I do not wish to go into the general subject of aphasia more than is absolutely necessary, and therefore I shall use scarcely any of those extremely technical terms which have grown into use of late years. I rather prefer to take it, as it were, from the physiological side, and to leave the anatomical questions as much as possible out of consideration. Still I cannot help saying that word or two. Twenty years ago, aphasia was chiefly regarded as localised in, and associated with, what is called Broca’s convolution—that is to say, the foot of the third or inferior frontal convolution, which, with a part of the foot of the frontal convolution, constitutes what is called Broca’s lobe considered as a speech centre. But we are now obliged, partly from the physiological and experimental evolution of the subject, and partly from the actual clinical developments of it, to recognise that there are at least four centres of localisation in the brain, lesions of which may affect the power of speech and of writing language. There is the Broca’s convolution, and there is the auditory centre which lies somewhat further back, these playing upon one another, the auditory centre transmitting to Broca’s convolution the impressions of spoken words through the ear, and the mechanisms of speech, again, being set in motion from Broca’s speech centre in the brain; so that these two centres are concerned chiefly with the reception and the production of words. When these two centres are connected by a general ascending system connected with graphic language, with written or printed words—that is to say, the speech which goes by the sight. The two centres just mentioned are concerned in the communications of speech by the way of going into, and going out, while the other two refer to the communications through the eye and the hand, both going in and going out. I think that is almost all I shall think it necessary to trouble you with on the subject of localisation. There is a fifth centre, but I think Dr. Lister and most people admit that the localisation of this is not very easy. It is supposed to be the centre of ideation of the word as apart from the mechanism for the production of the word. That centre is still not definitely localised, and therefore to a great extent we must keep it out of account. It will be sufficient for the present purpose to take account of what I am in the habit of calling the ingoing and outgoing mechanisms, and if we still further divide these into those that spring from the auditory centre (those that go by the ear to the speech centre) and those that go by the eye to the speech centre, and the corresponding ingoing mechanisms of utterance and writing, I think we have got enough of subdivision for our present purpose.

THE MENTAL STATE OF APHASICS.

Now when we come to consider further, we are confronted, in the first place with this ideal question, which also becomes a practical question: Is aphasia consistent at all with integrity of the mind? In other words, is a man who is an idiot necessarily deprived of all the powers of his mental capacity, that is, to say, does he, in respect of his infirmity, necessarily depart somewhat from the normal condition of mind, so that you must regard insanity as a part of his complaint? That is a very difficult question to begin with, and I cannot afford to deal with it at length. Most of you know the ingenious argument which Professor Max Müller has founded upon the Greek word logos, and although I do not go to the extent of Max Müller’s contention, yet I admit there is a great deal in it. “Logos,” in Greek, signifies the word, but “logos” also means the thought, the reason. Max Müller says that one expression does for the word and for the thought which the word represents. In point of fact, he says these are two different aspects of the same thing, and they are practically inseparable. If that is the case, then you might infer that, philosophically speaking, a man who is aphasic is to that extent deprived of reason, but I do not think we can accept that as a conclusion. I say, and I am willing to concede, however, that a human being who had never been otherwise than aphasic, who was congenitally deficient, let us say, in Broca’s lobe, or in any of the mechanisms which go to make the speech faculty, could never grow to the use of logos, and so on. Of the two, I think the one above the level of a dog, an elephant, or a horse. That is what I should be willing to concede. But when we come to the case of a man
who is, by a sudden accident, lamed as regards the mechanism of this particular faculty, having had all his reasoning processes well developed beforehand, I am unwilling to admit that he necessarily suffers any derogation at all of the higher faculties, although I may be pressed into the admission that theoretically he suffers, or is likely to suffer; or, later, in some degree. Of course, practically, he may suffer in almost any degree, because other faculties besides speech may be incidentally involved, as, for example, when an aphasic is also comatose; but that is all I can admit. The complex or practical laming of one faculty interfere with a man's capacity to make a will? I do not think that is a question which can be answered in any general sense, but in order to get on the lines of our subject I must direct your attention to what is the legal position in making a will, how much intellect it requires, what, even in cases that are not aphasic, are considered to be difficulties or doubts in the way of constituting a legal disposition of property, and on the other hand, the extent to which the legal instrument, commonly called a will, maintains itself against difficult positions by the force of its own character, as it were. These are all very curious questions, and I should hardly trust myself, not being a man of any legal information, to give an answer to these processes. It is not very lucky for me that we have had the subject presented within the last few days by the Lord President of the Court of Session, Lord Robertson, in words which can hardly be exceeded in admirability. The position he has taken up to the least thing with nothing to do with aphasia; but, nevertheless, if you are dealing with a lordship a statement as to the legal position in respect to testamentary capacity; a statement which I have never seen exceeded in precision for our present subject. There are, no doubt, Englishmen here present, and perhaps it may not be quite clear to some of them how far the legal position is the same in England; but all I have to say upon that is that if the law and the state of the facts is not the same in England, you will have to show cause, as the law would be different, and it is not any may depend upon it that we Scotchmen will maintain that our way is the right way, and that the Scotch law, founded on the civil law, and coming down to us in a long process of generations, is a much superior law to the English judge-made law, which is a thing of shreds and patches. Taking the Scotch law, I take it for granted that I am presenting the real first principles of the whole subject; and the English law, so far as it is not in accordance with those principles, and which as a law is as good as principles, is not as a law good as principles. I think, therefore, that Lord Robertson said this: "He must remind them (that is, the jury) that they had not got to try the question whether in the general sense the woman was sane or insane. The question was not what the law would say, but to what extent the person is capable of expressing a particular will—and had she enough mind to understand it, and did she understand it?—because there were many people in this world who had got what might be called a crack in them, and were really eccentric, and yet their wills were perfectly good. They might think that it was too complicated for the woman; and if so, then they would find against the will. On the other hand, they might think, although they had heard a good deal of trash about the woman's eccentricities—"observe the contemptuous way in which his lordship brushed as if all mere theoretical inferences tending to aptly state—"[that still she had enough sense to make a will if it was a will that she could understand. It was to be observed in favour of the will that it was not very complicated if they thought the woman really wanted it, they would have to consider whether there was satisfactory evidence that her mind was applied to it; but in the meantime, as regards the woman herself, no doubt she was a person of rather low intelligence. She had not been well-educated, and she was in a curious sort of case. Had the jury gone into the details of the case, with which I will not trouble you, and then comes this important statement: "They were left a good deal in the dark as to what share this woman had in the will. It was a will of M. Pasteur. His lordship's own impression was that she did not want the money. But it was for the jury to say whether this will was her will. They must not break the will unless they really thought that either she was unfit to make it that she had not sufficiency of mind to make it, or that she was weak and was led into making it by other people." I think that is very much in accordance with the way in which I put it in a letter to the British Medical Journal not long ago (June 12th, 1897), but in reference to an aphasic case that was written in a regular document, which is drawn up in reasonable language and signed by two independent witnesses, maintains itself in the eye of the law—it proves itself, as it were; in other words, it throws the onus probandi entirely on those who dispute its validity, and afterwards prove that he did not make the will or that he did not know what he was about, that he was not fully conscious of what he was doing when he made it, or, on the other hand, that he was misguided by interested parties, the will holds, and must hold. That is the position of the law at present in Scotland, and I believe also in England.

How is that position altered by the case of aphasia? To make a long story short, I would say that my view of it is briefly this. I might say a great deal more about the details, but my view of the principle is briefly this, that the fact of aphasia shifts the onus probandi. The fact of aphasia (unless it be very limited in extent), interferes either with the graphic and visual speech processes or with the auditory and vocal processes and throws the onus probandi upon those who consider the will genuine, or wish to prove the will genuine. It makes a difficulty in the way of a testator giving expression to his true desires and his true will, and those who suppose that the difficulty was successfully overcome. This is not saying that the will is technically bad because it was made by an aphasic person; that is not the position I am taking at all. I hold that an aphasic person—I will push it to the full length of saying it is a man completely aphasic, but not otherwise insane or stupid—has, as regards his inner mind, probably the full capacity of making a will of some kind. I do not say as good or as elaborate a will as you or I could make, with the assistance of a lawyer, but he has quite sufficient to meet those requirements required for a simple and natural disposition of this means.

I take for an illustration of this the case of M. Pasteur, who had a left-sided paralysis, a lesion therefore on the right side of the brain, when I met him in London in 1881; nevertheless, he continued to manage that admirable laboratory of his, was the administrative head of a large scientific research department, and of his mental capacity no mortal can entertain a single doubt for a moment, even for much more complicated and difficult work. Happening to meet once, an aphasic, of course; but he might have been so, had the lesion been on the other side of his brain. Now M. Pasteur made the shortest and the simplest will that I ever heard of. It was this: "I give all my goods,动词, and possessions that I have to my son. For the purpose of that, instead of being on the right side of his brain, that lesion had been on the left side of his brain, even if Broca's lobe, or the auditory centre, had been destroyed, that M. Pasteur would not have been able to form that will in his own mind, would not have been able to make a valid will, and leaving everything to his wife, provided he could have, somehow or other, by signs, or in some way, positively and clearly impressed everyone that that was his will, and had got that intention, somehow, put into a proper legal form? I have no doubt whatever as to that leg, which, nevertheless, may be quite clear if the testator could only get it out.

Now the question is, how far these difficulties go in a particular case. Dr. Bramwell, who I hoped would have been in this Section, has the industry, the completeness, and the only fault of it is that he has made it so excessively complicated in his way of stating it, that I am quite sure if I read the whole of it you you would be quite overwhelmed (as, indeed, I am myself) with the ex
treme subtleties of the argument. There are, perhaps, one or two points where I should be disposed to differ from him, but I am not going to speak on that juncture. There is quite concur with him in his general statement of principle that the question whether an aphasic person can make a will and how far he can make a will, is a question of detail entirely; it is a question which must be submitted to a jury on the basis of the individual facts and circumstances to which we have got to be brought in a court of law, not upon any abstract principle at all— I have stated the principle as far as I think it will go— but upon the individual details of the individual case. In fact, I apply to aphasia just the same rule as I apply to Boethus. There are expedients, as I have said, which is not a general question of law, it is not a thing which can be put into legal or into physiological categories at all. The question in that individual case was, Did the woman know what she wanted? Did she form a clear conception of what she wanted, and did she succeed in giving effect to that conception in the particular document that passed for her "will"? Or was that document not really her will at all, but inspired or instigated unduly by others taking advantage of her失效ness? Was he concerned where the question of interference and of the legal matters must have been to the court about the case; because even as regards the simple assent or dissent to a simple proposal it was found impossible to obtain a clear or consistent "Yes" or "Nay." Yet this gentleman said, in a general way, clear enough in his intelligence except as regards language, and there was no apparent ground for questioning his sanity.

Another case which I want to refer to is the one I myself stated in a letter to the British Medical Journal of June 12th, 1887, but as it is all in print, and as it contains a great deal of the substance of what I have said, I will not detain you with it. It is the only case in which I have been personally concerned where a dispute has arisen about an aphasic will; and it would have been a very curious case indeed had it come into court.

There is just one more case to which I must briefly refer. I saw in consultation a great many years ago a gentleman who became aphasic as the result of a hemiplegic attack. A friend of mine had married his daughter, but I did not see much of this patient latterly, as he went away to reside in England, where he died. Since this discussion arose I took occasion to enquire whether he had written a will after he became aphasic. I found he had not, and further enquired whether he would have liked to have done so, but the conscientious people who were about him did not think he was competent to do it, and thus, although he was, in a sense, all right as to his mind, he was so deficient in the power of expression as to have been regarded as not competent to give effect to what he would have liked to have done. And thus (as his son-in-law wrote to me lately), though almost any change in the disposition of his property after his daughter's death, he had made it, would have been more or less in the interest of her family, and although his own wishes were not stated, it was all right to have what he wanted (in a general way) were known to them, yet the difficulties to be surmounted were such that (although the son-in-law was a medical man) no attempt was ever made to put anything on paper, the original disposition (made before the aphasia) remaining unaltered to the last.

I regret very much that the exigencies of time and of space preclude me from making any more detailed references to these and other cases, and also from discussing the general subject more at large with relation to the different kinds of aphasia and agraphia.

POSTSCRIPT BY SIR W. T. GARDNER.

As this case is a really curious one, and is certainly not to be more particularly recorded, it may be as well here to insert the precise terms of the letter referred to by my friend whom I shall call Dr. X. The aphasic patient is referred to as Mr. Y.

"In reply to your letter, Mr. Y. made no will after his seizure; the estate was dealt with in terms of a will made before his marriage with his present wife before his marriage to my wife's death; my wife died before her father. For convenience of all parties interested he signed a document giving power of attorney to his two sons to give receipts for dividends, etc. I do not think he knew what he was doing then, but it was a matter in which everyone was in agreement. Had he been able he would, I am sure from a conversation I had with him after his daughter's death and about a year after his seizure, have altered his will somewhat. We were very much surprised to find that after his daughter's death would have occurred before his own he would have arranged differently. But he was never in a condition to give a clear assent to any special point. He was to the end confusing and misnaming coins, dates, and occasionally people.

II.—WILLIAM ELDER, M.D., F.R.C.P.F.,
Physician to Leith Hospital.

Whether a patient who suffers from aphasia is capable of making a valid will (or exercising his civil rights) is a question which it would be as absurd to answer with a "Yes" or a "No" as it would be to answer in a corresponding affirmative or negative fashion the question whether a patient suffering from cerebral tumour is capable of making a will or not. Each case must necessarily be judged on its own merits, and an answer given according to the symptoms which the patient showed at the time that the will was made. At the same time the general principle which I am putting forward must be taken into consideration in all cases of aphasia. To state it briefly, it is this: What amount of intelligence or mental capacity in a person is necessary in order that the testamentary act which has been executed by that person may legally stand as his will—or what amount of intelligence or mental capacity is it necessary for a person to show in order to give directions to his property? What amount of mental capacity or mental power of thinking or using the mind must a person have in order to make a valid will, and what amount of intelligence, or mental capacity is it necessary for a person to show in order to give directions to his property? What amount of mental capacity or mental power of thinking or using the mind must a person have in order to make a valid will, and in order to make a valid will, must that person have the use of his lucidity of thought and of space?
capable of carrying out in his actions what he psychologically intends; because, as is well known, to take a simple case it is quite possible that a person may mentally desire to say “No” and “Yes” by the outward expression of his mental action.

It must be laid down as a general principle that no one can make a will which does not possess the power of understanding and of producing language of some sort; I use the word language rather than speech because it is not so apt to lead to confusion. If a will is to come to be used in almost as general a sense as “language,” in order to make a will it is necessary for an individual to be able to communicate to others by means of some form of language what he would like to be done after his death.

It is necessary by law that the wishes or desires of the person be put in writing. It would not, for instance, be held to be a will if a person simply indicated by signs before he died that he wanted such and such a thing done, nor would it be held to be a will if a person gave directions by word of mouth.

The simplest and most primitive form of will is a holograph will—that is, a will written and signed by the testator himself. The law, however, recognises a will that has been written by someone else, provided it is signed by the person making it. In these cases, however, it is necessary for the signature to be attested by witnesses. The point I wish to make just now is that it is necessary for a person to be possessed of at least some language in order that he may make a will, although the amount of language may not necessarily be much.

He must be capable of understanding language, so that he knows either what he reads or what is read to him. This implies that he can hear and understand words, if he cannot read nor understand pantomimic language; but if he can read and understand what he reads, it is not necessary for him to hear nor understand pantomimic language. If he can understand pantomimic language, the question might arise whether it is necessary for him either to be able to hear or to read. Of course, for a person’s intelligence to be reached in other ways, as, for instance, by means of the muscular sense. On the other hand, given that a person understands what is in a document by any of these methods, it is not necessary that he be able to speak in order that he may execute a testamentary deed. He may indicate what he wishes by means of writing, or by pantomime, or in other ways. How, therefore, would the symptoms of the different forms of aphasia affect the testamentary capacity of a patient in each form of aphasia?

From the one form of aphasia of Broca, the varieties have increased till at least one author recognises twenty-eight, but these varieties are only theoretical, and practically there are four clinical types, although I believe several varieties of more or less resemblance of each of these types are seen occasionally. Of these types, two are sensory, and are an interference with some part of the reception and understanding of language mechanism, and two are motor, and are an interference with some part of the mechanism which has to do with the production of language. The sensory are: (1) auditory aphasia or word-deafness; (2) visual aphasia or word-blindness. The motor are: (1) motor aphasia or aphemia; (2) graphic aphasia or motor agraplia.

There are the general symptoms affecting the mental or intellectual capacity of the patient which may be shown by the subject of any cerebral lesion, and have a very direct bearing on the question of testamentary capacity. I put aside, however, those symptoms, and limit myself to the symptoms peculiar to each variety of aphasia.

AUDITORY APHASIA.

A person suffering from complete auditory aphasia would be incapable of making a will. Complete auditory aphasia not only implies word-deafness but also word-blindness, because it is necessary for the auditory word centre to be capable of acting in order that a person may understand what he reads, so that the person with auditory aphasia would not as a rule be able to read inter alia nor would he be able to understand what was spoken or read to him. The understanding of pantomimic language might also be lost, but if it were present it would certainly be very difficult to communicate to such an individual the contents of a testamentary document. It is possible, of course, that a person both word-blind and word-deaf might have acquired the power of reading by the touch and muscular sense, but such a case would be very exceptional.

Being able to understand any form of language, he would in all probability not be able to communicate his wishes by producing any form of language. In auditory aphasia, if the motor articulatory centre acts at all, the patient is paraphasic, that is, he can speak words but these words do not necessarily imply the correct ones, nor is he able to correct himself, because he cannot hear what he has said. Often such cases talk gibberish, especially if the auditory centre is not completely destroyed, or if the right auditory centre is particularly active.

His other productive language centres are even less capable of communicating with his fellow-men than his motor articulatory centres. If he can write at all, it is only some very familiar words or letters, such as his signature or even the first letter of his signature, and he may show “letter or familiar word intoxication” in writing. It is to be noted, therefore, that a signature present on a document is no evidence that the person understood a word of what was in the language, nor is it evidence that the person had command of any language, but is efficient even to write. The signature in such a case is written automatically by the graphic centre, and is analogous to a reflex act.

As a complete auditory aphasia is therefore incapable of making a will, so probably are all cases in which there is a distinct impairment of the auditory word-centre. In cases in which the impairment is very slight, then the symptoms of paraphasia and paraphasia are often more distinct, the patient on the one hand being able to understand spoken and written words better, but on the other hand producing language more freely, but often quite inaccurately. In such cases it would often be very difficult to say whether such a patient was capable of executing a will, and the same might apply in cases of conjugation aphasia, in which the auditory and visual word-centres escaped altogether, but the patient only showed the symptoms of paraphasia and paraphasia with word-intoxication. These cases understand what is said to them, and can read writing and speak printed language, but there is a tendency to speak or write, they use the incorrect words and repeat themselves. They know, however, that they have spoken or written incorrectly, but still it might be difficult to say whether they were capable of making a valid will.

There is one very rare form of auditory aphasia that must be put on a different footing from the others, and that is the infrapictorial or subcortical variety, where the patient cannot hear words, but can understand written and printed language. Such a case would be capable of executing a will provided he had education sufficient to read, but he would, of course, not understand what was read to him.

VISUAL APHASIA OR WORD-BLINDNESS.

