almost invariably recover and a proportionate minority of "late" cases of which many die. The adventitious and constantly varying relation between these two classes determines the total death rate and explains the irregularity of hospital statistics. It is here, therefore, again necessary to judge the efficacy of the treatment by its effect on individual late (usually secondarily infected) cases, and I have no hesitation in testifying to its value. Diphtheria, however, is the disease in which the beneficial results are most manifest. In early cases, of course, the serum treatment overshadows them; but at Plaistow Hospital (where late cases, coming from the low-

lying district of East London beyond the Lea, are unfortunately so numerous as to have lately necessitated the issue of a circular to medical practitioners emphasising the expediency of early removal) the effect of the treatment has been to reduce by one third the mortality among patients too far advanced to benefit by injections of antitoxin, or complicated by secondary infections which the serum (notwithstanding recent statements to the contrary) does not appear to influence.

This essay cannot be more fitly ended than with the detailed report of a case involving the system of treatment which it advocates. The case submitted is by no means unique, but will bring home the value of the treatment in a more practical way than can be done by means of a mere statistical return.

> E.H. aged two and a half years, was admitted to Plaistow Hospital on December 31st,1896, suffering from Diphtheria of four days' duration. There was nothing requiring remark in his past or family history. He was moderately well nourished. His face was pale and he was in a condition of apathy. The lungs and heart were normal. The respirations numbered 20 and the pulse 108. The latter was small, weak, and inclined to be irregular. The temperature was 99.6° Fahr. A specimen of the urine could not be obtained. Both tonsils were covered with thick membrane which extended backwards on the walls of the pharynx and encroached slightly on each side

ABBREVIATED CHART OF E.H.S CASE.



upon the soft palate. There was a slight muco-purulent discharge from the nose and the sub-maxillary and cervical glands on each side were distinctly enlarged with infiltration of the surrounding tissues. I confirmed the diagnosis of diphtheria by the culture method and an unfavourable but guarded prognosis was given. The pharynx and nose were directed to be syringed with a saturated solution of Boracic Acid four hourly. No drug was prescribed by the mouth as there was a history of repeated vomiting before admission. Three thousand units of antitoxin were injected at 2 p.m.; two thousand at 3.20; and two thousand at midnight - in all seven thousand units. The diet consisted of over-zyminised milk, given two hourly with one drachm of whiskey, and this the patient swallowed easily and willingly.

Jan. 1. The patient was reported to have had a good night, keeping warm, and passing urine freely in bed. Although still swallowing easily he was less willing to take milk, of which only twelve ounces had been administered. The membrane was found to have spread over the greater part of the front of the uvula. During this day the nasal discharge increased, but there was no other change.

Jan. 2. No change was noted during the night except that the patient was extremely difficult to feed, although swallowing with ease. The pulse was noted to be irregular during the afternoon and sulphate of strychnine($^{1}/_{450}$ gr.) hypodermically or-

dered four hourly. A large piece of membrane was removed by syringing at 3 p.m. and the patient was slightly sick afterwards, Bowels moved.

Jan. 3. The patient only took eleven ounces of milk during the night and, for the first time, no urine was passed. At noon the pharynx was found to be much clearer, the membrane being mainly on the front of the uvula and between its base on each side and the soft palate. The bowels were moved towards evening, with very little urine, At night the nasal discharge was noted to have disappeared (often, when sudden, a bad sign) and at midnight the pulse was distinctly weaker.

Jan. 4. No urine was passed during the early part of the night. Feeding with the nasal tube was commenced at 1 a.m. with a hard zyminised meat suppositary at similar intervals. A large poultice was applied over the kidneys at 6 a.m. While it was on the patient passed urine freely and shortly afterwards his pulse and general condition were noted to be distinctly improved. Later the bowels were moved. The poultices were ordered to be applied night and morning at 6 o'clock.

Jan. 5. The patient's condition was improved, and the pharynx clearer. Urine was passed abundantly. The poultices were discontinued in order to observe the effect on excretion. For the first time two ounces of urine were saved and found to contain "a marked quantity" of albumen. Slight coughing at intervals was reported during the day.

Jan. 6. The patient had a quiet night but was occasionally disturbed by cough due to bronchial catarrh. The respirations increased, reaching 36 towards the morning. The pharynx was then clear but its mucous membrane granular. Since admission the temperature had risen to a maximum of 101° Fahr. on the 3rd, and then fallen to normal at certain times on the 5th. Early on the 6th it rose to 102.8 and the respirations to 40. Bronchitic râles were audible over both lungs and the percussion note towards the lower part of the right posterior axillary fold was thought to be slightly impaired and the breathing tubular. The diagnosis was secondary broncho-pneumonia, pyogenic cocci with and without the diphtheria bacillus having been found in the bronchial secretion in post-mortems of similar cases. From the time that the temperature began to rise (3 a.m.) until the evening of this day the patient only passed a trace of urine. During the day he was repeatedly sick. A poultice was ordered as before, and 5 minims of spirit of camphor added to the nasal feeds, which were reduced to three ounces of over-zyminised milk and an equal quantity of water added. A steam-tent was also erected and terebene used in the kettle. After the poultice the patient was noted to have passed "a fair quantity" of urine in bed.