Here we would practically have to consider whether we had to do with a case of pure word-blindness (infrapictorial or subcortical visual aphasia), or of cortical word-blindness (pictorial or cortical visual aphasia). In subcortical (or pure) word-blindness, the patient would not be able to read and understand either printed or written matter, but he would be able to hear and understand spoken language, and he would be able to speak and write correctly. Such a patient, therefore, might be quite capable of making a will, provided the contents were read to him or he wrote them himself; but the case would be different with a patient suffering from pictorial or cortical word-blindness. In that case he would not be able to read nor understand written or printed language, nor would he be able to write either voluntarily or to dictation. It is to be noted that here also, I believe, such a patient is quite capable of writing his signature, or very familiar letters, by the automatic action of the graphic centre. But even then the fact of the presence of his signature to any document, even although he might understand what was in the document from having it read to him, raises the very interesting question as to whether such a document would stand, provided he carried out the legal formality necessary in Scotland of getting a notary to sign for him in the presence of
witnesses. I believe that in a case of uncomplicated cortical word-blindness the patient is quite capable of making a will, provided the contents are accurately read out to him before he gives instructions to the notary to sign for him. The patient has practically in the position of a person who is blind, with, of course, the additional general symptoms due to the fact of his having a cerebral lesion.

Motor Aphasia or Agraphia.

In this condition the testamentary capacity would vary according as the lesion was in Broca's centre alone (pictorial or cortical motor aphasia), or subcortically to Broca's centre (infrapictorial or subcortical motor aphasia), what Bastian calls aphasia, Banti, however, and I believe, almost always agraphic. If infrapictorial or subcortical motor aphasia, the patient can read and understand written and printed language, can hear and understand spoken language, and can write either voluntarily or to dictation, and therefore could write his own will; but it might be difficult for anyone to take directions from him for the making of his will, as he would not be able to speak; but if an educated person, his knowledge of language would be so perfect that he would be able to read will before he signed it. Hysterical mutism I believe to be the functional form of this variety, and hysterical mutes, therefore, are capable of making a valid will.

In cortical or pictorial motor aphasia we have a different condition, however, and I am afraid there must still be some difference of opinion as to the testamentary capacity of patients suffering from the uncomplicated form of this disease. Until within the past few years it has been believed that patients suffering from this form were almost always agraphic. Bastian has, however, produced evidence which he believes proves that patients with a lesion in Broca's centre, if limited to the third left frontal, do not suffer from agraphia. The chief part of that evidence is a case published by Guido Banti, but I cannot say that that case nor the evidence that Bastian has adduced is quite convincing, and the question is therefore still in doubt. This, however, is not the place to enter into a discussion of this question. Sufficient is it to mention it, and to get over the difficulty by stating that clinically by far the majority of cases have agraphia as well as motor aphasia, and therefore these cases would not be able to write a will, and if they signed such a deed, the signature would be an automatic one, and the will, to be legally executed, would in Scotland require to be signed for him by a notary in the presence of witnesses. But there is another point about these cases still somewhat in doubt, that is, whether a patient with pictorial motor aphasia can read and understand what he is reading. I believe that some can read and understand what they reading, and some cannot—the difference depending on the particular psychic constitution of the individual and the method of his education. Patients with cortical motor aphasia can, however, understand what they hear, so that if a deed was read over to them they would understand its contents, and they could give instruction by pantomime to a notary to sign for them in the presence of witnesses. Here a legal question might arise as to whether the instructions given by pantomime would be considered sufficient.

Graphic Aphasia.

No true case of cortical graphic aphasia has been authenticated, but in such a case the patient would be able to hear and understand spoken speech, to read and understand written and printed language, and to speak correctly, so that his knowledge of language would be complete except that he would not be able to write. He could, however, give instructions to a notary to sign for him in the presence of witnesses.

Similarly with cases of paralysis of the right hand due to subcortical lesions or lesions of the cortical centres for the right hand, the patient could execute a testamentary deed by giving instructions as in the last case, or he might write with the left hand. In this connection a very interesting point might arise, if in those cases of lesions subcortical to the centres for the right hand the patient sometimes, especially if he has been an expert writer, may, when he attempts to write with the left hand, write in the peculiar way called mirror writing. I have elsewhere given my views as to the explanation of this. I believe that the left hand in such cases is guided by the graphic or cheiro-kinesthetic centre on the left side, the impulses passing through the callosal fibres to the centres for the left hand in the right cerebral cortex; but whatever the explanation of such cases, a case might arise where a patient who, though left-handed, had a lesion in the internal capsular or subcortical lesion might write his own will in mirror writing with his left hand, or might sign his will, writing in this mirror fashion.

Such mirror writing, as I have pointed out elsewhere, is often an exact reproduction of his ordinary right-hand writing when looked at in a mirror. A person writing a will in this fashion ought, I believe, to be considered quite capable of executing a testamentary deed if his other symptoms did not point to incapacity, but it is questionable whether it would be held valid by law.

Conclusions.

The conclusions I would draw from a consideration of the whole subject are:

1. That organic diseases of the brain may render a patient incapable of making a will, and that some form of aphasia may be produced also as one of the symptoms of the organic disease.

2. That some forms of aphasia may render a patient incapable of will making.

3. That auditory aphasia, if at all well marked, incapacitates a patient from will making.

4. That some other forms of aphasia, such as pictorial word-blindness, pictorial motor aphasia, and graphic aphasia, may render a patient incapable of making a will, not necessarily from being mentally incapable, but from the difficulty of carrying out the legal formalities.

5. That these difficulties in carrying out the legal formalities necessarily vary according to the law of the particular country.

6. That simple uncomplicated cases of infrapictorial auditory, infrapictorial visual, and infrapictorial motor aphasia, are capable of valid will making.

III.—T. S. Clouston, M.D., F.R.C.P.Edin.,
Physician Superintendent, Royal Asylum, Morningside, Edinburgh.

Dr. Clouston said there were two points which he insisted every man must attend to. The first was the test question, whether it was the will of the individual, or whether it had been suggested to him. The second was that in making the will of any aphasic patient it was the duty of every medical man and lawyer to put the contrary case. A man had a property of which he was to dispose to his wife and his daughter—to A. and B. They were bound to ask him if it was for B. and C. or for D. and E. that he intended the money. No will of an aphasic, in spite of any judge or doctor, could be a legal and proper will unless the doctor had put the contrary case, because an aphasic could not act in a contrary way if put to him in a certain test case. It was essential that the mental condition of the would-be testator should be tested by a medical man. Dr. Clouston concluded by urging that two practical points in the actual making of the will must be attended to: (1) Test whether the document is his own, and has not been suggested by others; (2) Put the contrary proposition, or a different proposition, twice at least as to sums disposed of, and as to the persons to whom the money or property is left. No will can be valid where these two points have not been most carefully gone into.

[I was found necessary owing to the pressure of business to stop the discussion at this point.]

A DISCUSSION ON

THE PLEA OF INSANITY IN CRIMINAL CASES.

I.—Chas. A. Mercier, M.B., M.R.C.P.Lond.,
Lecturer on Neurology and Psychiatry, Westminster Hospital Medical School, and at the Medical School for Women, London.

The controversy between the medical and legal professions that has raged for so long round this subject is now rapidly extending. Judges, while adhering, as they consider them-
selves bound to do, to the terms of a well-known formula, contrive so to interpret that formula that upon the whole substantial justice is done. Medical men, recognising that upon the whole substantial justice is done, cease to contend for an absolute and perfect formula; they do not desire to contrive that such a formula might be found. after all, to be inapplicable to outlying and exceptional cases without that laxity of interpretation which renders the present law practically effectual. No useful object can in my opinion be served by a prolongation of this controversy, and I do not propose to have any more to say with regard to it.

**What Mental Conditions should Exonerate.**

The aspect of the plea of insanity which does demand discussion at the hands of medical men appears to me to rise upon this: Are medical men, who are physicians to the mental conditions which ought to exonerate a criminal from punishment, and if so, what are these conditions?

The first question must, I think, be answered in the negative. I know of no statement of such conditions that has received the general assent of the profession. Several propositions purporting to formulate these conditions have from time to time been proposed, but no one of them has succeeded in obtaining universal or even general support. To every one of them the doctors of the law have opposed, and been at least as strenuous as the opposition from without our ranks. While, therefore, we inhabit a dwelling so copiously provided with glazing, it would be well to refrain from the recreations of law and medicine with those agreements which have hitherto been adopted, and they added: “We are of opinion that this is punishment pure and simple”—or words to that effect. No further censure was uttered, evidently because it was felt that no further censure was needed, or indeed that no stronger censure was possible; the implication, the omitted premiss, being manifestly that no lunatic ought under any circumstances to be punished. With a full appreciation of the obloquy and odium that I shall incur by the statement, I affirm that for very many of their misdeeds the majority of lunatics ought to incur some punishment; and, further, I affirm that explicitly or implicitly this is the opinion of every practitioner who has had experience of the insane; and, furthermore, I affirm that punishment of the insane in any form or other is in practice in every institution for lunatics.

**Punishment by Withdrawal of Privileges.**

Come, gentlemen, let us clear our minds of cant in this matter. Who is there among you who, if a patient on parole comes in drunk, will not refuse him his parole next time he applies for it? Who is there among you who, when a woman has been fighting or smashing, will not forbid her to attend the dance? Who is there that would stop the smoking of a man who is discovered pilfering or bullying? Is it denied that these are punishments? It may be said that a woman who is so violently manicid as to be fighting and smashing is not fit to attend a dance, and is forbidden for that reason and not for punishment. And it may be said that the man who comes in drunk is refused his parole, not as punishment, but as precaution lest he should come in drunk again. But I expressly exclude the withdrawal of privileges as punishment for any such reason. I speak of “punishment pure and simple,” and I say that when a patient has been smashing and tearing her clothes, not in an access of acute mania, but in an outbreak of temper, she would be excluded from the dance, not because she was unhinged, but as punishment. If the patient refused the renewal of his parole as a precaution, then the refusal must be permanent. But it is not permanent. We rely upon the temporary withdrawal of the privilege to act as a check in preventing its abuse. However, that is no punishment. It is sometimes denied upon another ground that these are punishments; they are, it is said, not punishments, but withdrawal of privileges. Why, yes; and so to send a man in prison is to withdraw from him the privilege of going about at large. And to treat him to bread and drink and the plank bed is not punishment, but merely withdrawal of the privileges of sufficient food and sleep. I say that to stop a patient’s tobacco and to forbid him the weekly dance is “punishment pure and simple.”

**The Degree of Responsibility of the Insane.**

So far, I trust, that I have carried the sense of the meeting along with me, but my third proposition is one for which I not hope to obtain your immediate assent, although I trust to secure it before I have finished. It is this: Very few indeed of the insane are wholly irresponsible—by which I mean that there are very few indeed of the insane who could be deemed, if we put it with brutality plain, in many cases right and just to punish an insane person for wrong-doing. I am afraid that I have made your flesh creep. There is doubtless a very prevalent floating body of sentiment, which gets expressed from time to time with disquiet at the notion of ever punishing a lunatic under any circumstances for any act. The English Commissioners in Lunacy some years ago wrote in their report of a certain asylum that they had discovered a certain cold front had been adopted, and they added: “We are of opinion that this is punishment pure and simple”—or words to that effect. No further censure was uttered, evidently because it was felt that no further censure was needed, or indeed that no stronger censure was possible; the implication, the omitted premiss, being manifestly that no lunatic ought under any circumstances to be punished. With a full appreciation of the obloquy and odium that I shall incur by the statement, I affirm that for very many of their misdeeds the majority of lunatics ought to incur some punishment; and, further, I affirm that explicitly or implicitly this is the opinion of every practitioner who has had experience of the insane; and, furthermore, I affirm that punishment of the insane in any form or other is in practice in every institution for lunatics.

**IMMUNITY FROM PUNISHMENT.**

First, I ask you to agree that no insane person ought for any act to be punished with the same severity as a sane person ought to be punished for the same act. Or, in other words, the punishment of an insane person ought never to be as severe as that which would be inflicted on a sane person. That is an agreed proposition. This is a law of the law, and it is as true today as it was then.

Next, I wish to submit to your consideration the question whether, in any case, a person is to be regarded as insane. If, for instance, a man is drinking, is he to be regarded as insane, or is he to be regarded merely as skilly? And this is a question to be submitted to your consideration. If so, he is to be regarded as insane. That is an agreed proposition. If not, he is to be regarded as skilly. That is an agreed proposition.

But I wish to submit to your consideration the question whether, in any case, a person is to be regarded as insane. In the case of a man who is drinking, is he to be regarded as insane, or is he to be regarded merely as skilly? And this is a question to be submitted to your consideration. If so, he is to be regarded as insane. If not, he is to be regarded as skilly. That is an agreed proposition.
in fact, that all I have done is to refuse to call a spade an agricultural implement.

Let me point out that this proposition—that for certain offences lunatics are rightly punishable—is involved and implied in the propositions to which you have already assented. If it is not the case that no insane person ought to be punished with the same severity as a sane person, it is implied that the insane person ought to be visited with some punishment. When it is asserted that for every insane person there is a sphere of punish-ment, it is admitted. In case it is asserted that no insane person ought to be punished with the same severity as a sane person, it is implied that the insane person ought to be visited with some punishment. When it is asserted that for every insane person there is a sphere of punish-ment, it is admitted.

Mitigated Punishments.

The practical importance of these propositions with regard to the plea of insanity is this—that while there are some cases in which we may rightly ask the court to refrain altogether from punishing the criminal, there are many more cases in which we cannot justly demand such complete immunity, but in which we can fairly argue that the criminal is responsible to some extent but is not wholly responsible, and that, therefore, while he ought to be punished, he ought not to be punished with the same severity as an ordinary offender. If this attitude be assumed by a medical witness, I feel sure that not only will he present his plea in a more just and equitable form, but he will stand a fair better chance of having it admitted. His contention will be more in harmony not only with the justice of the case, but with the sense of the community, than if he holds the view that the insane is not guilty.

This, then, is the aim that, in my view, we should set ourselves to attain. The total immunity of some insane offenders for some acts, and the mitigation of punishment in more or less degree for all crimes done by insane offenders.

When should the Insane Criminal be Held Immune?

The acceptance of these principles, if they be accepted, will not help us much, however, to the solution of the practical problem that confronts us in concrete cases. For in the large number of cases in which insanity is pleaded, the prisoner has not been regarded as insane until the commission of the very crime for which he is now being tried. If our task were to establish the immunity, or partial immunity, of a person who is admittedly insane, it would be an easy one. What are we usually asked to do is to show why this offender, who up to the time of the crime has been sufficiently sane to be allowed, rightly or wrongly, to be at large, should now that he has committed a crime, receive the benefit of the plea of insanity.

Conclusion.

The speaker then briefly summarised the circumstances which, if proved, would establish the plea, namely:

1. Exoneration does not prejudice us in concrete cases, for in a very large number of cases in which insanity is pleaded, the prisoner has not been regarded as insane until the commission of the very crime for which he is now being tried. If our task were to establish the immunity, or partial immunity, of a person who is admittedly insane, it would be an easy one. What are we usually asked to do is to show why this offender, who up to the time of the crime has been sufficiently sane to be allowed, rightly or wrongly, to be at large, should now that he has committed a crime, receive the benefit of the plea of insanity.

2. Such confusion of thought that the accused was incapable of rightly estimating the circumstances or the consequences of his act.

3. Extreme inadequacy of motive.

4. Extreme imprudence in the act.

5. The non-concurrence in the act of the volitional self.

I. John F. Sutherland, M.D.,

Deputy Commissioner in Lunacy for Scotland.

I have no fault to find with the criterion of responsibility laid down by the judges in 1843 in response to the request of the House of Lords for a definite ruling. The criterion—a simple one—amounted to this: Did accused at the time of committing the crime know the nature and quality of the act, and did he know the act was a wrong one? This is a good enough definition for all purposes, and I have not known any injustice to insane persons result from it in Scotland. It may not be a perfect law, but on the whole it has worked, thanks to the fairness of the Bench of this country, remarkably well. If you wish this judicial formula changed, as some seem to think, we have the right to ask—(1) What do you propose to take its place? and (2) to state in what degree it has operated unfairly to accused persons. Cases in which the plea is possible are few, because the number of crimes of violence committed by insane persons is infinitesimal when the whole is taken into account. The bulk, perhaps no less than 95 per cent., of these indictable offences, were committed by persons in a state of intoxication. In regard to such authors of crimes of violence, how does the law and how do experts stand? The "judge-made" law of 1843, as some people term it, would exculpate them from responsibility, for it exactly meets the point that the intoxicated person does not know the nature and quality of the act, or that it was a wrong act, because intoxication is insanity of the most perfect type, no matter how transient. But while "insane at the time" is a plea with reference to what many classical writers will enter the witness box and testify to that effect? If they did, I do not believe any jury would convict of the capital charge.

The judicial dictum of 1843 is not, at all events in regard to them, at fault. It is not the law that is at fault, rather is it the hesitancy of medical witnesses to take a proper stand, which is blameworthy, and likewise the fact that the accused as a rule, being poor, have not the means to secure legal aid commensurate with the gravity and responsibility of the case. Consequently such cases, for the most part, fall into the hands of inexperienced lawyers, and matters are made worse by the knowledge that the aid of the specialist cannot be got. No fund for such special cases is available in Scotland. Were it in existence, several of the verdicts of recent years would have been altered. The only case of the few cases there was practically not the semblance of a defence.

It is in this direction a change is needed. In regard to such cases I would venture to point out some of the judicial fallacies that have arisen. One hears the learner of the Bench say, "This case is one of the drunken attack, the "voluntarily" induced state of mind of accused, and not least that the death sentence is a "terror" to drunkards. In none of these views can I concur.

Can a drunkard "do a "wrong"? I should be inclined to think that this is highly problematical, and that it does not even afford that presumptive evidence required in a court of law. Much might be said against the theory of "voluntary" drinking. Who can say with a degree of certainty in the advanced stage of a chronic drunkard's being "induced drinking" was voluntary? For that would imply the certainty of an absence of latent or patent physical and mental degeneration induced by the vicious or the diseased habit. The former in time merges into the latter. All is uncertainty. Then there is the supposed deterrent effect which the scaffold is said to produce in the minds of drunkards. There could be no greater delusion, and drunkards were as numerous on the next "pay day" as ever they were, and deal out violence as freely and as maniacally as ever they did. The marvel is, that instead of having thirty indictments for murder every year, there are not 1,000, and as a consequence capital punishment multiplied a thousandfold. This is an aspect of the question which is overlooked. The violence of the drunkard is subdued, not by the menace of the scaffold, but by the strength of the state of his mind. It could not be otherwise real; consciousness either does not exist, or is of the dimmest. The intoxicated authors of crimes of violence are insane; the duration of the insanity from a medico-legal point of view is of no moment, and by the criterion of a possibility laid down in 1843, the drunkard should not be responsible, and would not if the expert looked at the matter from the point of view now submitted. But if this view be not accepted, then the crime should be reduced from murder to culpable homicide, as is the case in many countries. Some Scottish judges view it in this light. If "insane at the time" were proved, there would still be the protection for society by detention in a safe place of custody.

II. Geo. F. Blandford, M.A., Oxon., M.D., F.R.C.P. Lond.,

Visiting Physician, Newlands and Otto House Lunatic Asylum.