Jan. 7. A good night was passed, although cough was somewhat frequent. There was also a tendency to sickness, but no actual vomiting. Urine

was passed freely after both poultices. The pulse continued stronger and more regular throughout the day while the respirations only averaged 26.

Jan. 8 to 11. There was some improvement on the whole in the general condition, but the stools were slightly offensive.

Jan. 12. Suppositories were stopped as patient passed three very offensive liquid stools. Chlorine solution was ordered to be added to the nasal feeds.

Jan. 13. The stools were much less offensive-partly due to clearing out the lower bowel with an enema.

Jan. 14. The patient passed abundant urine, but the albuminuria was found to have increased. Slight cramp of both hands was noted by the night-nurse. The strychnine injections were discontinued.

Jan. 15. Tetanic fixture of the fingers of both hands in the "dinner-fork" position was noted. The feet were also slightly affected. The pulmonary condition had improved, but the left ear was discharging; abundant urine was passed: also stool "fairly consistent and not offensive."

Jan. 17. The head was slightly retracted. "At 9.30 p.m. the patient had a prolonged convulsive attack when his face and lips became blue" (Nurse's report). The patient was semi-conscious throughout this day, when only a small quantity of urine was passed. The syringing of the pharynx was discontinued.

Jan. 18. The patient had slight convulsions at 2 a.m. At 5.30 p.m. he had a severe fit - "hands clenched with thumbs in palms, head very much retracted and respirations slower" (Nurse's report). The extremities were difficult to keep warm. The pulse averaged 112 and there was no change in its character. The bowels were well moved and a fair quantity of urine passed. The patient was in a condition of stupor.

Jan. 19. There was sickness after all feeds from shortly after midnight until 2 p.m. Six hourly suppositaries were recommenced. At 4 p.m. a nasal feed of water was given, two drachms of milk added to the following one, and this quantity doubled until the undiluted milk was being retained. Urine was passed freely after the evening poultice. As the whiskey in his feeds seemed to induce retching, two drachms with two ounces of water were ordered to be given midway between the suppositaries. The respirations were 24 and the pulse 120.

Jan. 20. "The child had a quiet and comfortable night without vomiting or inclination to vomit" (Nurse's report). At 11 a.m. the patient's condition was unchanged. No urine had been passed since the evening poultice: one was now applied without result. Patient had a slight convulsive attack at 1 p.m. with internal squint and was subsequently sick. The whiskey, even when administered by the gravitation method, was rejected. A poultice was

ordered at 4 p.m. for one hour, to be repeated at 8 o'clock. A small quantity of urine was passed after the second one. The patient appeared to be exceedingly weak at 8 p.m. and his pulse was almost imperceptible.

Jan. 21. Whiskey was once more added to a feed but rejected. Half an ounce of champagne, however, was retained and this quantity was ordered to be added to each nasal feed. The poultices were continued four hourly, and the patient passed urine three times in fair quantity. The pulse towards night distinctly improved.

Jan. 22 - 25. Urine passed freely. No change except that the spasm of the hands and feet became gradually less and had disappeared by the latter date.

Jan. 26. The patellar reflexes were found to be absent. The pupils were sluggish and there was slight internal squint. The flaccidity of the muscles and absence of movements indicated wide-spread paralysis.

Jan.27. The patient was lower and quite insensible, the pulse being very irregular and extremely difficult to count.

Feb. 1. The patient was now at his worst. From the time that the tetanic condition began to disappear - that is, with the incidence of paralysis - rapid emaciation was noticeable - and he was now extremely thin. The pulse was uncountable and between 2 and 3 a.m. he was in a state of collapse and apparently moribund. The only favourable elements in the case were that he was not sick and

urine was passed freely after a poultice.

Feb. 2. The patient passed a large quantity of urine and there was no sickness. Towards the evening a very marked improvement in his condition was apparent.

Feb. 4 - 5. The improvement steadily increased. Urine abundant. Cough almost ceased.

Feb. 6. The patient was distinctly brighter.

Feb. 10. The steam-tent was discontinued. The patient refused food by the mouth.

Feb. 12. The patient for the first time, took distinct notice of his surroundings and even attempted to play with a toy for a few moments. A little candy was given to him to suck, this being the best method of inducing young children to resume feeding by the mouth when the nasal tube has been used for a lengthened period.