Dr. Blandford remarked with regard to the vexed question of responsibility and knowledge of right and wrong, and the nature and quality of the mental disturbance that induced the accused to do wrong, but they knew it as lunatics. A dog knew right from wrong, a child knew right from wrong, but knew it as a child. A lunatic knew right from wrong, but the knowledge was that of the unformed mind. The whole point was the point to be proved. It might be right that he should be held to be responsible to a certain extent—and it would be for the benefit of many lunatics that they be held responsible to a certain extent—but instead of hanging a man who com-
mitted a murder through drink, he would send him, not to Broadmoor to smoke his pipe for the rest of his life, but to penal servitude, where he could do some useful work.

IV.—John Glaister, M.D.,
Professor of Medical Jurisprudence and Public Health, St. Mungo's College, Glasgow.

Professor Glaister said that he generally accepted the propositions laid down by Dr. Mercier, but he was not quite sure that they would all be agreed as to the degree of acceptance. Any amount of general discussion on the general question might prove largely interesting and of some value, but, after all, when the responsibility of those who engaged in a crime became a question of importance, perhaps of death, then only did the importance become of greatest significance. In his view there was less possibility of injustice being done to the insane than to the public. He was of opinion that the growing sentimentalism of the public regarding the responsibility of certain criminals, shown by petitions for modification of sentence and post hoc pleas of insanity, was a distinct danger.

V.—Alex. Robertson, M.D., F.F.P.S. Glas.,
Professor of Medicine, St. Mungo's College, Glasgow.

Dr. Alex. Robertson said that in the early part of his professional career he had published a paper entitled Modified Responsibility in Mitigation of Punishment, in which conclusions practically the same as those of Dr. Mercier in criminal cases were drawn, with that knowledge. It appeared to him that of late years judges and juries had made very full allowance for mental defect or disorder, when these were proved to exist in criminal cases, and that justice was done. He regarded the proposition maintained by Dr. Sutherland as dangerous to society. His proposition was that if in a condition of drunkenness one should murder another, the mere fact of his mind being disordered by alcohol—in other words, that he was intoxicated—should reduce his charge against his mind to culpable homicide. Dr. Sutherland appeared to advocate a change in the law to that effect. If such change were made, would there not be a temptation to anyone who had a feeling against another, probably known only to herself, to take two or three glasses of whisky, feign full intoxication, and kill the man against whom he had this feeling? For he would comfort himself with the thought that in any case he would at any rate not be hanged. But, even though there was no question of feigning, it was very doubtful in the case of any drunkard who killed another when drunk, whether the charge should be modified. In all such cases the criminal had many times previously been violent under drink. It was incumbent on all who were dangerous under drink to refrain from their observation; for, if they took it with that knowledge, they were clearly culpable and responsible for their acts. All such cases might safely be left to the common sense of juries.

VI.—Professor Sir William T. Gairdner, K.C.B.

Sir William Gairdner, speaking not as a specialist but as a teacher of the art of medicine in general, said what he had consistently taught had been in accordance with Dr. Mercier's doctrine. What he had held and taught all along was that there never was in fact justice in regard to the insane until there was a different form of verdict allowed from the present. The jury could say that a prisoner was guilty or not guilty because of insanity. He desired that there should be a third verdict allowed—guilty, but insane.

About a Discussion on the Agglutinating or Sedimenting Properties of Serums and Their Relation to Immunity.


Before a discussion as a means of differential diagnosis between different kinds of allied bacteria, the validity of the principle has attracted a very considerable amount of support, notwithstanding Pott's attempts to throw it into discredit as a test method. The importance of the agglutinating principle has been raised into a high position by the observation that the blood serum of typhoid-fever patients may acquire this property of clumping cultures of the typhoid bacillus. This observation was made first in the Hygienic Institute of Vienna by Dr. Grünbaum, working at the suggestion of Professor Gruber. The subject was first brought forward by Professor Gruber at the Congress for Innere Medicin in April, 1896. But it would not be profitable to occupy time with questions which are mere matters of history. With increasing knowledge of the varieties and species of bacteria, we are confronted with ever-increasing difficulties in finding criteria whereby the different kinds may be distinguished. Whilst many important differences may be demonstrated by the use of culture media of various composition, yet these not infrequently leave us in the lurch at the critical point. We still have a resource to fall back upon in the action exhibited by the serum obtained from artificially-immunised animals.

Specific Immunity.

There are various ways of applying this principle of specific immunity; these may be put under the following three headings:

1. Protective in respect of their power of affording protec-
tion to normal animals which are infected with the bac-
terium in question.

2. *Lysogenic,* in respect of their power of determining 
the rapid degeneration of the bacterium in the peritoneal 
fluid of a normal animal (Pfeiffer's test), or in the presence 
of perfectly fresh blood or serum from a normal animal (Bordet's 
test).

[Strictly speaking, according to my own belief this property 
should not be included here. The lysogenic power is pos-
sessed by normal sera in the absence of antimicrobial 
activity; the part played by the specific serum is merely that 
of weakening, whereby the bactericidal bodies are able 
not to be defeated by means of other injurious agencies such as heat 
similar effects can be produced.]

3. *Agglutinative,* in respect of their power of causing clumping 
(agglutination) and sedimentation of the bacterium.

We have to consider how far these different modes of ex-
perimentation are equivalent to one another as well as how 
far the action of sera is truly specific; that is to say, have we 
evidence that races or kinds of bacilli which are recognisably 
distinct by cultural methods are uniformly and equally with-
out reaction when exposed to one or other form of serum test? 
As far as present knowledge goes, this question cannot be 
answered with an unqualified affirmative.

**THE ACTION OF NORMAL AND HETEROLOGOUS SERUMS.**

Before entering upon the subject immediately before us, I 
will allude to the qualities with which certain "normal" and 
heterologous serums are endowed. In the days antecedent to 
the recognition of agglutination as one of the properties 
of certain specific serums, it was shown that some specimens of 
normal sera had distinct protective properties: the protec-
tion afforded by such serums is in contrast with that given by 
specific serums, in that extremely minute doses of the latter are 
sufficient, whilst comparatively large doses of the former are 
required. The purpose of testing specific effects, it is 
necessary to use samples of serum which are efficient in 
quantities of 20 to 100 cm. or less; probably doses of serum 
must not exceed about 50 mg. Control experiments must 
include those in which serum from the same kind of animal 
is used (this is particularly necessary in the case of serum 
derived from the horse, since even 50 mg. will sometimes 
cause very distinct retardation of death apart from any special 
or specific action). Some such serums will also determine a 
lysogenic effect in a space of an hour or so.

Turning now to agglutination, we find that many kinds of 
serum obtained from normal animals possess some degree of 
clumping power; however this, like the protective action, 
disappears when the proportions are sufficiently reduced. In 
observations of the protective action, it is desirable to test the 
serums at a constant antigen concentration, and other exper-
iments with old kept serums and alcohol precipitates, hardly 
show more than that low protective and lysogenic powers were 
associated with low clumping power. One form of experiment is 
designed to show growing cholera vibrios in cholera serum the 
agglutinating power is entirely destroyed, whilst the protective power is only 
diminished. Pfeiffer had previously described an almost 
equivalent experiment which was repeated several times by 
Professor Gruber and myself with serum and culture sent by 
Pfeiffer. Although we followed his instruction to the letter, 
we were never able to obtain his results. Since then the 
experiment has been modified, and some loss of protective 
power is admitted. In his last communication on the place 
of production of protective substances, he remains significantly 
silent, and passes over the agglutinating power of the organ 
extracts with the few words that it was increased in certain 
cases.

**PFEIFFER’S TEST REACTION IN RELATION TO THE CLUMPING TEST.**

It has already been pointed out that Pfeiffer's test is not 
merely associated with a complete protection. In reality 
the destruction or degeneration of the bacteria introduced 
is only partial at the end of the time limit; for by killing 
the animal when all the bacilli in samples of the free perito-
neal fluid are turned into spheroidal bodies, it is found that

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abundant untransformed individuals are present upon the omentum, etc. I believe that the previous agglutination of the bacteria forms an important adjuvant to the production of this degenerative process in the free peritoneal fluid; for it has been a very striking fact that these two factors have always been associated in the large series of experiments with vibrios which I carried out at Professor Grüber's Institute. Some recent work of Ransom and Kitashima is of interest in this connection; they obtained a race of cholera vibrios which was not affected by a certain cholera serum (this was effected by growing a number of successive generations in the diluted serum—in fact, we have reason to believe that the more susceptible individuals being gradually weeded out). The virulence of the culture was not appreciably affected thereby. This race of vibrios yielded a negative reaction to Pfeiffer's test, although the original race was both clumped by and afforded an almost complete positive Pfeiffer reaction with the same serum.

Another observer has given some experiments in which he shows that a preliminary dose of opium prevents the complete occurrence of Pfeiffer's reaction, although efficient serum is employed. This result he explains by the assertion that the leucocytes are paralysed; but if I may be allowed to put a different interpretation on this complex experiment, I am inclined to ascribe the result to the paralysis of the intestines whereby the sweeping mechanism of the peritoneal cavity is annulled, consequently all those vibrios which in a normal animal would be gathered up and disposed upon the omentum, etc., remain freely suspended in the fluid.

**Comparative Agglutinating, Lysogenic, and Preventive Action of Serums Obtained from Sufferers in an Epidemic Associated with the Presence of a Variety of B. enteritidis (Girten).**

**Intrapерitoneal Injection.**

**Limit Agglutinative Power Serum No. 19 = 0. No. 8 = 1 : 500. No. 13 = 1 : 500.**

<table>
<thead>
<tr>
<th>Guinea-pig</th>
<th>Dose</th>
<th>Examination of peritoneal fluid after</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, 360 g.</td>
<td>1 loop</td>
<td>No serum.</td>
<td>Very abundant active bacilli. Abundant bacilli.</td>
</tr>
<tr>
<td>B, 375 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 19.</td>
<td>Mostly active. Many bacilli.</td>
</tr>
<tr>
<td>C, 220 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 8.</td>
<td>Few bacilli. Not many active.</td>
</tr>
<tr>
<td>D, 320 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 13.</td>
<td>A few swollen non-motile bacilli.</td>
</tr>
</tbody>
</table>

**Limit Agglutinative Power Serum No. 80 = 0. No. 25 = 1 : 500. No. 23 = 1 : 1,000.**

**Intrapерitoneal Injection.**

<table>
<thead>
<tr>
<th>Guinea-pig</th>
<th>Dose</th>
<th>Examination of peritoneal fluid after 1 hr.</th>
<th>Examination of peritoneal fluid after 3 hrs.</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, 390 g.</td>
<td>1 loop</td>
<td>No serum.</td>
<td>Many active bacilli.</td>
<td>Died in 23 hrs.</td>
</tr>
<tr>
<td>B, 280 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 30.</td>
<td>Many active bacilli.</td>
<td>Died in 22 hrs.</td>
</tr>
<tr>
<td>C, 230 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 25.</td>
<td>Many active bacilli.</td>
<td>Died in 47 hrs.</td>
</tr>
<tr>
<td>D, 266 g.</td>
<td>1 loop + 20 mg.</td>
<td>Serum 27.</td>
<td>Many active bacilli.</td>
<td>Died in 60 to 70 cm.</td>
</tr>
</tbody>
</table>

According to my own observations upon sixteen kinds of vibrios (six cholera and seven not cholera, three reacting like cholera), positive Pfeiffer's reaction and complete sedimentation effect, combined with permanent protection, were invariably obtained together. The concordance was too striking a fact to be overlooked.

The following observations on other bacteria are similarly in harmony with the view that protective (and lysogenic) property and agglutination go together.

One more instance may be quoted in illustration of this association. It may not be generally known that it is perfectly possible to obtain a clumping serum by the administration of a non-pathogenic organism. By treating an animal with the non-virulent B. Pfeiffer, and subsequently succeeding in obtaining a serum which had considerable power of sedimenting this bacillus, whilst the animal to which another kind of serum was given with the bacilli afforded a typical control.

**Proportional Relationship between Protective, Lysogenic, and Clumping Power.**

The question as to whether there is any evidence of the existence of a proportional relationship between the protective and the clumping power of a serum entails the consideration of several matters. One finds doubt, necessarily, that the susceptibility of a race of bacilli to a given serum is a variable quantity. Early in our researches on vibrios, it appeared that the less virulent races were more susceptible to the agglutinins produced by the use of virulent cultures than were the virulent varieties themselves; moreover, in harmony with this, the serum obtained by means of the less virulent kinds, although very efficient upon these kinds, had slight influence upon the more virulent sorts. This was subsequently confirmed by Pfeiffer and other observers, from more recent observation I fear that it is not simply a matter of virulence, for a less virulent stock of B. enteritidis was found also to be less influenced by a given serum. It is better, therefore, to speak of greater and less resistance and susceptibility to clumping serum.

Again, everyone who has watched the process of agglutination under the microscope must have been struck with the difference between individual bacilli, certain individuals being influenced long before others; indeed, some may escape altogether. Now, in measuring the agglutinating or sedimenting potency of a serum by means of determining the limit dilution at which a visibly recognisable effect is engendered in a given time, we get some idea of the action upon the susceptible individuals, but the resistant and less susceptible ones are not heeded. This method of measurement could hardly be expected to yield any proportional comparison between the protective and clumping power of the serum. The following example may be cited in this connexion. A sample of typhoid serum was found to have a sedimenting value of 1 : 20,000 when tested for the ultimate limit of dilution at which recognisable effect was produced; when tested with the same culture upon an animal it was found that as much as 50 mg. only just protected against about twice the minimal fatal dose; in a word, it was not a powerful serum. How, then, can we reconcile so high an apparent clumping power and so low a protective capability with any association between these two properties? The answer to this is: By testing the total effect of the serum upon a given quantity of bacilli. Even in a strength of 2 per cent. this serum could not cause complete precipitation of all the bacilli; according to this test the serum could not be called a potont one. In contrasting the protective and clumping efficiency of serums we must take heed of the effect produced upon the more resistant as well as upon the more susceptible individuals. In working with vibrios it was found that serums which were capable of causing the complete sedimentation of about 2 cm. of the culture with a 1 per cent. dilution were also capable of producing positive results in Pfeiffer's test, with permanent survival of the animals, in a dose of about 10 to 20 mg. Whilst the ultimate limit dilution at which agglutination can be discerned is totally out of proportion with the protective capacity, yet it may be in concordance with the relative protective capacities of two or more samples of serum when tested with the same culture; the experiments tabulated above may be
cited as instances. Some authors have argued that since a serum has high clumping power on a weak race and yet insignificant protective action against a virulent stock, the existence of any link between these two phenomena cannot be entertained. It would perhaps be kindest to say nothing about such an argument.

**Relationship between Clumping Power and Certain Inhibitory Effects.**

When bacteria are grown in the presence of even small quantities of efficient agglutinating serum, they exhibit departures from their normal habit of growth; the reducing power of a cholea vibrio may be checked, the phosphorescence of a luminous vibrio can be stopped, the production of the pigment “pyocyanin” by the B. pyocyanus may be inhibited; morphologically also we have the tendency to grow in chains or threads by microbes, which naturally do not present this feature. No one has as yet succeeded in separating out a pure agglutinin, so that we are not able to say whether these inhibitory actions are due to the agglutinins themselves or to substances which are associated with them; we are, in fact, in the same position with regard to these inhibitory phenomena as we are in the case of the protective agents. All that we can say is that a combination of clumping, inhibitory, and protective substances is extremely suggestive of a close relationship in their nature. One author, Salimbene, regards the agglutination phenomenon as a property which is only acquired by the blood, etc., after it has been shed; he states that it does not take place within the living animal. This is entirely at variance with my own experience, for numerous observations upon peritoneal injections in immunised animals have always shown that agglutination occurs within the peritoneal cavity. If the examination of the peritoneal fluid is made later than about five minutes after the time of the inoculation, all or most of the clumps have disappeared, for they have been swept away by the abdominal movements to the walls of the cavity. Salimbene also asserts that the presence of oxygen is a necessary factor for the occurrence of clumping, inasmuch as it fails to occur in vacuo. Here again my observations are in opposition for on endeavouring to repeat his results I find that agglutination takes place in the vacuum, in the oxygen-free atmosphere produced by means of pyrogallol and caustic soda, and in an atmosphere of coal gas just as well as in the controls exposed to the air. As his observations have been frequently quoted, it would be of importance if others would give their experience in this matter.

**Bactericidal Action of Serums with Clumping Properties.**

Before the days of agglutination many authors examined immunised serums for bactericidal action. For instance, Sana-rell, working with cholera and other vibrios, found that consider-able destruction took place. More recent observations (Bordet, Landsteiner) show that these serums are only really bactericidal when they are quite fresh; sera which have been kept or which have been heated to 55° C. lose the power of absolute destruction although they may cause profound effects upon the appearance and growth of the organisms; the bactericidal effect, however, is regained by the addition of perfectly fresh normal blood or serum, which by itself is unable to produce a like effect if the bacteria are sufficiently resistant (virulent).

**The Differential Destruction of Agglutinins in Vitro and in Vivo.**

It has been established that by growing the special microbe in a given homologous serum the power of clumping is diminished or entirely destroyed, according to the method of experiment. On the other hand, in the growth of insusceptible heterologous bacteria, moulds, etc., practically no diminution occurs. The same observation has been made with regard to the protective power of such serums—namely, that the like sort destroys, the unlike leaves intact. Here, then, we have another instance of the parallelism between agglutinins and agglutinative. It must be admitted that certain authors aver that agglutinins are not destroyed by the presence of the homologous organism. This is due to the fact that undiluted serums were infected, so that the growth of the bacilli was interfered with too much. The following experiment illustrates the effect of varying dilutions:

<table>
<thead>
<tr>
<th>Portion A. Inoculated with typhoid serum</th>
<th>Portion B. Inoculated with typhoid serum and half strength of Gärtner's bacillus serum</th>
<th>Portion C. Inoculated with Gärtner's bacillus serum</th>
<th>Portion D. Inoculated with Gärtner's bacillus serum and half strength of Gärtner's bacillus serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 hours after inoculation</td>
<td>+</td>
<td>Slight</td>
<td>0</td>
</tr>
<tr>
<td>50 hours after inoculation</td>
<td>Trace</td>
<td>0</td>
<td>Slight</td>
</tr>
<tr>
<td>52 hours after inoculation</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

With the typhoid infection the loss is greater the higher the dilution.

It will be noticed that the presence of Gärtner's bacillus also caused some loss, whilst the colon bacillus was quite indifferent at these dilutions.

Another method of testing this differential loss of clumping power is to do it within a living animal. By giving a homologous dose to an animal which already possesses some agglutinating power in its blood the agglutinating value of the blood can be made to decrease. It is somewhat inviting to suppose that as the agglutinins are used up during the struggle against the new infection they take some share in the process, and are useful and not merely ornamental substances. If the dose is recovered from the reapper in larger quantities than before, on the other hand, the animal may die of intoxication before they are completely destroyed.

Four guinea-pigs were prepared by giving them equal doses (2 loops 2 mg. of living typhoid bacillus approximately) of these serums, but without success. Each one then received a large dose of bacillus in its peritoneal cavity (6 loops of young agar culture in each case). On the previous day the blood was taken in order to test its sedimenting power.

**Sedimenting Values for Typhoid Bacillus (all were tested with the same suspension).**

<table>
<thead>
<tr>
<th>Sedimenting Value</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:2000</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>1:3000</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>1:4000</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

It will be observed that the result is merely a repetition of the experiment in vitro to which I have just alluded, for the typhoid had most marked effect, the coli moderate effect, the other two with B. enteritidis being intermediate. Guinea-pig B, which received Gärtner's bacillus, deserves a few more words. A control normal animal which received only 1 loop (that is, one-sixth the quantity given to B) died within 21 hours; B
survived 60 hours. A sample of its peritoneal fluid withdrawn immediately after the injection showed that most of the bacilli had already become clumped, and only a few were free and motile; after the death there were very few bacilli in the peritoneal fluid; there were, however, very many spherical degeneration forms which on culture gave rise to a pure growth of Gärtner's bacillus.