Feb. 15. Patient very much better in every way and less emaciated.

Feb. 19. Towards the evening a new probationer, who was given charge of the patient for a few hours, allowed him to become markedly chilled. His extremities were quite cold and his pulse almost imperceptible. He was wrapped in relays of hot blankets, surrounded with hot-water bottles, and a drachm of whiskey with hot milk given by nasal tube every hour. Only a trace of urine was passed at midnight after a poultice.

Feb. 20. The urine continued very scanty.

Hot blankets and bottles were required continuously.

Feb. 21. The patient passed urine abundantly after the morning poultice. During the day there was rapid general improvement.

Feb. 22. The patient had quite recovered, passing urine freely. A specimen was saved, and found to contain no albumen. The specific gravity was 1115.

Feb. 23. The patient was taken round the ward wrapped in a blanket and was bright and alert.

Feb. 26. The patient was propped up in bed with a pillow, and took semi-solid food by mouth without coughing. Water, however, appeared to enter the larynx, and this was consequently still given by the nasal tube. The poultices were discontinued.

March 2. The nasal tube was no longer required.

March 4. The patient was put on a fairly full diet.

March 7. He was dressed for the first time and up for an hour in a baby's chair.

March 28. The patient was discharged. He was beginning to walk again, was well nourished, and in perfect health.

APPENDIX

It is proposed here to deal in the briefest manner possible with the commoner secondary infections complicating the individual fevers. Many, as regards their local features, are trivial, but, as I have endeavoured to make plain in the text of the essay, it is their constitutional influence on an antecedent pathological condition which makes them important. Extensive research has convinced me that this relation between local affections, often of a minor character, and grave general disturbance, has not been sufficiently recognised or accepted as a basis for definite treatment.

The subject of the Appendix involves a controversial element which will be avoided, my own opinion having been declared at the outset. Signs have not been wanting of late that the growing assurance of the bacteriologist as to the pathogeny of certain microbic affections has not been accompanied by a proportionate readiness on the part of the physician to accept the facts as proved. It seems to me that this is the result of the too early specialisation of a subject which involves such important clinical issues. It is the physician-bacteriologist, rather than the laboratory worker, with whom the verdict lies, and it is to be hoped that, in the near future, clinical bacteriology will assume the place which cannot be rightfully claimed either by medicine or bacteriology as a separate science.

ENTERIC FEVER

The necrotic lesion produced in the intestine by the primary Eberth-Gaffky bacillus provides the chief local lesion for secondary infection in Typhoid cases. The primary micro-organisms penetrate the mesenteric glands and are also found in the spleen. Gaining access to the blood-current their selective action comes into play and, in consequence, they are seldom to be isolated from it. The much-discussed question as to whether they are ever the cause, per se, of suppurative lesions bears upon secondary infection and is probably to be answered in the affirmative. They have been found alone in periosteal abscesses, parotitis, renal abscesses, and rarely, in post-typhoid ulcerative endocarditis. Experimental evidence suggests that if these infections had been originally mixed the secondary rather than the primary organisms would have survived.

The conditions induced by Enteric Fever are specially favourable to secondary infection. The conveyance of extrinsic secondary micro-organisms to the primary local lesion is made possible by the perversion of the gastric secretion. More than this, the disease is peculiar in that there exists normally in the region of the primary lesion a special secondary organism - the Bacillus Coli Communis - which multiplies with enormous rapidity under the abnormal conditions. It has been suggested that the primary toxins augment the virulence of the Bacillus Coli On the other hand the general toxic effect of the latter

must be very slight if Widal's reaction is to be taken as a measure of the resulting immunity. The Bacillus Coli follows the distribution of the primary bacterium, penetrating by means of the ulcers. It is abundant in the mesenteric glands and a common factor in the production of various remote suppurative lesions. The pyogenic cocci also obtain access to the tissues by means of the ulcers and are present with or without the Bacillus Typhosus and Bacillus Coli in various distant lesions such as meningitis. Bouchard has shown that the natural putrefactive process in the intestine is greatly increased during an attack of Enteric Fever and though the bacteria involved may not have the power of invasion the absorption of poisons generated by them beyond all doubt adds to the general intoxication.

A catarrhal condition of the respiratory mucous membrane is almost invariably present in typhoid cases, while ulceration, especially laryngeal, is by no means uncommon. In addition to the primary micro-organism streptococci and pneumo-cocci may be implicated in this condition. Among other complications due in part or wholly to pyogenic bacteria are otitis, empyema, and parotitis. Pneumo-cocci alone or with the primary bacilli are present in the congestive and broncho-pneumonic patches which constitute the commonest lung-complications. Secondary infection by way of bedsore should, in these days of scientific nursing, be impossible.

It is evident that intestinal antisepsis, while indicated in all zymotic diseases, is specially called for in

Typhoid Fever. Its wide vogue appears to be due to a belief that it modifies the virulence of the primary infection. If it could be adopted at the very outset, before the bacteria have penetrated the tissues, no doubt this result would be obtained and, in ordinary cases it may prevent that form of relapse due to infection of fresh areas. Holding this view I have prescribed, as a prophylactic, chlorine solution for persons subjected to exceptional danger of infection and with apparent success. That intestinal antiseptics can modify or abort the primary infective process when given after a clinical diagnosis is possible I do not believe, since no case of the kind has ever come under my notice. The great value of such substances lies in their power of inhibiting secondary infection, whether by the Bacillus Coli or the pyogenic bacteria and their still more remarkable efficacy in preventing intestinal putrefaction. As regards the drug to be selected, I am strongly opposed to the use of guaiacol, phenol and their compounds on the ground that their effect in intensifying the uraemic condition, probably by hampering excretion, far outweighs their undoubted power of arresting intestinal putrefaction. This is, of course, contrary to the generally accepted estimate of their value. Their reputation seems to be founded on their use in very small doses and in mild cases. My results in 100 cases of <u>severe</u> Enteric Fever, treated with creasote, can only be described as disastrous. The Sister who had charge of the series contracted the disease towards the end and absolutely refused to take the

drug! As already stated, I regard Yeo's chlorine-water as the best intestinal antiseptic. Free administration is essential, as much as two ounces being given to an adult every two hours. Although not pleasant to take, it is ant-emetic rather than otherwise. In spite of its reputation as an ideal non-poisonous intestinal antiseptic Naphthol appears in some patients to induce sudden coma, sickness and collapse. This is, also, contrary to the view commonly held. It has occurred to me that, in the cases above-mentioned, conditions favourable to absorption may suddenly arise. It is usual for the comfort of the patient to cleanse his mouth from time to time with such preparation as boroglyceride. In severe cases, instead of or in addition to such treatment I order the mouth, pharynx and nose to be thoroughly syringed with boracic lotion four-hourly, in order to discourage the lodgment of the secondary micro-organisms to which reference has been made. Patients seldom find this process irksome, and, indeed, many welcome it.

TYPHUS FEVER

This rare disease, of which I saw about a score of cases when in Liverpool, is peculiarly free from secondary microbic complications, abscesses in the cervical region alone being sufficiently common to require mention.

VARIOLA

Small-pox is specially interesting, as being a disease in which almost all the dangerous symptoms are due to secondary invasion and intoxication, the only exception to this rule being those strictly malignant cases - especially of the haemorrhagic type - in which death occurs in the earlier stage. The vesicles, when forming, do not contain secondary bacteria, but later, in addition to saprophytes, the Staphylococcus Aureus, with the Staphylococcus Cereus Flavus, always appears. In some cases the Streptococcus Pyogenes is also present. The incidence of these micro-organisms seems to be an essential feature of the unmodified disease and it would be a fair inference that the general preventive methods suggested in the text would have little or no influence upon it. Nevertheless, Bianchi has obtained favourable results by rendering the surroundings of his patients as nearly as possible aseptic. An improved application of the seropathic method is now foreshadowed as a prophylactic and curative method, but the difficulties are great. The red-light treatment appears to have a doubtful effect in modifying the bacterial activity. Having regard for the fact that in the stage of maturation the small pox patient is infected by a vast number of secondary pyogenic organisms the common occurrence of suppurative, and allied, complications is explained. Among such are conjunctivitis and corneal ulcer with its possibilities, including panophthalmitis (rarer than formerly); adenitis; otitis media and its

extensions; laryngeal ulceration, perichondritis and necrosis of the cartilage; bronchitis, lobular pneumonia and empyema; boils, abscesses, erysipelatous inflammations and cellulitis. Lobar pneumonia is comparatively rare and pyaemia no longer common.

Thorough syringing with boracic lotion controls some of the above conditions, especially the eye-complications. Anti-streptococcic serum, at best, can only influence one of the diverse infections, not always present in a considerable degree.

Owing to the strict isolation of small-pox cases invasion by other then ubiquitous pyogenic bacteria is rare.

VACCINIA

The question of mixed and secondary infection through the artificial lesion caused by vaccination is, needless to say, a burning one. No doubt the secondary organisms are more often introduced subsequent to vaccination, owing to want of care or cleanliness; but a recent public enquiry indicated the grave results which may follow mixed infection at the time of inoculation. Statistics following the general adoption of glycerinated lymph will throw an interesting light on the question of mixed versus secondary infection.