We had, therefore, the passive protective action of typhoid serum on Gärtner's bacillus, we find that it is capable of giving distinct retardation of death with doses of bacilli which are rapidly fatal to control animals; just as the agglutinating effect is less in degree than is the case with the typhoid bacillus, so also the protective action is in lesser degree. There is much variation, however, between the inter-actions of different samples of typhoid serum and different varieties of B. enteritidis.

**Comparison of Agglutinative, Lyogenic, and Protective Serum Action of Typhoid Serum on B. Enteritidis (Gärtner).**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>loop Gärtner</td>
<td>50 mgm. vibrio serum. Agglutinating power: 0. Complete precipitation in 1 hour.</td>
<td>loop Gärtner</td>
<td>50 mgm. Typhoid serum. Agglutinating power: 0. (1) Complete precipitation in 1 hour.</td>
</tr>
<tr>
<td>Immediately: Abundant active bacilli, no clumps.</td>
<td>Immediately: Abundant small clumps, also many active free bacilli.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 1 hour: Abundant active bacilli, no clumps.</td>
<td>After 1 hour: Many bacilli, none motile, many deformed bacilli, and many spherules.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 3 hours: Abundant motile and non-motile bacilli.</td>
<td>After 3 hours: No bacilli; many swollen spherules.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bear in mind that floccular action of the serum has not been obtained.</td>
<td>Bear in mind that floccular action of the serum has not been obtained.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneal Sample Taken:</td>
<td>Peritoneal Sample Taken:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>immediately:</td>
<td>60 hours. T. 37-6° C.</td>
<td>60 hours. T. 37-5° C.</td>
<td></td>
</tr>
<tr>
<td>72 hours. T. 37-8° C.</td>
<td>72 hours. T. 37-8° C.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| *Both these sera were taken 31 years previously and kept sealed up in sterile condition in glass tubes. The typhoid serum has not apparently lost much of its agglutinating power since April, 1895.*

**Effect of Heat and Time.**

So far as present knowledge goes it appears that both agglutinins and protective substances become destroyed at about the same temperature; thus both suffer but little at 60° unless the heating is prolonged. Both are fairly well preserved after long keeping, although some loss does occur. In the animal economy after active immunisation with living bacilli both substances persist for considerable periods; in some of the original experiments with Professor Gruber well-marked agglutinating power was present in animals more than a year after their infection. According to Pfeiffer the agglutinating power may be lost earlier than the protective property, judging from a very few cases.

**Fatal Issue During the Presence of High Agglutinating Power of the Blood.**

So far, no one, I believe, has proved the existence of agglutinins apart from any protective power of the serum. At first sight it may appear strange that an animal should die of a particular infection, although a few tiny droplets of its serum are capable of protecting numbers of other animals from a like infection. But this is an old and well-established fact, which, moreover, must have been confirmed by nearly every worker in the field of immunity. What the mechanism of the fatal issue may be (whether some toxic product or some interference with some important organ) in such cases, I must leave on one side. It is clear, however, that the fact that an animal may die with large quantities of agglutinins in its blood is no argument against the association of these substances with protective bodies, unless it is also shown that the latter are absent. And this has not yet been demonstrated. One of the best samples of serum which I obtained at the commencement of my researches was taken from a moribund animal; it possessed high agglutinating as well as high protective power.

Kraus found that floccular coagula were produced by the action of specific serum upon filtrates of cultures of the homologous bacteria. He maintains, and his observations show, that the reaction is quite specific. In the low dilutions in which these experiments were made (1 in 10, 1 in 20) it would not be likely that specific differences would be well marked when the strains are brought out by the confirmatory work of C. Nicolle.

**Conclusion.**

The actions of normal and homologous sera (clumping and protective) may be left on one side as hardly germane to our subject. We have evidence that when agglutinins are present, inhibitory and protective properties are also to be found. Hitherto an agglutinin free from these other substances has not been obtained. Agglutinins act within the living body by causing clumping as well as in the test tube. Destruction of agglutinins occurs in an actively immunised animal after infection with the homologous bacterium.

There is no definite relationship between the limit dilution at which clumping can be recognized and the limit dilution at which complete effect is produced upon a given amount of the bacteria. From the latter some clue as to the preventive efficiency of a serum may be obtained.

Lastly, although the association of agglutinins with protective substances may be shown to be fortuitous in future experience, yet it will always have attached interest from the fact that the now well-established method of serum-diagnosis in typhoid fever and other diseases owes its birth to this association. The knowledge that protective qualities are acquired by the blood of typhoid fever patients led to the probability that the clumping property would also be developed. This resulted in Gruber's world-famous suggestion that this agglutinating property should be worked out in typhoid and cholera patients.

### II.

**A. S. F. Grünbaum, M.D.,**

Senior Demonstrator of Physiology, London University, London.

Dr. Grünbaum said that he had worked chiefly with human sera, the agglutinating action of which was often small. He thought that it was important to note that in low dilutions the agglutinative power did not go hand in hand with the protective power. He pointed out that even inanimate substances—for example, particles of French chalk—might be agglutinated by various sera, and that, therefore, the agglutination was probably a physical process which prepared the bacilli for the action of other substances later on. Even non-motile organisms might show less of Brownian movement in the presence of certain sera, probably from the swelling of a membrane round them. He suggested that a fourth property might be attributed to the specific sera in addition to those mentioned by Dr. Durham—namely, a paralyzing action on motile organisms.

### III.

**E. J. McWeeney, M.D.,**

Professor of Pathology and Bacteriology, Catholic University, Dublin.

Professor McWeeney said that in the course of his work on the action of typhoid bacilli he had arrived at the following results: (1) The typhoid bacillus when caused to grow in broth containing typhoid serum displayed a number of characteristic phenomena which were not observable in broth containing normal serum, such as a rapidity of growth and the formation of flated, convoluted chains made up of short individuals; (2) this mode of growth could, under
certain circumstances, be utilised for clinical purposes; (4) the cases in which it might be advantageously used were those in which the clumping by the ordinary Gruber-Widal method was slow in coming on, or for any other reason left the observer in doubt. The method consisted in diluting the suspected serum with broth containing a small number of typhoid bacilli and preparing hanging drops, which were examined after varying periods of time. A moderately active serum, diluted 100 times with sterile broth, and inoculated with a few typhoid bacilli, yielded distinctly con- 
voluted chains after about six hours at 37° C. By the aid of this method he had been able to clear up the nature of a case of typhoid fever, the symptoms of which resembled those of meningitis, and which had been admitted under the care of Dr. Murphy to the Mater Misericordiae Hospital, Dublin. The method was one that could hardly be carried out by the ordinary clinical observer on account of the absolute sterility required in all the manipulations. Professor McWeeney concluded by giving a short lantern demonstration in illustration of his results.

IV.—G. SIMS WOODHEAD, M.D.,
Director, Research Laboratories of the Royal Colleges of Physicians and Surgeons, London.

Dr. Woodhead said that he could not help thinking that this was a subject which might with advantage be left to experts, because it lay outside of or rather as one who was interested in the question from a general point of view. There now appeared to be several actions in serums which undoubtedly ran parallel for long distances, but which appeared to diverge in various directions. He was very much struck by Widal's experiments in regard to this in connection with ricin and antiricin. He had already said in this Section that the toxins were by no means the simple substances that were at one time suggested, and they had just heard that the serums were equally complicated. He thought it extremely unfortunate that the agglutinative serums of cholera, typhoid, etc., could not be raised to such a high degree of immunising activity as the immunising serums of diphtheria and tetanus in which, however, the agglutinative power was comparatively low. He hoped that some time they might come across some organism which would enable them to produce a serum in which both powers were highly developed. He was certainly inclined to agree with Dr. Durham as against Widal that a high agglutinating power in either cholera or typhoid could scarcely be associated with a low immunising power. The observations of Weigert and Ehrlich on the separable properties produced by the action of micro-organisms and toxins on cells would indicate that neutralisation of certain powers might be carried out in the bacteria themselves by substances separated from the tissue cells. He would like to ask Dr. Durham whether he had used higher temperatures than 55° C. or 60° C. for the purpose of determining whether there was any difference in this respect between the agglutinin and the antitoxin—the globulin precipitating temperatures, for example. He agreed with Dr. Durham as to the necessity or non-necessity for the presence of oxygen.

V.—Donald H. Hutchinson, M.D.,
Edinburgh.

Dr. Hutchinson said that he had inoculated himself with dead typhoid bacilli according to Wright's method, and had afterwards examined at short intervals of time his serum as regards its effect on living typhoid bacilli. He found in so doing that the first effect to appear was an interference with the motility of the organisms, that is, the serum appeared to develop a paralysing action before it caused distinct agglutination.

Dr. Durham thought that too much importance should not be ascribed to the paralysing effect; absolute loss of motility did not obtain in any complete agglutination, for certain individuals could be seen exhibiting whirling movements. Moreover, fresh serum and leucocyte peritoneal fluid had much paralysing influence apart from any specific action. Since Dr. Woodhead and others had been unable to obtain Staheli- ben's results they might be put aside. The antitoxic serums of diphtheria could not be compared with the class of so-called "antibacterial" serums of typhoid and cholera. Many observers showed that the antitoxin prepared by means of filtered diphtheria toxin did not afford so efficient a protection against living bacilli as one prepared by immunising with living culture. The effect of heat depended largely upon the degree of dilution of the serum before heating; serum diluted with distilled water, kept at temperatures of clumping power, against higher temperatures for a longer time than undiluted serum. By adding to the diluting fluid "nutrose" or phosphates which prevented coagulation of the albumen still greater resistance to heat was produced.

POST-DIPHTHERIAL PARALYSIS.

[Abstract.]

By G. Sims Woodhead, M.D., F.R.C.P.Edin., F.R.S.E.
Director, Research Laboratories of the Royal Colleges of Physicians and Surgeons, London.

STATISTICS.

The great attention aroused in diphtheria during recent years has caused us to study diphtherial paralysis more carefully. How important this question is may be gathered from a study of the following figures. During the year 1896 there were examined at the laboratories 7,832 cases that had been certified 'diphtheria.' Of these 5,868 had diphtheria in the throat and 1,966 were paralysed by paralysis of a more or less marked kind. Of these cases, 1,096 had been treated with antitoxin, and there were 273 deaths amongst them; 266 received no antitoxin (that is, they were most of them mild cases in all probability), and there were 814 of the cases examined in which no diphtheria bacilli were found, there were 177 cases of paralysis with 59 deaths; 59 of these cases were treated with antitoxin—31 deaths. There were, moreover, 88 not treated with antitoxin, 28 of these succumbing.

DATES OF ONSET OF PARALYSIS.

Mr. A. Miller, M.B., B.C., gives an account of a number of cases of paralyses observed by him at the South-Eastern Hospital during the years 1896 and 1897, in which the onset was primarily (1) in the muscles of the palate; (2) in the oculo-motor muscles; (3) in the muscles of other parts; and (4) in cases of paralytic heart failure. He collects 494 cases, of which 185 were primary paralyses of the palate, 197 strabismus, 10 paralysis of other muscles, 102 cases of cardiac paralysis, 91 of which died and 1 recovered. The bulk of the palatal paralyses occurred between the fifth and the fifteenth day, none before the fourth. Of the oculo-motor paralyses the bulk occurred between the fourth and seventeenth days, none before the fourth; of the primary paralyses of other parts, half of them occurred between the fifth and the tenth day, and the other half before the earlier date. A case of primary paralysis of the palate occurred as late as the sixty-fifth day; of primary oculo-motor paralysis the ninety-first day, and primary paralysis of other parts on the fifty-first day. The bulk of the cardiac paralyses occurred between the fifth and the tenth day: a few cases occurred even as early as the second day, whilst this condition occurred in a severe form (that is, ending fatally) in 2 cases on the fifty-fourth day and in 1 case which recovered on the fifty-ninth day.

It is evident, then, that in the human subject these paralyses occur at a comparatively early date, although in numerous cases they come on at very much later stages; and one cannot help thinking that we have evidence of the primary affection of the nerve fibres of the vagus by the poison on the muscular tissue in the fact that cardiac paralyses occurred relatively at so much earlier a period than the other forms of paralyses. The affection of the cells of the vasomotor centres and perhaps also of the ganglia of the heart muscle, which is constantly in action, than in the case of other muscles, which in most cases are practically at rest, and in which therefore the demands on both the motor cells and the muscular tissue itself are comparatively slight.

MORBID HISTOLOGY.

Without going into the theory of the causation of paralysis, I may refer to the segmental nerve degeneration described...
by Meyer, Sidney Martin, and others. Comparatively rare, and almost always limited to the certain part of the body, and certain temporary changes may be observed during the first twenty-four hours in which toxin may be acting on the nerve cells. It is maintained that the cells so affected either atrophy or recover at an early date, but that the nerves for which these cells act as trophic centres under degenerative changes, perhaps of a Wallerian type, and that only then do we meet, with the characteristic diphtheritic paralysis. I have examined two cords from experimental animals treated with full doses of toxin, and in one case the chromatolytic changes were so marked that there was no perceptible deviation from the normal. It appears, as pointed out by Mouravieff, that when there is no great demand on their functional activity these changes appear to produce few or no symptoms; but, owing to the trophic changes, the peripheral nerves over which they preside become markedly altered in structure, a kind of Wallerian degeneration going on, with the result that they lose their conductivity, and paralysis is the result. In this way, too, may be explained the peculiar want of co-ordination that sometimes occurs, and the patchy distribution of the nerve lesions, a few fibres of a nerve undergoing degeneration corresponding to the large or small numbers of nerve cells in the cord that are affected.

Pernot, in a series of post-mortem examinations, five in number, found that in patients that died early after infection there was marked inflammation of the meninges of the brain and cord, any other changes being the result of complications. In all instances, there was evidence of inflammation and degeneration of the perivascular tissue and of the cells, not only of the anterior horn of the spinal cord, but also of the brain cortex. They found, however, in connection with these cells, that it was only the protoplasmatic processes which were affected. These changes are observed very rapidly after the toxin gets into the circulation; and it would appear that, especially in acute cases, toxin acts directly from the blood vessels especially on the protoplasmatic processes of nerve cells, and that, as a result of the changes in these trophic centres, the medullary sheath, and perhaps also the axis cylinder itself, may afterwards become degenerated, the process extending from the cell along the trunk nerve.

Paralysis in Animals.

Escherich notes that post-diphtheritic paralysis is a comparatively rare phenomenon in the guinea-pig, and he attributes this to the fact that in them in most cases the course of the disease runs only over a few days, though he points out that it has also been shown that certain animals survive a subcutaneous injection of toxins or bacilli, where the process has been so severe that a necrotic area has been formed, and which afterwards ulcerates, there is paralysis, especially of the hinder limbs, and of the posterior portion of the body. Loeffler, in 1860, drew attention to this fact, but he also showed that this paralysis in some cases passed off, and that the animal afterwards was to a certain extent immune, and he looked upon this paralysis as one of the symptoms of a severe attack of the disease—an attack such as would confer a certain degree of immunity, and an immunity which would last for some little time.

Madsen points out that paralysis, when it occurs, as a rule, follows the infiltration which results from the injection of a dose of toxin not fully neutralised. Although this swelling disappears, there very frequently occurs, some nineteen or twenty days after the injection, the first symptoms of paralysis, which manifests itself in the form of a rolling of the hinder part of the body and of the hind limbs whenever the animal attempts to make any active movements. This paralysis gradually becomes more distinct, and after a time may involve the fore limbs. The animal at rest usually lies on its side, but can raise itself when it makes a special effort. As a rule, there is a complete loss of strength, comparatively slight in muscles, but in many cases the loss is very marked. Madsen also notes that although recovery is possible, this condition usually ends in death. The animal retains muscular power longest in the head and neck, and in certain cases the only remains of strength that remains to it is by pulling itself on by its front teeth.

In most of these cases the temperature falls sometimes a couple of degrees, and the respirations and even the heart beat have been diminished in number. It is curious that although there should be this marked muscular weakness, the animal is still very bright, continues to feed as long as there is food within reach, is on the alert for sounds, and gives the peculiar cooing noise so characteristic of a guinea-pig. In any case, makes a sharp noise in its neighbourhood. Even in those animals which recover there is impairment of the muscular movements for a considerable period. In point of time the majority of the cases appear on the 21st to the 23rd day after injection. In connection with this are the cases of appearance of paralysis, Ehrlich has observed that in most of the cases of paralysis in the guinea-pig which have followed injection of nearly neutralised toxin the symptoms have manifested themselves at the end of the second week, instead of at the end of the third week as in Madsen’s cases, and he suggests that this may be due to the fact that Madsen used the original method of testing, that is, neutralising with a roth of an antitoxin unit, Ehrlich’s observations being made on animals in which the neutralising amount of serum was one unit. The bearing of this will be presently noted. The amount of swelling is certainly no indication as to the probability of the occurrence of post-diphtheritic paralysis, as we have observed some cases in which the amount of swelling comparatively slight in which there has been paralysis, whilst in other cases where there has been a large amount of swelling there has been no paralysis at all. Examples of this are given in the specimen cases which are merely a few selected for the purpose of illustration from a considerable number. They have been taken from records made in the second six months of 1897 and the first six months of 1898. Madsen refers to an exceedingly interesting fact, the bearing of which will be seen immediately. When the French method of neutralising antitoxin is used, that is, where a single large lethal dose only is neutralised by the antitoxin, paralysis is of very infrequent occurrence, and when it does occur it usually disappears in the course of a few days.

13 Cases of Post-Diphtheria Paralysis (Guinea-pigs): Cases Selected from a Series of Animals used for Testing the Strength of Antitoxin.

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>Local reaction</th>
<th>2nd day</th>
<th>4th day</th>
<th>14th day</th>
<th>25th day</th>
<th>35th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>245</td>
<td>Slight local swelling</td>
<td>Distinct indurated swelling</td>
<td>-45</td>
<td>-6</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>272</td>
<td>Large firm swelling</td>
<td>Large deposit</td>
<td>-15</td>
<td>-8</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>265</td>
<td>Narrow medium</td>
<td>Broad hard band</td>
<td>-5</td>
<td>-35</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>270</td>
<td>Traces of firm swell.</td>
<td>Nil</td>
<td>Nil</td>
<td>Not recorded.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>285</td>
<td>Traces of swelling</td>
<td>Slight strand</td>
<td>+35</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>280</td>
<td>Small firm swelling</td>
<td>Swelling nearly gone</td>
<td>-5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>255</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>275</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>295</td>
<td>Narrow strand</td>
<td>Firm narrow strand</td>
<td>+30</td>
<td>-70</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>270</td>
<td>Large soft swelling</td>
<td>Firm swelling</td>
<td>-30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>260</td>
<td>Broad band of firm</td>
<td>Narrow firm band</td>
<td>-30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>270</td>
<td>Large firm swelling</td>
<td>Large hard swelling</td>
<td>-15</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>255</td>
<td>Very large</td>
<td>Firm large hard deposit</td>
<td>40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It will be seen at once with reference to the table that the date of onset has little to do with the severity of the local swelling. Indeed, if we were to take the local reaction as giving any indication at all it would appear that the less the local reaction the more rapidly does the paralysis make its appearance, for in case No. 1 we find very slight local reaction on the second day, although there is a distinct indurated swelling on the fourth day; whilst in case No. 12 although there is very firm swelling on the second day and a large hard deposit remaining on the fourth day, the paralysis is not well developed until the twenty-fifth day. It should be remembered, however, that the paralysis may in several instances have occurred a little earlier than is here noted, where means only, which is always a somewhat hurried day, and Sunday, in which observations would not be made, intervene; whilst in other cases the first symptoms of
paralysis may have been overlooked. As regards weight, it will be noted that, speaking generally, the greatest loss occurs at the two extremes of the table, and it would appear that such loss of weight occurs: (a) When the general toxic action is very acute, as is Case 1, or where there is time for considerable local disturbance to come in, as the cases 10, 11, and 12, in which the onset of paralysis was delayed the most, and in only one was there anything but a marked diminution in the weight on the fourth day. In most of the other cases the loss of weight was very marked, but in only one or two instances has this weight been recorded.

Bearing in mind the fact that in the earlier experiments very few cases of paralysis among guinea-pigs were recorded, although in later experiments such a comparatively large number arose, this seems to explain fact and this appears to be offered by the fact that paralysis amongst an equal number of guinea-pigs used for testing purposes is greater when Ehrlich's new method is used than when the older method was employed.

**LOCAL AND CONSTITUTIONAL ACTION OF THE TOXIN.**

In describing toxin hitherto we have had its action divided into what may be called local and constitutional, the constitutional again being divided into those causing rapid death and those giving rise to rise of temperature and nutritional changes or reactions. So far as the cases that I have noted here are concerned, it is evident that the paralyzing substances are not the same as those which produce the local tissue reactions.

Martín pointed out that the albumoses separated from the body—not highly poisonous substances—give rise to comparatively slight local reactions, but when injected in small doses into the vein they cause marked rise of temperature, some wasting, and slight paralysis.

Cartwright Wood, who got rid of the enzymes from the albumoses by heating at 65° for one hour, was able to differentiate the actions of the enzymes and the "albumoses" somewhat more sharply. This rise of temperature following injection of the latter is accompanied by comparatively little though more prolonged local reaction; but, on the other hand, these substances give rise to slight paralytic symptoms even when injected in large quantities. In animals in which paralysis occurs there is at first a slight rise of temperature; this is almost invariably followed during the paralytic stage by a fall, sometimes of a couple of degrees and in one or two instances the temperature was as low as 98° a couple of days after the onset of paralysis. I hope, however, to collect more accurate information on this point.

**FURTHER ENQUIRIES NECESSARY.**

The following statement may afford an indication as to the lines on which it would be necessary to investigate further the causes of this paralysis. This paralysis occurs more frequently in animals used for testing the strength of antitoxin serum, the greater the number of lethal substances used in the test dose—that is, there are more cases of paralysis when a theoretically ten times lethal dose is than when one is used, and still more when the test dose is again multiplied by ten—than is, when it equals one.

As Ehrlich has pointed out, there are certain substances formed along with all toxins and also formed as the result of a slight rearrangement of molecules of toxins, which, although they combine with antitoxins, have to a great extent lost their power of killing guinea-pigs. Some of these substances, however, only combine with the toxin after the latter has entered into combination with the antitoxin, so that one can readily understand that these epitoxoids, as he calls them, may be present in large quantities uncombined with the actively lethal toxins and have all entered into combination with the antitoxin, so that the greater will be the danger of a considerable amount of this epitoxoid being left over after the neutralization of the actively lethal toxin. We should, therefore, expect that if some such substance as this exists, its amount of the paralysis, the greater would be the proportion of paralyses as the test dose of the toxin becomes larger.

**REFERENCES.**


**DISCUSSION.**

Dr. F. W. Mott, F.R.S., congratulated Dr. Woodhead upon his valuable paper, and the important statistics based upon a large amount of observation, of which he was greatly forward. He referred to the large proportion of cases of diphtherial paralysis, and asked whether those inimical to the antitoxin treatment had any grounds for explaining it by the increased use of antitoxins. No doubt Dr. Woodhead would satisfactorily dispose of this question, but he made the remark so that there should be no uncertainty in the minds of the public. Dr. Mott said that he had examined the nervous and muscular tissues in five cases of diphtherial paralysis. He had found generally fatty degeneration early and late of the muscles and sometimes Wallerian degeneration of the nerves. He had observed extreme early fatty degeneration of the heart, and yet no degeneration of the vagus nerve. He was of opinion that pro- bably the diphtherial paralysis. In his opinion, early antitoxin treatment was of the greatest value in diminishing the number of cases of paralysis in diphtheria.

Dr. E. W. Goodall (London) said that since the introduction of the antitoxin treatment the incidence of paralysis following diphtheria had diminished. There was evidence of this we believed to be that patients now recovered, or at any rate lived long enough to show symptoms of paralysis, who without antitoxin would have died at an earlier period. But though the number of the cases of paralysis, relatively as well as absolutely, had increased, the number of fatal cases had diminished. Moreover, if the serum treatment were commenced early enough, the number of cases of paralysis would be lower instead of higher than before. This was well shown in the large diphtheria cases in the Metropolitan Asylum Board's Hospitals during 1886. These cases were all under skilled observation from the very commencement, and the serum treatment was begun early. Among them the number of paralysis cases was considerably less than among the diphtheria cases admitted from outside during the same period, and there was only one case fatal from paralysis.

Dr. Woodhead, in reply to Dr. Mott, said that he was not thoroughly satisfied that antitoxin had no power of setting up post-convulsion by itself. He had given it to large in guinea-pigs and rabbits, but had never seen a case in which by itself it had produced any paralytic symptoms. He was very the patient to hear Dr. Mott had said regarding the action of the toxin on the processes of the nerve cells; it bore out very much the view that the action of the toxin was rapid and potent on the nerve cells. As he had indicated in his paper, he believed that the heart failed earliest and most frequently because it was the organ which really got least rest. He had contended for the same thing in his article on Tetanus in the
Allbutt's System of Medicine. This condition of over-work and ill-nutrition was the great factor, even in those paralysies that appeared later. The poison did its work, but it was only when muscle and nerve were called into functional activity that the damage was unmasked and the tissues give way under a strain in which they are normally able to stand. He quite agreed with Professor Baginsky and Dr. Goodall that cases of paralysis were not now so frequent as formerly, and that those which did occur were less severe. He thought that the practical outcome of the whole matter was that, if possible, the antitoxin should be used before degenerative changes had been set up, and that enough antitoxin should be given to neutralize not only the lethal action of the diphtheria toxin, but also its local and paralysis-producing action.

A NOTE ON THE LOCAL ACTION OF CRUDE DIPHTHERIA TOXIN.

By J. J. DOUGLAS, M.D., F.R.C.P.E.,
London.

INTRODUCTORY.

While much work has been done on the cellular changes following the injection of diphtheria toxin, attention has been chiefly directed to changes occurring in organs more or less remote from the seat of inoculation. Thus, Balgassari investigated changes in cells of liver and kidney, and Barbucci in cells of liver, spleen, and lymph glands. Welch and Flexner, however, while examining spleen, liver, and kidney, also investigated the histological changes at the seat of inoculation; they, however, used living cultures of the bacilli. These observers demonstrated the affinity of the toxin for the nucleus of cells, resulting in its fragmentation or in a modification of its staining reaction. They also found evidence of proliferative changes. It was to study the local changes subsequent to the injection of a filtered culture that this research was undertaken. With the object of investigating the local antitodal effect of antitoxin doses of this were injected in certain cases along with the crude toxin.

METHODS, ETC.

The animals used were guinea-pigs. There were three series of experiments made: (1) with toxin alone, (2) with toxin and a half-neutralising dose (as regards its lethal activity) of antitoxin, and (3) with toxin and a fully-neutralising dose (as regards its lethal activity) of antitoxin. The full test dose of toxin was given in each case. The injections were given subcutaneously in the abdominal wall. The animals were killed at varying periods after injection, e.g., 20 minutes, 1 hour, 2 hours, 3 hours, 5½ hours, 10½ hours, 24 hours, and 30 hours. The skin of the abdomen was shaved and portions of the abdominal wall removed, hardened in 2 per cent. formalin, in Müller, embedded in paraffin, and cut in the ordinary way. Sections were stained with Ehrlich's haematoxylin and eosin. It will be convenient in what follows to speak of 1-hour, 2-hours, etc., sections, meaning thereby sections of specimens taken from animals killed 1 hour, 2 hours, etc., after injection. Attention was directed to the subcutaneous tissue of the area into which injection had been made, and in it to (a) the presence or absence of edema, to (b) the condition of fixed connective tissue cells, to (c) the condition and relative number of wandering cells, and to (d) the condition in the subcutaneous tissue apparently endothelial in character.

TOXIN ALONE.

(1) Series treated with toxin alone. It was not found possible to get a 24-hours' specimen, as the animals did not live so long.

(a) Presence or Absence of Edema.—The earliest section to show undoubted edema was the 5½ hours' one. It was more marked in the 1-hour's specimen and still more in the 24-hours' one. In the earlier sections there was a condition which might possibly be edema, but which might also depend upon undissolved fluid of injection.

(b) Condition of Fixed Connective Tissue Cells.—These in all periods, from 1 to 24 hours, appear swollen. This swelling seems to vary directly with the length of the period up to 24 hours. In some cases the cells show a lateral bulging. At no period are there discernible signs of fragmentation of the nucleus, nor of proliferation of the cells, unless indeed the above-mentioned lateral bulging may be taken as evidence of this. In many cases the cells seem to have taken up the stain very faintly. In 1-hour and 2-hour sections there are a few vacuolated cells.

(c) Condition of Relative Number of Wandering Cells.—The number of these tends to vary directly with the length of the period up to 24 hours. In 1-hour and 2-hour sections the majority show almost a uniform staining with haematoxylin, the nucleus not being clearly defined. In the earlier of these two sections, however, there are cells showing apparently a normal staining reaction with distinct nucleus. In both, where nucleus is definable, it appears single. Seen for the first time in 2-hour section, and being present in increasing numbers in 3-hour, 5½-hour, and 10½-hour sections, are round cells very faintly or not at all stained, and having a granular appearance. This appearance is not a question of faulty technique. These phantom cells are present in greatest numbers in 5½-hour sections. In 24-hour sections they have altogether disappeared. Appearing for the first time in 5½-hour section are polymorpho-nuclear cells with eosinophile granules—finely granular oxyphile cells. These are also present in 10½-hour sections and in 24-hour sections. Fragmentation of nucleus is seen most markedly in 24-hour sections, though it is also seen, but to a less degree, in 10½-hour sections. In the former the nuclei appear shatterd, recalling the appearance of pus cells.

(d) Cells apparently endothelial in character. These are oval cells with apparently one large nucleus and very little protoplasm. The chromatin network stains faintly with haematoxylin, but is distinct. They are present in all sections, perhaps in greatest numbers in the latest ones.

In most sections there are signs of cloudy swelling of the superficial muscular fibres.

TOXIN HALF NEUTRALISED.

(2) Series treated with toxin and a half-neutralising dose of antitoxin. Studied in a like manner it was found impossible to be sure of the reality of edema before 5½ hours after injection. From this period on, edema increased up to 24 hours. Connective tissue fixed cells appeared swollen in 20 minutes' section, and this swelling was present in all sections, and was more marked in late specimens.

The changes in the wandering cells seemed to be very similar to those in Series 1. There were present uninuclear cells with distinctly staining nucleus, cells staining uniformly with haematoxylin, and having indistinct nucleus, gradations between these and phantom cells, phantom cells, finely granular oxyphile cells, and cells in which the nucleus was fragmented. All of these appeared at nearly identical periods to those at which they appeared when antitoxin was not used. Endothelial cells were also present in most of the specimens.

TOXIN FULLY NEUTRALISED.

(3) Series treated with toxin and fully neutralising dose antitoxin. What has been said of Series 2 practically applies to this one. The changes appear almost identical, save for the earlier appearance of badly staining cells.

SUMMARY.

In conclusion the points elucidated by this research seem to be: (1) That the cellular changes are degenerative, and that there is no indication of proliferation of affected cells; and (2) that antitoxin, whatever may be its antagonistic effect generally, does not locally act as a chemical antidote to the toxin.

Toxin Alone.
Toxin alone: 1 hour after injection showing "false oedema."

Toxin alone: 2 hours after injection showing "false oedema."

Toxin alone: 2½ hours after injection showing marked oedema.

Toxin alone: 24 hours after injection showing marked oedema.

Toxin alone: 24 hours after injection showing commencement of true oedema.

Toxin alone: 3 hours after injection showing swollen fixed connective tissue cells.
Toxin alone: 3 hours after injection showing "phantom" cells, one of which is marked x.

Toxin alone: 3 hours after injection. Endothelial cell marked x.

Toxin alone: 5½ hours after injection showing "phantom" cells marked x.

Toxin half neutralised: 24 hours after injection showing marked oedema.

Toxin alone: 24 hours after injection. The cells have fragmented nuclei; though this does not appear distinctly in photograph.

Toxin half neutralised: 24 hours after injection showing cells with fragmented nucleus.
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<tr>
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<th>20 min.</th>
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<th>90 min.</th>
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<tbody>
<tr>
<td><strong>Toxin Half Neutralised.</strong></td>
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<tr>
<td>Uninuclear cells with normal staining reaction</td>
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<td>+</td>
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<tr>
<td>Cells uniformly staining</td>
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<td>Phantom cells</td>
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<td>Finely granular oxyphile cells</td>
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<td>Cells with fragmented nucleus</td>
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<td>Cells of endothelial type</td>
<td>+</td>
<td>+</td>
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<th>12 hr.</th>
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<th>36 hr.</th>
<th>48 hr.</th>
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<tr>
<td><strong>Toxin Wholly Neutralised.</strong></td>
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<tr>
<td>Uninuclear cells with normal staining reaction</td>
<td>+</td>
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<td>Cells uniformly staining</td>
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<td>+</td>
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<tr>
<td>Phantom cells</td>
<td>+</td>
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<td>Finely granular oxyphile cells</td>
<td>+</td>
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<td>Cells with fragmented nucleus</td>
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<tr>
<td>Cells of endothelial type</td>
<td>+</td>
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<td>+</td>
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</tbody>
</table>

**REFERENCES.**


**DISCUSSION.**

Dr. Muir referred to the need for control experiments with antitoxin as regards the time of appearance of the finely granular oxyphilic cells. The fact that they appeared at an earlier date, when the antitoxin was injected with the toxin, than when the toxin was injected alone, was suggestive in relation to the general question regarding the meaning of the local leucocytosis. It would be of value, if it could be absolutely shown that, by reducing the quantity of the toxic agent, the leucocyte emigration took place earlier and was more marked. Such changes should also be studied in relation to the blood or general leucocytosis.

Dr. Lazurus-Barlow felt sure that if the specific gravity of the affected tissues were taken, evidence of output of fluid by the blood vessels would be found far earlier than the 53 hours after injection which Dr. Donahue had first recognised it. He thought that research should be further conducted on the lines indicated by the author, as in that direction might perhaps be found an answer to the question whether endothelial cells play a part in ordinary repair besides the new formation of the blood vessels.

**ON NEISSER'S DIAGNOSTIC STAIN FOR THE DIPHTHERIA BACILLUS.**


**[ABSTRACT.]**

A new differential staining method for the diphtheria bacillus was recently published by Neisser. The formula is as follows:

1. One gramm of methylene blue (Gruber's) is dissolved in 20 c.cm. of alcohol (95 per cent) and mixed with 930 c.cm. of distilled water and 5 c.cm. of glacial acetic acid.
2. Two grammes of benzidin are dissolved in 1,000 c.cm. of boiling distilled water, and the solution is filtered.

Cover-glass specimens prepared from fresh serum cultures are stained in No. i for 5 to 30 seconds, rinsed in water, counter-stained in No. ii for 5 to 30 seconds, washed in water, dried, and mounted in Canada balsam.

So treated, the diphtheria bacillus appears as a slender, longish rod, stained brown, and generally containing granules of a deep blue or inky tinct. There are usually two granules, situated at the poles, occasionally a third at the middle of the rod. The method has been tested on about 50 cultures from diphtheria throats, and the characteristic appearances have been obtained in every case. The pseudo-diphtheria bacillus of Hoffmann does not give the granulation. A slightly longer treatment than that recommended by Neisser has seemed to yield better results—namely, five seconds in the blue and ten seconds in the brown.

An attempt has been made to extend the method to swabbing or membrane from the throat. With swabbing the results were not very successful, an error of about 14 per cent, occurring in 30 cases.

With fresh membrane, care being taken to avoid fallacy from the presence of fragments of lepto- and diplo- bacillus, which may simulate the diphtheria bacillus, Neisser's method often affords a rapid means of positive diagnosis. If a negative result be obtained recourse must be had to culture methods.

**REFERENCE.**


**NORMAL SERUM IN RELATION TO THE DIAGNOSIS OF THE TYPHOID BACILLUS.**

By S. R. Christophers, M.B.Vict.,

From the Pathological Laboratory, University College, Liverpool.

In the event of a positive reaction being given by any suspected typhoid organism and the typhoid serum, there are two possibilities which should be taken into account before the diagnosis is definitely decided. The first, which has been amply demonstrated by Durham, is that of the mutual serum action of the typhoid bacillus with that of Gartner’s bacillus. The second, which has not been received much attention, is that of normal serum, apart from any specific reaction whatever, may with certain organisms give reactions equal in power and extent of dilution to so-called specific ones. The fact that normal serum has some action on some of organisms has always been recognised, but that this action in some conditions is immensely increased has received but scant notice.

So long as the reaction is used as a clinical test for typhoid fever the importance of this increased normal serum action is not very great. The cultures of typhoid used are of pretty uniform virulence, and human serum does not act on such as a rule above 1 in 10 dilution. But so soon as one has to deal with organisms from various sources and of various degrees of attenuation then this normal serum action becomes of very great importance indeed.

Trying serum reactions upon numbers of typhoid-like and colon-like organisms isolated from shell fish, milk, and water, I was struck by the great action at which normal serum acted, and strongly agglutinated many of the organisms. In many instances in dilution of 1 in 100 normal human serum caused extremely marked agglutination, large clumps of motionless bacilli being formed, and the preparation exactly resembling a decided typhoid reaction. Here is a pronounced action of normal serum upon certain organisms appeared to be a specific one, for it equally in degree and extent of dilution even strong reactions given by the serum of typhoid patients upon the typhoid bacillus. But further investigation showed that in no way could this action be called specific, and that it was in some way entirely due to a great susceptibility of certain organisms to be agglutinated by all serums. Those of the organisms most susceptible to human serums were also those most susceptible to the serums of the horse, monkey, rabbit, and even of the frog. So uniform was the action of different serums upon these organisms, that I came to the conclusion that it was not a selective action due to the serums, but depended entirely on varying susceptibilities of the organisms. In every case the non-susceptible forms in small doses proved fatal to guinea-pigs, whilst the susceptible forms in enormous doses failed to have any effect whatever.

The majority of these organisms resemble very closely the bacillus coli communis; others are extremely difficult to distinguish from the typhoid bacillus. The following table
shows the reactions of some of the more typhoid-like of these organisms and their behaviour with different sera.