VARICELLA

Chicken-pox runs its course in the great majority of cases without complications having a secondary origin. A notable exception is the condition known as Varicella Gangrenosa in which there is probably a tubercular element.

EPIDEMIC INFLUENZA

The influenza bacillus is almost always associated with the pneumococcus or with pyogenic bacteria in the early respiratory complications which so commonly effect this disease. On the other hand the primary organism has been found alone in suppurating pulmonary foci and even in otitis media and meningitis. In lobular pneumonia it is usually associated with the Streptococcus Pyogenes or the pneumococcus: in empyema the latter organism is commonly present without it. The primary organism seems to exalt the virulence of the pneumococcus. Hence the lobar pneumonia of convalescence is most fatal, while the appearance of the diplococcus in distant secondary lesions, such as meningitis, is a further indication of this effect.

If the seropathic treatment of conditions due to invasion by the pneumococcus is placed on an assured basis, one of its most useful purposes will be the prevention of influenzal secondary infection.

WHOOPING COUGH

Pertussis, after diarrhoea, is the great cause of zymotic infant mortality, death being generally due to secondary lobular pneumonia. When this condition is followed by caseation of the bronchial glands the latter may become foci for a general tuberculosis.

RUBEOLA

This affection is practically free from secondary complications and it only requires mention to repudiate the theory ascribing it to a mixed infection by Scarlet Fever and Measles, against neither of which diseases an attack of Rubeola is protective (Goodall and Washbourne)

MEASLES

Measles, per se, is seldom dangerous, death being almost invariably due to secondary infection. As the primary disease is frequently regarded as a domestic ailment, and its connection with grave secondary complications is not always evident to the medical man called in late, or admitted by the child's parents, it is likely that the mortality due to it is much higher than is shown by statistics. The primary local lesion is an extensive catarrh of the respiratory tract and the conjunctiva, and, in a less marked degree, of the mouth and pharynx. In-

vasion by pyogenic bacteria commonly follows and the Streptococcus Pyogenes may be specially noted as the usual cause of broncho-pneumonia. Among other complications of the same class are cervical lymphadenitis and cellulitis; cancrum oris; pleurisy with effusion - usually purulent; blepharitis, conjunctivitis, corneal ulcer and panophthalmitis; otitis and otorrhoea; and noma vulvae. Lobar pneumonia is comparatively rare. There is susceptibility to other primary infections affecting the same tract as measles - as, for example, Whooping cough and Diphtheria, The latter is much commoner than is generally admitted and is of a most fatal type, being generally laryngeal. It especially affects the stage of defervescence, and its recognition is a matter of vital importance since the early injection of antitoxin provides a certain cure. During convalescence from Measles and for a considerable period afterwards, patients are prone to contract tubercular affections, generally pulmonary, but occasionally in the form of meningitis or peritonitis. For reasons stated elsewhere the complications due to pyogenic organisms are best prevented and mitigated by making the patient's surroundings approximately aseptic. This is borne out by the fact, generally admitted, that insanitary surroundings prejudicially affect the epidemic type. Antiseptic douches are, of course, also indicated, As regards tuberculosis, all milk taken by the patient during the period of susceptibility should be boiled and association with individuals suffering from tubercular infections avoided.

The following case is of interest as throwing a special light on the value of preventive methods I was called in by Dr A. to see A.C., aged 5, suffering from a severe primary attack of Measles then approaching its acme. The child's past history revealed a number of minor ailments, but nothing important, while, previous to falling ill, it had been in good health. Much anxiety was expressed by the parents as two brothers had died of measles with pulmonary complications and a sister had also suffered from a severe attack. Nevertheless a favourable prognosis was given although the mother expressed herself as resigned to the loss of the child, Precautions of an extreme kind were taken as regards cleanliness and antiseptics freely used. A.C. made a rapid recovery without bronchitic or pulmonary complications.

SCARLET FEVER.

In its malignant form simple Scarlet Fever is very fatal; but strictly malignant cases are rare and it is to the auxiliary or distinct effect of secondary complications that death is usually attributable. Whatever may be the nature of the primary organisms it appears to foster the growth and increase the virulence of the Streptococcus Pyogenes which is almost invariably present in cultures from scarlatinal throats. In certain cases, under favouring conditions, the streptococcal infection

becomes predominant, the immediate result being a marked aggravation of the local lesion, constituting Scarlatina Anginosa. Other cocci may be involved and, by extension, a variety of lesions may result. Among these are gangrenous conditions of the pharynx, suppurative tonsillitis, laryngeal oedema and ulceration; bronchitis, lobular and lobar pneumonia and empyema; rhinitis, otitis; adenitis and cervical cellulitis; blepharitis, conjunctivitis and corneal ulcer. Pyaemia originating from otitis or severe septic sore throat, may supervene, with such consequences as suppurative arthritis and periosteal and other abscesses. Scarlatinal nephritis is to be regarded as having a primary toxic source although streptococci have been found in the kidneys in some cases. Scarlatinal rheumatism in light of its age-incidence, is probably not due to a secondary infection and appears also to differ from ordinary acute rheumatism. Certain considerations suggest to me the possibility that it is caused by the natural Scarlatinal antitoxin formed during the acute attack and circulating in the blood: this, however, is little more than a surmise. The so-called typhoid type of Scarlet Fever is apparently a modification of Scarlatina Anginosa. In the latter the local toxic effects overshadow the general toxaemia, while in typhoid cases the reverse obtains.

There is a form of toxaemia, appearing sometimes with, but usually after, the primary defervescence, which has a striking individuality, and, indeed, possesses all the clinical features of a distinct disease. Generally

there is slight diffuse pharyngitis and the mucous membrane at each side of the base of the uvula is ulcerated, so that there results a crack or chink with a greyish-yellow floor in consequence and the uvula appears to be somewhat elongated. The general toxic symptoms closely resemble those of diphtheria, minus the paralysis. The Bacillus Diphtheriae is absent. The onset is evidenced by a slight and transient rise in temperature, with sore throat. This is followed by apyrexia, the pulse becoming progressively weaker. In a few days, sickness, more or less persistent, sets in, and there is often oliguria. The patient's mental condition remains clear until death which is seldom postponed beyond a week. Rapid emaciation is invariable. These symptoms might be regarded as uraemic; but many considerations place such a view out of court. I have seen about a dozen fatal cases. The affection appears to be described by Goodall and Washbourne as a variation of Scarlatina Anginosa. I am satisfied, however, that the conditions are distinct. Nevertheless, cultivations from the throat reveal no additional elements.

Post-scarlatinal Diphtheria is a form of secondary infection both common and grave. It may be, as some hold, that the virulence of the Diphtheria bacillus is exalted by association with the primary micro-organism or the secondary streptococcus. It is more likely that the primary lesion provides a specially favourable nidus. In any case, growth is usually vigorous and the larynx frequently implicated. Although the infection usually

supervenes after defervescence, the occurrence of membraneous exudation on the tonsils in the acute stage should always be followed by a bacteriological examination - or, if this is impossible, antidiphtheritic serum should be injected. The fact that this serum, in preference to the anti-streptococci preparation, has been recommended for Scarlatina Anginosa without a diphtheritic element, makes this treatment doubly justifiable.