<table>
<thead>
<tr>
<th>Laboratory Typhoid</th>
<th>Typhoid Like</th>
<th>Colon Like</th>
<th>Bacillus Coll.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram's stain</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Glucose media at 20°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indol formation in peptone salt solution</td>
<td>No indol</td>
<td>No indol</td>
<td>Indol</td>
</tr>
<tr>
<td>Milk in 48 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth on acid potato</td>
<td>Not coagulated</td>
<td>Not coagulated</td>
<td>Thick</td>
</tr>
<tr>
<td>Growth on cellulose gelatin</td>
<td>Very thin</td>
<td>Thin</td>
<td>Thick</td>
</tr>
<tr>
<td>Acid formation in neutral litmus whey 1 day</td>
<td>7 per cent.</td>
<td>20 per cent.</td>
<td>20 per cent.</td>
</tr>
<tr>
<td>Acid formation in neutral litmus whey 3 days</td>
<td>7 per cent.</td>
<td>20 per cent.</td>
<td>20 per cent.</td>
</tr>
<tr>
<td>Motility of bacilli</td>
<td>Very active</td>
<td>Very active</td>
<td>Sluggish</td>
</tr>
<tr>
<td>Flagella of bacilli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum reactions:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typhoid serum (a)</td>
<td>1 in 90</td>
<td>1 in 100</td>
<td>1 in 100</td>
</tr>
<tr>
<td>Typhoid serum (b)</td>
<td>1 in 90</td>
<td>1 in 100</td>
<td>1 in 100</td>
</tr>
<tr>
<td>Strongly reacting normal serum</td>
<td>1 in 100</td>
<td>1 in 100</td>
<td>1 in 100</td>
</tr>
<tr>
<td>Weak normal serum</td>
<td>Not in 10</td>
<td>1 in 90</td>
<td>1 in 100</td>
</tr>
<tr>
<td>Immunised rabbit's serum</td>
<td>1 in 500</td>
<td>Not in 10</td>
<td>Not in 90</td>
</tr>
</tbody>
</table>

Professor McWeeny said that he had repeatedly isolated from samples of drinking water coliform bacilli, which gave a typical clumping reaction with every specimen of human serum, normal and pathological, with which he had tested them. He had carried the dilution of the serum as far as 1 per cent., but not beyond that. The bacilli that gave this reaction were short, actively motile rods, growing rapidly at the room temperature, and actively fermenting glucose and lactose. He had not tested them on sugar agar. Crystals of trichlor phosphate, or a diffused cloudiness, regularly appeared in old gelatine cultures. He regarded them as excessively attenuated micro-organisms, perhaps derived originally from a bacillus coli.

ON AN EPIDEMIC OF GASTRO-ENTERITIS ASSOCIATED WITH THE PRESENCE OF A VARIETY OF THE BACILLUS ENTERITIDIS (GAERTNER), AND WITH POSITIVE SERO-DIAGNOSTIC EVIDENCE (IN VIVO AND IN VITRO).

[Abstract.]

(From the Pathological Laboratory of the University of Cambridge.)

By HERBERT E. DURHAM, M.B., Grocers' Research Scholar.

The symptoms of the cases were similar to those which have been described in outbreaks associated with the presence of the bacillus enteritidis of Gärtner and varieties thereof. About 185 persons were affected.

From a piece of the liver of a fatal case various bacilli were isolated; a large majority of these were found to agree in character with Gärtner's bacillus. The preponderance of these bacilli was suggestive of a causal connection with the epidemic. Eleven cases of these bacilli from the liver were compared with the three other cases of bacillus enteritidis in my possession—Gärtner, Günther, and Vienna—by means of their reactions to the serum of animals immunised against two of these varieties. It was found by this test that they resembled the cases "Vienna" and "Günther" more closely than that of Gärtner.

Blood serum was obtained from 29 individuals who had suffered from the epidemic about four weeks previously. Differential diagnosis was tried against five varieties of the bacillus enteritidis and also against the typhoid bacillus. At a dilution of 1 in 100 it was found that 18 of these blood samples gave good positive reaction with one of the cultures obtained from the liver; some were potent enough to react at higher dilutions, as 1 in 1,000. A comparison of the effects of these sera upon different races gave the following results:

<table>
<thead>
<tr>
<th>Culture</th>
<th>Strong Reaction at 1 in 100</th>
<th>Strong Reaction at 1 in 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver 1...</td>
<td>14 times</td>
<td>11 times</td>
</tr>
<tr>
<td>Vienna ...</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Günther</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Gärtner...</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

The sera reacted more strongly often with a culture obtained from the fatal case (Liver 1) than they did with the other cases (especially Günther). This is in concord with the results of the comparison with the bacillus upon experimentally produced sera. The remaining 11 samples exhibited no agglutinative effect at 1 in 100; some also failed to react at lower dilutions. Since it is hardly to be doubted that they suffered from the same disease, these cases may be compared to those of enteric fever in which either no reaction or but a slight and fleeting one is developed towards the typhoid bacillus.

Further, 8 serum samples were tried in doses of 20 mg. (see p. 590) for protective qualities against culture from the fatal case. Two of these had no agglutinative effect and no evidence of any protective action and a negative Pfeiffer reaction. The remaining 6 not only had agglutinative action, but also gave distinct evidence of protective action as well as positive results with Pfeiffer's test (lysogenic). Thus the evidence in favour regarding the bacillus as the cause of the outbreak is made more complete.

Guinea-pigs which were fed upon living and killed cultures of the bacillus acquired agglutinating properties in their blood.

Out of the 29 cases examined 5 gave minimal traces of reactions at 1 in 100 against the typhoid bacillus. At lower dilutions (especially by bringing undiluted serum in contact with 6 and 19 drops of culture) some of these gave well-marked clumping with typhoid culture; so that in the absence of differential tests they might have been returned as having been obtained from typhoid fever patients.

The importance of making use of several different cultures for the purpose of serodiagnosis in vitro (Gruber's reaction) as well as the necessity for comparative dilutions is well illustrated by these cases. Only one sample reacted sufficiently strongly against the race "Gärtnert" (that is, 1 in 500) for really decisive information. If this race and typhoid bacilli had alone been put to the test much of the nature of the sera and of the epidemic would have remained undisclosed.

Judging from experimental work, it is not improbable that an epidemic caused by the race "Gärtnert" might be less easy to distinguish from enteric fever by the serum reactions than in the present instance, for these bacilli are rather more susceptible mutually to their respective sera than are the races with which the epidemic was associated.

For controls 28 samples of serum were tested against all the races above mentioned. None of them reacted at 1 in 100 with two of the cases obtained from the liver, nor with the races Gänther and Vienna. Twelve of these sera were from persons who had never had typhoid fever, the rest had either had or were suffering from that illness. One of these normal controls was from a person who was associated with those who were affected by the epidemic.

The nature of the bacilli found in the fatal case together with the serum reactions and the clinical symptoms in the majority of the sufferers affords considerable presumptive evidence that the epidemic was causally related to the bacillus. Several of the outbreaks hitherto recorded have been associated with the meat of diseased animals (especially cows). No such origin was traceable in the present instance.

More information is required about the distribution, modes of infection, etc., of the "Gärtnert-like bacilli" of Nordmann's pittagocia and Thomas's bacilli appear to be varieties, not only in this country but also elsewhere, as in India, where choleraic disease is endemic. The observation of Grübaum that cases of febrile jaundice may give "lyphoid reaction" should be kept in mind.

[The indices of the microscope slides were shown to illustrate the morphology of the bacilli found in connection with]
THE PATHOLOGICAL EFFECTS OF DEAD TUBERCLE BACILLI.

By Stewart Stockman,
Professor of Pathology, Dick Veterinary College, Edinburgh.

Experiments with Dead Tubercle Bacilli. Such experiments have been undertaken before. Koch showed that dead tubercle bacilli produced an abscess in guinea-pigs when injected subcutaneously.

Prudden and Hodenpyl experimented more fully on guinea-pigs and rabbits. In their experiments they used dead tubercle bacilli from cultures on glycerine, agar, and broth. In some of their experiments they used bacilli that had been freed from their soluble products, but they found that the results were the same whether they used bacilli from agar or broth, and whether these had been washed free from the soluble products or not. They concluded that the lesions produced were due to some substance—bacterio-protein—set free by disintegration of the microbes in the tissues, or extracted in some other way. They incline more to the former view.

For the subcutaneous inoculations that were made in from two to six weeks. Tubercle bacilli stainable by the ordinary methods were found in the pus. By intraperitoneal and pleural inoculation with a milky emulsion of bacilli they produced nodules of various sizes on the serous membranes. These were made up of a central creamy-looking part surrounded by fibrous tissue. The central part consisted of epithelioid cells and giant cells. Tubercle bacilli were abundant in the central part; well-marked caseation was not found. Intravenous inoculations went directly into the avenues of rabbits. The animals were killed and examined at intervals of from one to sixty days. A few died after the third week. In animals killed after one day the bacilli were found in the lungs, liver, and spleen, most abundantly in the first-mentioned organ. The older the tubercle the fewer seemed to be the bacilli. After five days white nodules were found in the lung, some being microscopic, others quite visible to the eye. They were present up to the sixtieth day, the longest period of observation. Their structure consisted of epithelioid cells, giant cells, and leucocytes. Bacilli were found between the cells and inside giant cells. Later the nodule was denser and made up of epithelioid cells and loose connective tissue. After three weeks microscopic tubercle bacilli and lyphatic tubercles were found in the capillaries, were found in the liver. After five or six weeks visible nodules were found in the latter organ. Prudden and Hodenpyl conclude that the nodules originate in a proliferation of the vascular endothelium under the stimulus of dead and disintegrating tubercle bacilli. They say that "the dead bacilli seem to act as foreign bodies simply, curiously stimulating, it is true, but only foreign bodies after all." I think too much is made here of the foreign body question. Every foreign body does not produce this tissue reaction, although the power to do so may not belong exclusively to the tubercle bacillus. The action of the dead tubercle bacillus is in large part, at least, special to it, and it is the foreign body of this order that we are most likely to meet with in the tissues.

At the conclusion of their paper these authors offer some suggestions as to the influence of the products of the living germ on the degenerative changes in a true tubercle. They suggest, too, the possibility of the more fibrous tubercles being due to dead bacilli.

Curiously enough it was that last idea and a wish to further test an opinion which I had formed as to the origin of tuberculous giant cells, that led me to undertake these experiments with dead bacilli before I knew of their paper. I have since read it very carefully, and wish here to acknowledge my indebtedness to the authors. I have performed most of my experiments on different animals, but many of them confirm those of Prudden and Hodenpyl.

I must also mention that Straus and Gamaclia have to some extent confirmed the results of the American authors by experimenting on guinea-pigs, rabbits, and dogs. They say little about lesions in the liver. They found giant cells in the nodules. That may be because in their experiments too few bacilli were arrested in one part, or because the centres of the nodules were not examined. Many of their animals wasted and died. When the clumps of bacilli were broken and well distributed in the blood vessels the animals died and all the same, but no lesions were found. Evidently several dead bacilli are necessary in one part to produce a lesion. If the number of bacilli was very small the animals wasted, then recovered, and appeared quite healthy, but if a second small dose were administered they wasted and died. By using very small and ever-increasing doses of the dead bacillus they immunised the animal against it. With the products of the bacillus in artificial culture they could produce no lesion.

TUBERCULOSIS OF THE UDDER.

If one examines a number of tuberculous udders from the cow, one generally finds distinct caseous nodules, but that is not the only form that the tuberculous lesion may assume. At the Edinburgh abattoir during the last few years I have found a considerable number of tuberculous udders without any appearance of a caseous nodule in their substance. On examining these microscopically I have found tubercle bacilli and tuberculous giant cells, although the former were not very numerous. The size of the tuberclebacilli has been slightly underestimated. These udders, however, will not very much increase the amount of tuberculous-infected milk, because the affected quarters give little or no milk, and the cow is soon to be sent the abattoir.

I doubt that the last is true. The bacilli enter the udder in one way or because of foreign bodies. Much of the tuberculous udders has been slightly underestimated. These udders, however, will not very much increase the amount of tuberculous-infected milk, because the affected quarters give little or no milk, and the cow is soon to be sent the abattoir. The bacilli enter the udder in two ways: first, by the ordinary way of the blood vessels, and secondly, by the invasion of the blood vessels. The former is the old story of the tubercle bacilli found in the ox and pig. They are often surrounded by a rim of fibrous tissue, which is invading the caseous centre. Moreover, the tuberculous lesions of the muscles—muscle is considered a bad medium for the growth of the tubercle bacillus—which I have described in the pig were distinctly fibrous. I may say, too, that I have once found tubercle bacilli in fibrous nodules under the mucous membrane of the fourth stomach of the ox, and have several times found them in various thickenings of the subcarnal regions of the ox. These are the observations which have led me to undertake these experiments.
killed by three hours' steaming. The bacilli came from a glycerine broth culture that had been kept for five months. An abscess formed and burst three days afterwards. A month later a second injection of bacilli in thick emulsion was given under the skin. The latter came from a glycerine broth culture that had been in the incubator for four months, and afterwards killed by three hours' steaming on the third day. Swelling about the size of a hen's egg formed at the site of inoculation. The skin over this abscess was asciticified, and some pus was aspirated into a sterilised syringe by means of a needle passed into the cavity. The culture was then inoculated into a sterilised syringe by passing a portion of the contents through a needle. The results of both injections were negative.

In order to see if the bacilli were still present in the second abscess, which was removed from the animal during the operation, the fluid in the syringe was inoculated into cultures for the tubercle bacillus. They were all negative.

One might draw the following conclusions from this experiment: (1) That the soluble products of the tubercle bacillus produce little effect on the healthy organism, although they have a very decided action on animals whose bodies contain the tubercle bacilli, living or dead. (2) That the dead bacilli are far more active than the soluble products, although this may be on account of their retaining a strong toxin in their bodies.

This bitch ran away and enjoyed perfect health for ten months afterwards. I was anxious to see if she would still react to the dead bacilli.

On the 29th March of this year the daily temperature ranged between 101.8° and 102.4°F. She received into her jugular vein the greater part of the bacilli from a 2 months' culture of the tubercle bacillus in 50 cc. of glycerine broth, which had been sterilised by boiling at 100°C. The 2nd March. Temperature 105.5°F. Animal rather dull. The 4th March. Temperature 104°F. Animal brighter. The 5th March. Temperature 100.5°F. Animal brighter. The 6th March. Temperature 105°F. Animal apparently quite well.

Up to the 9th April the temperature fluctuated between 103.5° and 104.5°F. From the 4th to the 8th April the daily temperature at 12 o'clock was over 105°F. On the 9th April (4 days after), at 9.15 a.m., when the temperature was 106°F. Two of the late cultures were injected. My reason for starting at this hour was, of course, to get the observation over in one day.

The annexed chart shows the temperature reaction.

### Chart I.

<table>
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<th>9:00</th>
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<tr>
<td>April</td>
<td>9</td>
<td>9.5</td>
<td>9.7</td>
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The variation was thus 1.2°, but it did not go much beyond the physiological limits. The results of tuberculin in the dog, however, have not been satisfactory, so far at least. Cadiot records the result of the test on 15 tuberculous dogs. The rise in temperature amounted to from 0.5° to 1.7° C. In 8 cases the temperature rose no more than 1°. In 3 cases there was no rise, but a diminution in temperature followed by death.

The animal was killed four months after intravenous injection of dead bacilli. The pleura showed a large number of fibrous nodules which contained no bacilli. There were no distinct nodules in the lung. The liver showed numerous tuberculous nodules.

**Experiment 19.**-Spoonish bitch. With a view to raising the temperature for a certain experiment of his own, Dr. Noel Paton injected some dead tubercle bacilli into the external saphena vein of this animal's hind leg. He killed her twenty days afterwards, and was good enough to let me have the lungs and portions of the liver. The lungs contained many small, firm, greyish nodules, the size of a pin's head. The liver was very slightly enlarged by the naked eye, but the microscope revealed small cellular collections identical with those found at the start of an ordinary tubercle caused by the living bacilli entering by way of the blood vessels. The temperature of this animal did not rise, but I think many bacilli were used.

The animal was tested with tuberculin on February 27th, 1898. It did not give any reaction. The normal temperature was 99.2°F. On February 28th two cultures of the B. tuberculin in 5 cc. of glycerine broth, which had been incubated for two months, were killed by submitting them to the boiling temperature for one hour. The fluid was then tested off. Animal and bacilli were left as a thick emulsion. As one can understand, the microbes were very numerous. At 4:30 P.M. the bacilli from the two cultures were injected into the left jugular vein of the pony with all antiseptic precautions.

### Chart II.

The above chart shows the temperature reaction after the inoculation, and also the result of the tuberculin test applied three weeks afterwards.

The reaction was 0° F. It will be seen that the temperature after the injection of dead bacilli fell to the normal just about the time that it should have been rising had the animal been inoculated with living bacilli. The animal was afterwards killed for the dissecting room, twenty-five days after the bacilli had been injected.

**Necropsy.**-The lungs were simply studded with small white nodules, varying in size from a pin point to a pea. They to some extent resembled miliary tubercles, but they differed from them in being denser and less yellow. One or two small areas about the size of a bean were very solid and of an amber colour. The latter much resembled the larger nodules that one finds in the lungs of sheep afflicted with parasitic pseudo-tuberculosis. There was also slight broncho-pneumonia. The jugular vein at the seat of inoculation showed a nodule in its wall. This nodule was about the size of a pea nut. It was comparatively firm, but showed one small softened centre. Cover-glass preparations, made with the softened material and stained by carbol fuchsin, showed numerous bacilli. None of the other organs showed lesions visible to the naked eye. With several nodules from the lungs guinea pigs were inoculated into the peritoneal cavity. They did not become tuberculous. The bacilli then were dead.

**Microscopic.**-The lung nodules were made up chiefly of epithelioid cells and loose connective tissue, containing a good many spindle cells. There were a few giant cells in some of the nodules. These giant cells, however, were fewer in number and not quite so distinct as those found in natural cases of tuberculosis. Numerous bacilli were present between the cells of the nodule, either as single rods or in clumps. At some places they assumed a somewhat circular arrangement, such as one often finds at the periphery of the giant cell in an ordinary tubercle. The bacilli were easily stainable by the ordinary methods used for the tubercle bacillus. There was no distinct caseation, but there were some very small homogenous patches which stained diffusely.

The best method of showing the giant cell is to stain with picric-carmine a section cut on the freezing microtome. It is difficult to find these sections cut in paraffin, although distinct giant cells are well enough seen in sections of ordinary tuberculous nodules cut in the latter way. Contrary to what one finds in the ordinary tubercle, those caused by the dead bacilli are vascular. The lumen of a small artery, however, is often narrowed by a periarteritis.

A nodule in the wall of the jugular vein had a similar appearance to those found in the lung. The cellular centre, however, was more extensive, and there was a tendency for it to drop out of unembellished sections.

It seems to me that the giant cells are most numerous in the larger nodules. On these contain the greatest number of bacilli.

I attempted to repeat this experiment on another horse, but the animal died of embolism, in great part, I think, due to air bubbles in the fluid.

I have now another animal under experiment, I will inject
him with tuberculin at several intervals in order to see if he will secrete it. In this case, the administration of the tuberculin
was started four days after the death of the animal, and the
animal was found to have lived for nine weeks without showing
any symptoms of tuberculosis.

Experiments with Tuberculin.-In the experiments with
tuberculin, the horse was used as the subject of observation.

1. Sept. 3, 1898.]

EFFECTS OF DEAD TUBERCLE BACILLI.