DIPHTHERIA

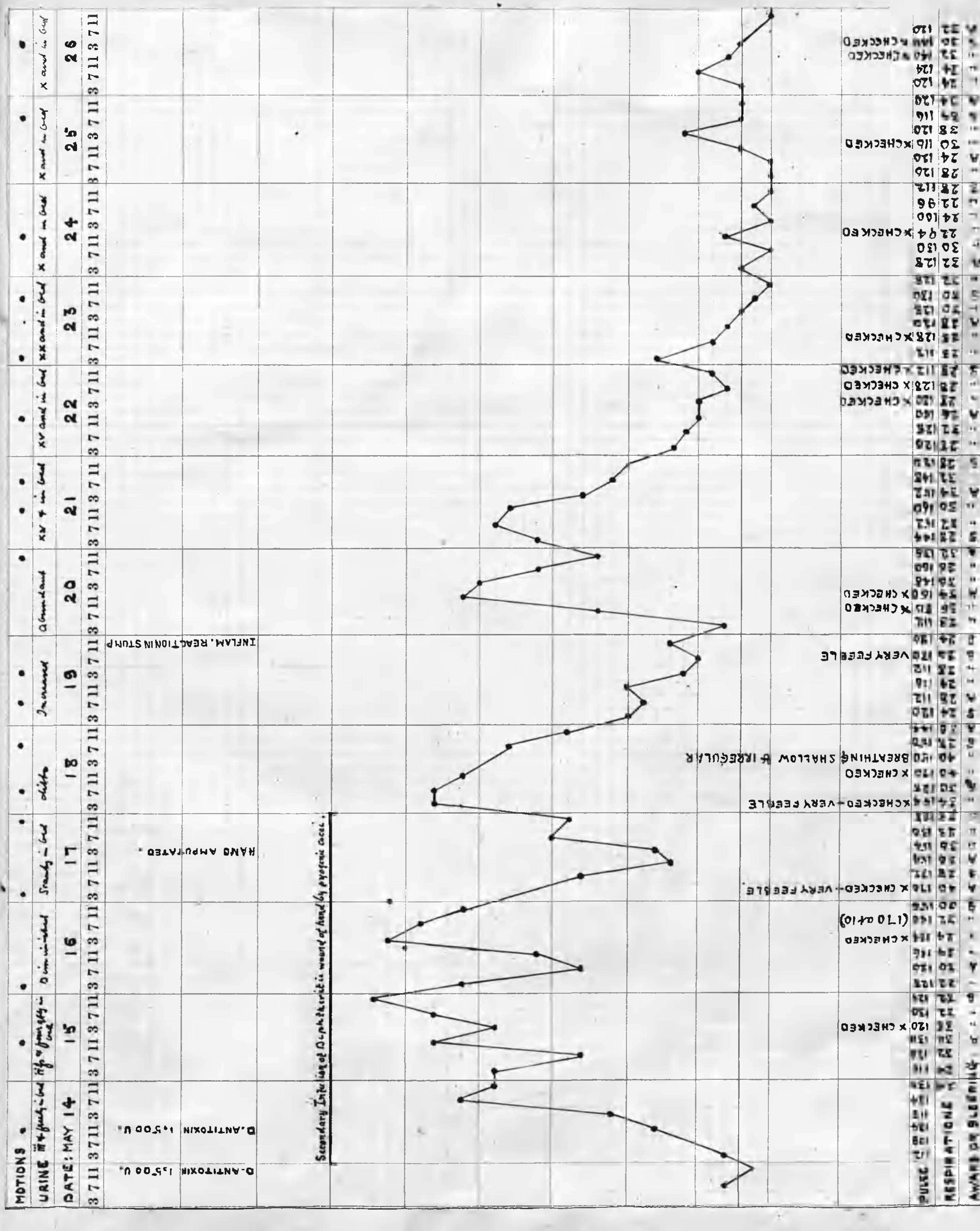
As in the case of Scarlet Fever, so in Diphtheria, the commonest secondary micro-organism is the Streptococcus Pyogenes. It is frequently associated with the Bacillus Diphtheriae in the local lesion, but penetrating more deeply. Some maintain that it exalts the virulence of the primary organism while others take the opposite view. Culture experiments favour the former opinion. My clinical experience is that, as a result of the mixed infection, the purely diphtheritic symptoms are mitigated but that the result is not necessarily more favourable, since the effects of the foreign intoxication - notably a prolongation of the febrile state - may add tp the gravity of the case. Oliguria-not necessarily associated with albuminuria - is more marked, prolonged, and dangerous than in any other infectious condition. The same mixed infection is the common cause of lobular pneumonia, the streptocuccus preceding the bacillus in the process of extension. The Streptococcus may, as in Scarlet Fever,

produce lymphadenitis, cellulitis, conjunctivitis, and otitis, Ulceration and gangrene of the pharynx and lobar pneumonia are also due to secondary infection. In these conditions the Staphylococcus,Pneumo-coccus, and, rarely the Bacillus Coli may be involved.

The following case is, I believe, unique as regards the location of the secondary infection and its removal by amputation. Wound diphtheria affecting the hand is not excessively rare, and is usually free from danger to the patient, but I have never known it to be followed by grave secondary infections. When the advisability of operating was under discussion I was unable to recall or find any record of a parallel case.

On May 12th, 1897, I saw Alfred P. aged 20 months in consultation with Dr Griffen. The patient was a fat, vigorous child with an excellent past and family history. Two weeks previously he had scratched the back of his hand somewhat severely in the space between the forefinger and thumb. The wound had almost healed without dressing. On May 3rd, he was noticed to be ailing, and on the following day the mother noted that his throat was sore. On the 5th she saw a milky deposit on the tonsils, but did not send for a doctor, although Diphtheria was prevalent in the street. On the same evening she remarked that the wound on the hand looked "angry", the patient being in the habit of sucking his thumb. On the 6th, Dr Griffen was called

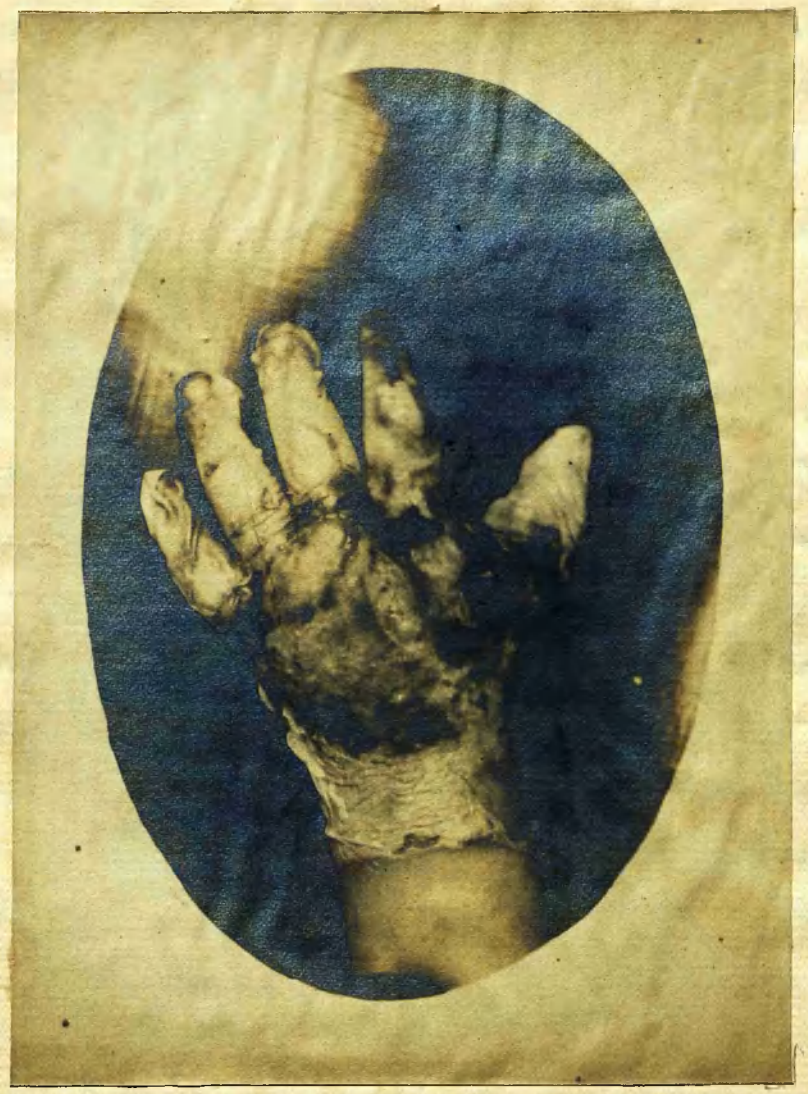
CHART OF A.P.'S CASE



in and diagnosed pharyngeal Diphtheria, but was not shown the hand. On the following evening, however, he found the wound covered with a distinct pellicle, the whole back of the hand being oedematous and the fingers slightly swollen. He ordered boracic fomentations four-hourly. Two days later the membrane on the wound was typical and the swelling had much increase, When I saw the patient on the 12th, there was still a diffluent patch of membrane on the left tonsil, with traces on the right. There was a slight discharge from the nose, but the cervical glands were not perceptibly affected. The urine contained a distinct trace of albumen. The temperature was 100° Fahr., the pulse 104, rather poor and small, but not irregular. The heart and lungs were normal. The left hand showed on the inner and posterior aspect of the base of the thumb a ragged purulent ulcer, fringed, near the upper end by a few threads of grey membrane. Dr Griffen had removed the greater part with forceps on the previous day, and in order to relieve the tension had made an incision almost in the centre of the back of the hand (faintly discernible in the photograph). My diagnosis was faucial Diphtheria with later infection of the hand owing to the patient sucking his fingers. The same evening he was removed to hospital and placed under my care. The diagnosis was then bacteriologically confirmed. Antitoxaemic treatment was adopted including the injection of 3,000 units of antitoxin. The hand

PHOTOGRAPH OF A.P.'S HAND TAKEN ON

THE DAY BEFORE AMPUTATION.



continued to be treated with the boracic dressings. On the morning after admission the pus from the incision was noted to have a faint blue tinge, and the Bacillus Pyocyaneus was demonstrated by cultivation. On the 15th there was no longer any trace of faucial exudation. The hand was gangrenous, all the fingers being hopelessly implicated. The organism of diphtheria could no longer be found, but a smear preparation showed many other bacilli and some staphylococci. At the wrist there was typical erysipelatous inflammation with a sharply defined advancing line. Blood from the margin, on incubation, showed the presence of numerous staphylococci and a few streptococci. The patient's pulse was now 170 and exceedingly feeble, while his temperature was frequently above 103° Fahr. His general comdition being extremely critical and the hand beyond recovery, Mr Allen saw the case with me and, on avowedly surgical grounds, advised immediate amputation. From the medical standpoint I considered that death could only be averted by the removal of the source of secondary intoxication - the more as the urine was running down in quantity. Accordingly on the 17th, after the desperate nature of the remedy had been explained to the paremts, Mr Allen amputated the hand above the wrist. The appended photograph was taken on the previous day. While under chloroform the patient very nearly died of syncope. He was afterwards in a very low condition and showed

no improvement until the 19th, when a sustained change for the better set in. The stump healed very slowly. Seen some months later, the patient was in vigorous health.