[The British Medical Journal 603

...are capable of proliferation, and that the tissues have
overcome many of the bacilli in certain nodules, and prevented
the changes from going further. The dead bacilli experimentally
injected certainly do not disappear from the nodule, and we may
expect those killed in situ to do the same. In the centre of the
so-called giant-cell one may find a single stain nucleus; usually
one sees only chromatin substance, but even that may be
absorbed. Many of the nuclei at the margin are breaking
up. It is at the margin of the giant cell that they are mainly
found, and they may be to the number of twelve or more. If
these nuclei be carefully looked at, one often sees that they are
in reality surrounded by the cell bodies in different stages of
degeneration. This is best seen in the tubercles provoked
by the dead microbes, possibly because the formation is neither
so rapid nor so marked as in the case of active living bacilli.

In some of the former one can see contiguous cells with
caseous bodies not yet fused. Their nuclei are still present,
but show up less distinctly. Some of the latter are in capillary
vessels, and seem to arise from the endothelial cells. As
caseation extends, other cells at the periphery are included.
The nuclei of the cells first struck with degeneration
become disintegrated, and the living ones are taken up at
the margin. By-and-by the degenerating patch may
increase to such an extent that the cell-like form is lost, and
it takes the appearance of a caseous area. Some of the cells
included at the margin resemble certain of the white
blood corpuscles; they are somewhat like these, and come out
to surround the dead patch and have perished in an attempt
to digest the bacilli.

These experiments seem to show so far that one may
inject milk containing dead bacilli. That, of course,
does not mean that cows with tuberculous udders should be
tolerated in byres. They also suggest the possibility that
some of the very chronic lesions in animals contain only
dead bacilli. To decide this, of course, one would have to
inoculate previous sections obtained from large animals
in question. The production of a lesion in the abdominal
organs of guinea-pigs would not in all cases be enough to prove
the vitality of the bacillus, because one might possibly inject
a sufficient number of dead ones to act. Artificial culture
on glycine agar, however, would decide the question.

REFERENCES.
1 Most of the work in this paper has been done in the Laboratory of the
Royal College of Physicians of Edinburgh, and I wish here to acknowledge
my obligations to that institution. Journal of Hygiene, June 2dth, 1895.
3 Veterinarin, March, 1896.

DISCUSSION.
Professor McFADYEN said that Professor Stockman's
experiments with cows containing dead bacilli followed only
when colossal quantities of the bacilli were introduced. He
could not agree that the formation of giant cells was similar to
caseation, which was an effect produced only by living bacilli.

Dr. WILLIAMS said he was interested in this paper because
a series of experiments which it had fallen to his lot to carry
out had given a number of "false results," if he might so say,
which had a bearing on the question. He found that
dead bacilli injected locally set up a local lesion in which
the bacilli could be stained. From this lesion, however, no
secondary infection could be obtained. Injected into the
veins, these dead bacilli made their way principally to the
lungs, where non-caseating, fibrous nodules were formed.
These nodules contained no infective material, and secondary
lesions could not be obtained. The bacilli, when not quite
dead, could be recovered. He thought this was a flaw in the
previous experiments of the author.

Professor GREENFIELD said that the previous speakers
had practically acknowledged the existence of a possible flaw
in their experiments. He asked if it were not possible that
some bacilli, if not killed, might be still living. From his own
reading, however, he had been led to the conclusion that dead
bacilli undoubtedly might produce elementary tubercle follicles with giant cells.
He asked at what period of time the lesions described by Professor Stockman were found in the liver after intravenous injection. He thought it unnecessary to assume that the bacilli producing them must have been living, as it was quite possible for dead bacilli to pass through the pulmonary capillaries and lodge in the liver.

Professor McWenney inquired whether Professor Stockman had determined the virulence of his cultures before injecting them. The same effects could hardly be expected to result from the presence in the tissues of virulent as from that of attenuated organisms, even though they had previously been devitalised. He was of opinion that a determination of the virulence of the bacilli in the living state would be of great value in the interpretation of results obtained by the injection of devitalised cultures.

Dr. Mott suggested that in the case of fibroid nodules produced by organisms presumably devitalised, inoculation experiments should be made from them in fresh animals.

A DISCUSSION ON THE NATURE AND SIGNIFICANCE OF LEUCOCYTOSIS.

I.—Robert Muir, M.D., F.R.C.P.Edin., Lecturer on Pathological Bacteriology, Edinburgh University.

The subject of the discussion which I have the honour of opening is at once one of the most important in modern pathology, and has also a most important bearing on clinical diagnosis and prognosis. It is, moreover, one which has very wide connections, being on the one hand closely involved with the tissue changes usually grouped together as inflammation and, on the other, intimately related to the defence of the organism against noxae of various kinds, especially against microbes. The subject is, in fact, so wide, that on such an occasion the present discussion must necessarily be treated in one or two of its parts. The object of the discussion is to imply a consideration of the whole question of phagocytosis and of the bactericidal or other antagonistic properties (direct or indirect) of the substances secreted by or contained within these cells. And further, the observations on the modification in the number of leucocytes within the blood as a whole, or the modification in the number of different varieties, as can only be treated in one or two of its parts. The object being the examination of open local increase, emigration of leucocytes, and their subsequent behaviour would imply in its discussion a consideration of the whole question of phagocytosis and of the bactericidal or other antagonistic properties (direct or indirect) of the substances secreted by or contained within these cells. And further, the observations on the modification in the number of leucocytes within the blood as a whole, or the modification in the number of different varieties, as can only be treated in one or two of its parts. The object being the examination of open local increase, emigration of leucocytes, and their subsequent behaviour would imply in its discussion a consideration of the whole question of phagocytosis and of the bactericidal or other antagonistic properties (direct or indirect) of the substances secreted by or contained within these cells.

Definition of Terms.
The term leucocytosis may be applied to any condition in which there is an excess of leucocytes over the normal, whether in the tissues or part of the vascular system, a local leucocytosis, or throughout the circulating blood, a general leucocytosis. We shall first speak of the latter. The general facts are well known—that in many acute inflammatory conditions, occurring naturally or experimentally produced, such as pneumonia, coryza, etc., and especially in supplicative conditions, the number of leucocytes in the circulating blood may be two- or three-fold the normal, or even more. Further, a similar condition may be produced by the introduction into the body of various chemical substances, of which the most important are those used in the treatment of inflammation, (a) bacterial products, especially the so-called bacterial proteins; (b) extracts of various organs or tissues rich in cells, such as spleen, bone-marrow, etc.; (c) a great variety of definite organic compounds—especially those derived from the crystalline matter of the blood or produced by so-called bacterial products, (d) extracts of various organs or tissues rich in cells, such as spleen, bone-marrow, etc.; (e) a great variety of definite organic compounds—especially those derived from the crystalline matter of the blood or produced by substances produced by substances produced by such substances is sometimes spoken of as toxic leucocytosis, but in its essence is closely related to that occurring in inflammatory conditions. One question has been raised which must first be answered—namely, is leucocytosis occurring in the conditions mentioned real? That is, does the total number of leucocytes in the circulating blood increase, or is there simply an accumulation in the peripheral vessels from which blood is usually drawn? Recent observations of those of Goldschneider and Jacob may be mentioned (with which I am in full agreement), that the increase in the peripheral vessels is clearly a general one and that in the peripheral vessels there is the same proportionate excess over the number in the blood of the heart as there is in the normal condition. There occurs therefore in leucocytosis an increase of leucocytes both in the circulation, and, in other words, an addition of leucocytes to the blood. Further, in the case of supplicative and allied conditions, there occurs an enormous emigration of leucocytes from the vessel, so that we see, for example, in clinical cases, several ounces of pus discharged daily, and during this time, it be noted, the number in the blood is much above the normal. In such conditions, where there is a continuous drain, and at the same time an excess of leucocytes in the blood, the production must be much in excess of the normal. In the case of leucocytosis following injections of chemical substances there must first be an addition of cells to the blood, but after this addition has taken place it does not necessarily follow that it requires an increased multiplication to maintain it, though such may occur.

There are two points which also must be kept in view: (1) The variety of leucocyte in excess in these conditions is almost exclusively the finely granular (oxyphile or neutrophil), active spheroid leucocyte, polymorphonuclear; (2) the enormous rapidity with which the leucocyte increase occurs—namely, a doubling or more of the normal number in a few hours.

Varieties of Leucocytes.—The Origin of the Finely Granular Leucocytes.
The varieties of leucocytes, as met with in the blood of man and animals, were shortly described. The distribution of these varieties is also of importance, but I wish specially to mention (with which I have agreed), as this seems to me a point upon which sufficient stress has not been laid. In the first place, as everyone knows, leucocytes multiply by mitotic division in lymphoid tissue, lymphatic glands, Malpighian patches of spleen, solitary glands, etc. The cells there undergoing division are small spherical cells, with relatively large nuclei and rather scanty hyaline protoplasm. These cells give rise to lymphocytes, which leave by efferent paths, and a certain proportion reach the blood by the thoracic duct. Secondly, leucocytes undergo division in the bone marrow. The great proportion of cells dividing there are of somewhat larger size than in the germ centres, and their protoplasm contains fine granules which have a definite (oxyphile, neutrophile, etc.) reaction. The coarsely granular lymphocyte cell is then in its initial position, though they are fewer in number, and their multiplication is less active, than is the case with the former variety. Now it is to be noted that division among the finely granular cells in the marrow in normal conditions is very active; in fact, so far as I have seen, as active as in the germ centres of lymphoid tissue. How do the leucocytes derived from these cells leave the marrow? One naturally concludes by the blood stream, but in the blood stream there are no cells with spherical or oval nucleus and with fine granules in the protoplasm, which have the same reaction. Examination of the marrow shows, however, that the cells there present show great variation in the configuration of the nucleus, and, in fact, one can trace all the intermediate stages from the simple rounded or oval nucleus through various degrees of lobulation to the markedly multipartite nucleus of the finely granular, actively ameboid leucocyte. And, if one examines sections, one can see that leucocytes of this character are normally found in varying number at the periphery of the blood channels, whilst the larger cells from which these cells, in my opinion, they spring, are, as a rule, further removed from the blood stream. According to this view, then, the finely granular cells after division undergo this peculiar change in the nucleus which specially characterises them and enter in their newly formed condition. I may add that I have failed to find any ameboid movements in the larger cells in the marrow. The acquisition of this property would appear to be developed pari passu with the change in the configuration of the nucleus.
Another fundamental question in the inquiry is whether any formation of the finely granular leucocytes with polymorphonuclear nucleus takes place in the blood from the larger hyaline forms with simple spherical nucleus. There is no doubt that the latter, indeed, in the action of oblation of the nucleus may be seen, but does the change go further? It will be found that authors disagree markedly on this point. At one time I considered that I could find in human blood transition forms between the “undenucleated” and “multinucleated” leucocytes, as they were formerly called, but such transition forms appeared to be exceedingly scanty and apparently quite insufficient in number in leucocytosis to account for the large number of multinucleated cells seen in such conditions. If we examine the bone marrow of the rabbit in which the corresponding cells have the granules much more pronounced, I think it will be impossible to observe transition forms, in fact, the whole appearance during the occurrence of a leucocytosis is as if a large number of cells of exactly the same kind were rapidly added to the blood. On carefully considering, on the one hand, the character of the cells in the blood, and, on the other hand, the cells in the marrow, there can be little doubt—in my mind there is no doubt—that the polymorphonuclear leucocytes are formed chiefly, if not entirely, from the latter, and enter the blood stream in their fully formed condition.

**Leucocytosis in Inflammatory Conditions.**

We must now pass on to the consideration of the evidence of increased multiplication of leucocytes in inflammatory conditions associated with leucocytosis. I may state, in a word, that neither in the tissues nor in the blood stream is there evidence of multiplication by mitosis amongst the polymorphonuclear leucocytes to account for the increase. The question regarding direct division is a difficult one, but here again facts are entirely wanting to show that such a process plays an important part in the changes which occur. If these cells are multiplied, it is only by the process of inclusions,—namely, Are any important changes found in the bone marrow when there is a constant drain on this variety of cell; in other words, when there is an increased production of this form of cell? To answer this question I have made a considerable number of experiments, and shall briefly detail the results. These experiments consisted in producing leucocytosis, or at least a removal of leucocytes from the blood, by subcutaneous or intraperitoneal injections of organisms, chiefly staphylocoeci. The experiments lasted for various periods of time up to four weeks and a half. The results are somewhat striking. I find that there occurs an important change which is readily recognisable. This change consists in a general absorption of the fat of the marrow and a corresponding hypoplasia of the cells; and in other important cases, the cells increased in number are the large finely granular cells which may be called finely granular leucoblasts, and which are the source of the finely granular leucocytes. It is possible that the cells which are newly formed are undergoing rapid multiplication. The coarsely granular eosinophile cells are relatively, and it may be absolutely, diminished. Erythroblasts or nucleated red corpuscles are also much diminished. The giant cells may undergo degenerative change and in great part disappear. (These cells do not contain granules, and are probably derived from the larger hyaline cells.) The marrow in such a condition presents a striking deviation from normal, and the change may be said to correspond superficially to what occurs in the erythroblasts after haemorrhage (great increase in number and increase in the mitotic figures). If we call the latter the "erythroblastic" type of marrow, then we may call that which I have described the "leucoblastic" type of marrow. This fact appears to me to throw light on the whole subject. If we consider the finely granular cells as a class—say in a case of suppuration—we find (a) locally an enormous number of finely granular leucocytes (pus corpuscles); (b) in the blood a great increase in the number of the same cells; and (o) in the marrow a great increase in the cells from which these leucocytes are derived.

Furthermore, it is very probable that the same cause would explain all these phenomena. It must now be accepted that bacterial products act as chemotactic substances, and are the chief agents in the leucocytic migration and accumulation. One cannot, I think, study the phenomena which follow, for example, intraperitoneal injection of various bacteria, without recognising that this process must be at work. Granted then a chemotactic substance, it may be in such quantity as only to act upon the bone marrow, by local inflammation or suppuration without leucocytosis, but if the local lesion be more extensive, then these substances which produce chemotaxis are absorbed by the blood stream in such quantities that they may be brought to the site of the lesion, and the result will be a general leucocytosis. This is in all probability the first step in the production of the leucocytosis quickly following the injection of chemical substances into the circulation. But there is another question, the question of transition from large leucoblasts (marrow cells), and this is probably due to a stimulating effect which these substances exert on the cells—it certainly cannot be explained on any mechanical principle. We have therefore the local leucocytosis and the general leucocytosis induced by the same agency. This view very closely corresponds with what Ehrlich and Lazarus have adopted in their latest publication.\(^1\) I may say, however, that I have arrived at these conclusions quite independently, and that, so far as I know, the changes referred to in the bone-marrow have not been previously described.

In interpreting the phenomena we may then say: (1) THAT the local leucocytosis is a most important means of defence; (2) THAT the proliferative changes in the bone-marrow are the means by which the leucocytes are supplied in large numbers at any given place of need; (3) THAT the leucocytosis in the blood is an indication at least that this supply is being maintained. We may also mention that the vascular arrangements in the marrow are such as, on the one hand, to permit a ready action upon its cells of chemotactic substances circulating in the blood, and, on the other hand, to allow a free and rapid passage of the cells into the blood.

It is to be noted that chemical substances must be the means by which a general leucocytosis is brought about, and therefore it is not surprising that it can be produced where there is no local inflammatory change. Whether in such a case the leucocytosis really acts as a means of defence by combining with toxins in the blood, for example, in the leucocytosis following injection of diphtheria toxin, must still be considered an open question. Another question worthy of study is whether, and if so to what extent, degenerating or broken down tissues act as chemotactic agents in the production of a general leucocytosis.

**Relations of the Finely Granular and Hyaline Leucocytes.**

I have said that in view of the chief sites of multiplication the great majority of leucocytes fall into two series, one including the lymphocytes and hyaline cells, the other including the finely granular leucocytes and the finely granular leucoblasts of the bone marrow, with possibly the eosinophile series. (The consideration of these organisms has necessarily been omitted; they certainly play a minor part in the questions under consideration.) An important question, and one exceedingly difficult to answer, is whether or not hyaline cells acquire granules as they lie in the bone marrow and become finely granular leucoblasts. This is a question which I am not prepared to answer, either in the affirmative or in the negative, but one must note, first, that during a prolonged leucocytosis mitosis in the finely granular leucocytes described, and suppression of excessive proliferation of one or other, we have an explanation of the two forms of leucocytocarhynia. In the one form, as is well known, there is an increase in the blood and tissues of the lymphocytes, and it may be of the larger hyaline cells. In the other form we have an increase of the finely granular leucocytes (marrow cells).

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1 Die Anämie, in Nothnagel's Specielle Pathologie und Therapie.
and an appearance of them in the blood, and at the same time a great increase in the number of finely granular polymorphonuclear leucocytes.

LEUCOPENIA.

A few words must also be said with regard to diminution in the number of leucocytes—leucopenia—and we may consider, first, the fall which may occur with comparative rapidity in inflammatory or infective conditions, or on the introduction of certain chemical substances into the blood. Here, it is to be noted, the fall is chiefly, sometimes almost entirely, on the part of the finely granular polymorphonuclear leucocytes. One may summarise thus the circumstances on which this fall may depend:

First, a fall after the injection of various chemical bodies is due in great part, if not entirely, to the accumulation of leucocytes in the capillaries of various organs, especially of the lungs. This has been proved by the experiments of Surgeon-Captain D. Bruce, of Goldscheider and Jacob, as well as my own. It can readily be demonstrated. Therefore one may say that the rapid destruction of leucocytes supposed by Lowit to occur in these circumstances has at least not been proved.

Secondly, after injections—for example, of organisms into the peritoneum—the fall may be due in part to accumulation of the leucocytes in the capillaries of the mesentery, peritoneum, etc., and in part to the emigration of leucocytes into the peritoneal cavity, the latter occurring very rapidly. It is, therefore, a necessary consequence of the inflammatory lesion that a sudden fall of the inflammatory leucocytes is due in the number of leucocytes. (Where, however, the inflammatory change is more gradually developed, as in most clinical cases, leucopenia may not be preceded by leucopenia.)

Thirdly, in severe septicemic and toxic conditions an enormous leucocyte degeneration and destruction can be traced in the spleen and to a less extent in the bone marrow, and in certain circumstances there is great leucocyte accumulation associated with phagocytosis in these situations. The removal of leucocytes from the blood stream by their being entangled in coagula forming in the heart before death—for example, in pneumonia—may also be mentioned.

Fourthly, the fall may be due to interference with the proliferative changes in the bone-marrow, as a result of the action of toxic substances. On this point further observation is necessary.

Fifthly, whether substances exert a negative chemotaxis on the leucocytes in the marrow or elsewhere and interfere with their passage into the blood stream must still be left an open question.

It will be observed that in many of the circumstances mentioned the conditions determining the leucopenia are of an unfavourable kind, whether they be excess of toxic substances in the blood, excess of leucocyte emigration due to a rapid inflammatory spread, rapid leucocyte destruction, etc. No doubt in cases of a combination of circumstances is at work—for example, in the fall of the leucocytes in pneumonia without a crisis. But it is extremely important that in all conditions where there is leucopenia the circumstances which bring it about should be accurately ascertained, not simply to establish scientific facts, but also to afford the basis of possible therapeutic measures.

Another interesting fact may be noted—namely, that in various grave inflammatory or infective conditions when the leucocyte number falls, there appears in the blood stream some of the finely granular leucoblasts of the marrow—the myelocytes which are so numerous in the blood in medullary leucocytæmia. Whether this is due to organic change in the marrow interfering with the normal relation of its cells, I at present cannot say. It, however, appears to be usually a bad omen.

Lastly, we may merely mention that the leucocyte number is diminished in several chronic conditions—for example, in pernicious anaemia, in some cases of chlorosis (as I pointed out several years ago), and in some cases of anaemia with splenic enlargement. Here, again, the diminution is chiefly on the part of the polymorphonuclear leucocytes; and this association with defective blood formation or with alterations in the function of the bone-marrow is worthy of note.

EOSINOPHILE LEUCOCYTOSIS.

Though leucocyte increase is usually due to increase in the finely granular leucocytes, attention has been given within late years drawn to the conditions in which eosinophile leucocytes are proportionately in excess, though this is not rarely the number of leucocytes may be little increased—the condition known as "eosinophilia." Local accumulation of the eosinophile cells is common in a variety of conditions. I have observed it in various grave conditions of the body; for example, in atrophic conditions of the gastric and other mucous membranes, around cancerous growths, especially some varieties of epithelioma; in some forms of malignant glanular affection allied to the lymphadenoma; also in some subacute affections—such as tuberculous conditions, and in several other conditions. The number of eosinophile leucocytes in the tissues may be very great. And further, it has been observed that in bronchial asthma the leucocytes in the bronchial secretion are chiefly eosinophiles. The discussion of the behaviour of these cells would occupy much too long, but it is interesting to note that a close analogy can be drawn between this form of leucocytosis and the ordinary form. There may be local accumulations of the eosinophile leucocytes without increase in the blood, but on the other hand if the area affected, for example a skin lesion, be extensive, there may be an eosinophile leucocytosis in the blood. It is to be observed also that large eosinophile leucocytes are sometimes found in the bone marrow, and that leucocyte figures may sometimes be observed in them. So also in the medullary form of leucocytæmia these cells, both the eosinophile leucocytes and the smaller eosinophile leucocytes may be implicated in the leucocyte increase. Important questions in connection with this subject are: Do finely granular leucoblasts ever become eosinophile leucoblasts, and do the finely granular leucocytes in the blood or in the tissues become eosinophile leucocytes? Some facts suggest that these two varieties of granular cells are closely related to one another, whilst others show that to a certain extent they behave as if they were independent. The great diminution of eosinophile leucocytes in the blood in acute inflammatory affection in the number of the eosinophiles, and it may be sometimes leucocytæmia is also worthy of note. This subject must be investigated along the same lines as the behaviour of the finely granular cells. The occurrence of local accumulations of lymphocytes and hyaline cells can only be mentioned as a subject also worthy of consideration.

CONCLUSION.

In conclusion, I express the hope that this discussion may aid in determining the position which the term inflammation is to occupy in the science of pathology. It appears that much discussion might be avoided if a sharper distinction were drawn between the active and the passive phenomena concerned. By the former, I mean those in which there is a defensive reaction, by the latter, those which are merely the evidence of the action of toxins or other noxe on tissues, especially on living cells. The former ought to be regarded in the light of evolution as a provision for the protection of the organism, the latter merely as evidence that living structures are necessarily capable of damage.

II.—W. S. GREENFIELD, M.D., F.R.C.P.,
Professor of Pathology in the University of Edinburgh.

The President, Professor Greenfield, complimented Dr. Muir on the able manner in which he had opened so important a subject. He did not think one could anticipate anything that might be said by others who wished to take part in the discussion; but he thought that the results obtained by Dr. Muir were of the highest value, and that they threw a fresh light on the whole question of leucocytæmia.

III.—D. J. HAMILTON, M.B., F.R.C.S.E., F.R.S.E.,
Professor of Pathological Anatomy, University of Aberdeen.

Professor Hamilton said that the subject was one of the greatest importance. There was this to be said about it, however, that, owing to the evidence on many points being as yet scanty, and often contradictory, no one was entitled to offer an opinion on any of the so-called facts of the process, and far
les upon the numerous theories bound up with the subject, which might in the smallest degree savour of being dogmatic. Thus, in the first place, there were evidently leucocytes and leucocytoses differing widely in their causation and significance, and it would be rash and foolish to conclude because, let us say, an excess of leucocytes in the blood had occurred in one case as a protection against the effects of noxious substances introduced into the system, that therefore leucocytes in other cases were to be looked upon in the same light. Even after what Dr. Muir had said of investigators being almost unanimous on the subject of leucocytosis being a general affection, that is to say, affecting the whole blood equally, yet he was not convinced that in the least degree it was of great importance. It might happen that a physician had considerable difficulty in distinguishing between typhoid and Malta fever, and he thought that a bedside examination of the blood would afford a rapid and reliable test. In further illustration of the value of a chemotaxis experiment, he predicted the difficulty that was often felt in knowing when to grant a patient suffering from appendicitis permission to rise. In his experience this could be told with precision; for, if leucocytosis was present, the patient should not rise even though all other signs and symptoms were negative. The patient might safely rise, even though some tenderness still persisted. In conclusion, he quoted the case of a patient whom he had seen for a sore throat. The state of health had been improved, but the temperature continued to rise. Examination of the blood revealed a marked increase in the polymorphonuclear leucocytes, and, in spite of the absence of any physical signs, he was thus enabled to predict the onset of an acute pneumonia or pleurisy, the latter hypothesis being verified on the following day.

V.—T. EDMONSTON CHARLES, M.D., LL.D., F.R.C.P.,

Dr. Charles said that in examining the blood in some acute cases of Malta fever he had been struck by the absence of the polymorphonuclear leucocytes, only lymphocytes with a single large nucleus were present. He thought that at first this appearance might be due to the particular stain employed in the cases which had been obtained the same results whatever stain he used, for example, eosine and methylene blue. In other fevers, for example, in typhoid fever, he had not found the same absence of the polymorphonuclear leucocytes, and he thought that this was a diagnosis of the largest importance. The absence of the polymorphonuclear leucocytes had been strikingly apparent in two cases of typhus fever, and he thought that a bedside examination of the blood would afford a rapid and reliable test. In further illustration of the value of a chemotaxis experiment, he predicted the difficulty that was often felt in knowing when to grant a patient suffering from appendicitis permission to rise. In his experience this could be told with precision; for, if leucocytosis was present, the patient should not rise even though all other signs and symptoms were negative. The patient might safely rise, even though some tenderness still persisted. In conclusion, he quoted the case of a patient whom he had seen for a sore throat. The state of health had been improved, but the temperature continued to rise. Examination of the blood revealed a marked increase in the polymorphonuclear leucocytes, and, in spite of the absence of any physical signs, he was thus enabled to predict the onset of an acute pneumonia or pleurisy, the latter hypothesis being verified on the following day.

IV.—G. SIMS WOODHEAD, M.D., F.R.C.P.E.,
Director, Research Laboratories of the Royal Colleges of Physicians and Surgeons, London.

Dr. Woodhead said that he had listened with great interest to the paper, which he believed was of special value from the fact that its subject matter had a bearing on very great questions in pathology. Its bearing on inflammation and immunity was of special interest to him, but he recognised its very great importance in connection with such a condition as leucocytosis. In regard to what Professor Hamilton had said, he thought that we should not allow a separation into two camps merely, for after all chemotaxis was conceived in Belgium, but was brought to a German, and worked at by a Russian in Italy and in France. He quite agreed that chemotaxis and phagocytosis should not be accepted as proved. Theories of this kind should not perhaps be dogmatically held, but he believed in their use as working hypotheses. Dr. Muir's work would, he believed, clear the ground for further investigation. The locality of the small granular polymorphonuclear cells having been fixed, and distinction being made between all those derived from the bone marrow and those from other sources, still further elimination became possible. He looked upon leucocytosis as evidence of a power of reaction in the tissues in which those cells were formed, or on the part of the cells themselves. In the local reaction of mild anthrax cases we had evidence of powers of the tissue to react and multiply in the presence of proteid poisons and other irritants.

VII.—HERBERT E. DURHAM, M.B.,
Grocers' Research Scholar, Cambridge.

Dr. Durham congratulated Dr. Muir on the success of his investigations on the bone marrow. He desired to emphasise the advisability of a routine examination of this tissue in infective diseases, since, in certain instances of bacillary infection, it was possible to demonstrate the presence of bacilli there, although examination of other organs proved negative. He also alluded to the period of resolution of a leucocytosis when many cells rather of the lymphocyte type were present; he had been unable to find transition forms between the polymorphonuclear leucocyte and these lymphocytic forms. He referred also to the rapidity of the changes and the similarity of the general type of the sequence of changes in the leucocytes in the different cavities (vascular, synovial, peritoneal, etc.) of the body after experimental injection. The enormous number of leucocytes which appeared after injections in immunised animals was compatible with the changes in "leucoblastic" bone marrow described by Dr. Muir.

VIII.—T. H. MILROY, M.D.,
Physiology Laboratory, University of Edinburgh.

Dr. Milroy said that in the experimental leucocytosis caused by the injection of nucleic acid there was an alteration in the
ratio between the amounts of nitrogen and $P_O_2$ exerted compared to that in health. This difference referred both to an absolute and relative increase in the $P_O_2$ compared to the nitrogen. He also stated that in medullary leucocytosis the $P_O_2$ seemed to have both absolutely and relatively decreased compared to the nitrogen, and said that this appeared to suggest a check in the breaking down of leucocytes.

**Dr. Miur's Reply.**

**After remarks by Dr. Copeman and Dr. Grünbaum.**

Dr. Miur, in reply, thanked the members who had taken part in the discussion for the kind way in which they had received his remarks, and briefly referred to some of the points which had been raised. With regard to Professor Hamilton's observations, he said that he had admitted at once the occurrence of merely local leucocytosis, but repeated that an increase of the total number of leucocytes had also to be dealt with. He considered that chemotaxis was the only agent which would explain the phenomena present, but that the stimulatory effect of the marrow was of equal, if not greater, importance. If lymphoid tissue was concerned, it had still to be shown where the cells coming from it became transformed into the finely granular polymorphonuclear leucocytes. The remarks of Dr. Edmondson Charles were of importance in showing that a fall of leucocyte number in one disease might not have the same significance as in another; in each case the circumstances determining it must be investigated. He agreed with Dr. Lazarus-Barlow as to the difficulty in many cases of distinguishing haematogenous leucocytes from swollen endothelial cells and in determining the part which they play. In relation to Dr. Durham's remarks, he said that the extent to which organisms accumulated in the spleen and bone-marrow respectively varied in different diseases; so far as his observations went, they were more numerous in the former, but it was interesting to learn that the converse might be the case. He did not intend to draw too close an analogy between the marrow changes after haemorrhage and those occurring in leucocytosis, as the increase of the two classes of mother-cells was the concern of the analogy.

**The blood changes after experimental thyroidectomy.**

By **Alfred G. Levy, M.D.**

(From the Department of Pathological Chemistry of University College, London.)

**Mode of Experiment.**

Numerous observations have now been made on the striking and diverse phenomena incident upon the removal of the thyroid gland of animals, but it is evident that we are still very much in the dark regarding the physiological functions of the thyroid secretion, and of the pathological process which must occur when the secretion is absent from the body.

The study of objective symptoms can only supply us with hints as to the seat or seats of the pathological processes which must take place when an animal is in a state of cachexia thyroidectomica. But these pathological processes have been but little directly investigated. The principal workers in this line have been Ducheschi, who has made some observations upon the urine, and infers thence a destruction of protein matter; Vassali, histological investigations of the central nervous system; and, contemporary with myself, Postoff has examined the blood, and last year published a short note on his work.

In experiments of this kind, it is, of course, essential that the parathyroids should be carefully removed with the thyroid gland, and this, fortunately, in the dog is easy to accomplish; but the small accessory thyroid bodies which are known sometimes to exist in the tissues around the aorta and large vessels, and which, according to Cunningham, have an active function, render it difficult to be sure that the thyroid influence is in all cases entirely withdrawn, and perhaps on this fact largely depends the somewhat variable character of the changes in the blood which I have observed.

**The corpuscular elements.**

The anemia which supervenes upon thyroidectomy was early pointed out; however, I cannot find that it is ever very intense, and it most certainly is not constant, in its occurrence. The red corpuscles are reduced in number, the maximum reduction I have observed being 25 per cent., and the fall in the hemoglobin is roughly proportionate to that of the corpuscles, so that the anemia is doubtless wholly due to a destruction of the latter.

For example, in one dog with marked symptoms on the third day showed red corpuscles 5,700,000 the normal being 7,500,000; hemoglobin 70, the normal being 90. Another dog, with intense symptoms, on the third day showed red corpuscles 7,400,000, the normal being 7,750,000 (showing a slight increase); hemoglobin remaining unchanged.

I may mention that after a pronounced anemia of this type the liver gives an iron reaction with potassium ferrocyanide.

Another well-known phenomenon is the leucocytosis which invariably occurs. Numerous small, newly-formed leucocytes may often be found the day after the operation. The numbers fluctuate very considerably, as the following example shows: normal 8,000; first day 32,000; second day 17,000; third day 44,000.

**Chemical Changes.**

The fibrin of the blood is known to fluctuate to some extent in certain pathological conditions, usually in the direction of increase, noticeably so after severe hemorrhages, and in some infectious and inflammatory conditions. After thyroidectomy, changes in fibrinogen, and other clotting substances besides fibrin, are in my experience, invariable, and often considerable; thus, for example, from a normal of 0.2 per cent. to 0.56 per cent., or 0.29 per cent. to 0.56 per cent., but the increase is not always quite so large.

The specific gravity, as might be expected from the diminution of the principal solid blood contents, becomes lowered. The fall of course is largely dependent upon any considerable anemia, but it is very evident that a change in the serum solids, such as we find in the athyroid condition, may have a marked effect upon the specific gravity, so that, to my mind, the method now in vogue of estimating hemoglobin from the specific gravity is not always a quite reliable one.

The proteins in the blood, which were estimated in every case, underwent a varying diminution, as also did the total nitrogen. When we come to consider the total solid contents of the blood, we find they always undergo a reduction, and in most instances their loss is more or less greater than that of the proteins, showing that one or more of the non-proteid material are destroyed under these circumstances. To take a single example, the solids are reduced from 22.8 per cent. to 20.37 per cent., and the proteins from 20.37 per cent. to 19.2 per cent., that is, a loss of 2.45 g. solids against a loss of 2.52 g. protein. But it occurs that the protein loss is more or less larger than that of the solids—for example, 1.2 g. loss of solids against 2.97 g. loss of proteins, indicating a considerable increase of some non-proteid material. So that these facts, taken in combination, may be held to point to a varying loss of some, and a varying gain of other, non-proteid matter. As regards these non-proteids, I have found that the blood ash does not vary to any substantial extent, so that there remains the carbohydrate and fatty substances and the effects for further consideration, but I have not yet had an opportunity of pursuing the investigation in this direction.

Of course when there is a considerable anemia a large part of the loss in proteins is directly due to this, but when the anemia is absent or insignificant a large loss of proteins may still occur. To quote one example, in one of my dogs the loss of hemoglobin, 0; loss of corpuscles, 5.8 per cent.; loss of solids, 10 per cent.; loss of proteins, 15 per cent.; so that here it is the serum solids which principally suffer.

**Conclusion.**

Throughout the experiments I gave careful attention to the housing and feeding of the dogs after they had been thyroidectomised, for an animal in this condition is especially susceptible to external debility. In all cases the outcome was the same; and in no case, I think, would it not be fair to ascribe its blood changes entirely to the
loss of the thyroid secretion, but when bled the majority of my dogs were in very good bodily condition, and one indeed increased in weight after the operation.

I may remark the striking want of interdependence among the various pleural changes observed; and that none of these bear any relation to the severity or rapidity of onset of the general symptoms of the cachexia. This apparently irresponsible accentuation of certain structural blood changes, as also of certain objective symptoms, may perhaps be partly referred to the "contiguous circumstances" of such temperature, hygienic surroundings, food, and, as I have already mentioned, to the existence of accessory thyroid bodies; but it is only a full knowledge of the physiology of the thyroid gland that can satisfactorily ascribe to these things definite causal relations.

To Professor Vaughan Harley my thanks are due for many helpful suggestions in working out this research.

Dr. Welsh said that he had removed the parathyroids alone in a few cases in cats, and, though he had never examined the blood during life, he had observed that the organs and tissues after death were often anemic, and showed evidence of fatty degeneration.

Dr. Morey thought that the tendons and connective tissues should also be examined in relation to these blood changes. The theory that an excessive accumulation of mucin occurred after removal of the thyroid was probably no longer held by anyone. He suspected that the reason why the relative loss of the proteins and of the total solids varied so greatly might be found in the variations in the nutrition of the dogs observed in the course of the various experiments.

Dr. Muir said that he examined the blood in several cases of myxœdema in man, and had found a slight leucocytosis in some cases, whilst it was absent in others. The degree of anaemia also varied, but was usually slight. His general results were that the changes in the corpuscular elements were not of a marked kind.

ON PLEURAL IRRITATION AND PLEURISY.

By W. S. Lazarus-Barlow, M.D.,
Curator of the Museum, St. George's Hospital.

Dr. Lazarus-Barlow considered the formation of "false membranes" and thickening of the pleura found when the pleura itself or the subjacent lung was the seat of inflammation. The commonly accepted view was that the false membranes, which were essentially associated with acute processes, were formed by deposition of fibrin from a liquid inflammatory exudation. Certain views (Grawitz, Schleiffarth, Neumann, Borst), had dissented from this opinion, and maintained that the false membranes were chiefly formed by a modification of the subendothelial connective tissue of the serous membrane. This modification had been termed "fibrinous degeneration" by Neumann, Neumann, in particular, maintained that in the pleural cavity the false membranes might frequently be found covered by endothelium, and not covering endothelium, as should be the case if the commonly accepted view were correct. Borst, working with the peritoneal cavity of guinea-pigs, agreed with Neumann, but in addition found that in the earliest stages of an acute peritonitis, induced by injection of a solution of iodine in potassium iodide, there was often a marked proliferation of endothelial cells.

The author had made serial sections of pleura parallel with its surface (following herein Neumann's suggestion) under the following conditions:

A. Pleura of guinea-pig:
1. after injection of diphtheria toxin into the pleural tissue, normal.
2. in hypostatic congestion.
3. in early pleurisy in diphtheria.
4. in acute pleurisy.
5. after injection of pneumonia.
6. later, but still early pleurisy in glands.
7. tuberculous.

B. Human Pleura.
4. "  " pneumonia.
5. "  " generalised military

[Photographs of these were thrown upon the screen.] The author found that there were, at least, three distinct forms of pleurisy: (1) A form in which "fibrinous degeneration" occurs along with marked infiltration of the pleura by cells; (2) a form in which there is a general increase of the connective tissue of the pleura without marked infiltration by cells and without "fibrinous degeneration" of the connective tissue fibrils; (3) a form in which the whole thickness of the pleura itself consisted of thickly vascular and very young cicatricial tissue. He agreed with Neumann that endothelium might be found covering the "false membrane," and that the connective tissue of the pleura itself might undergo the change which was well termed "fibrinous degeneration." But he did not agree that these changes were commonly seen. In the guinea-pig, in particular, the endothelium degenerated to form a part of the false membrane, or if this did not occur it could be found lying beneath the false membrane; in no case had it been found covering the false membrane. In the human cases all trace of the normal endothelium was lost, and reasons were given for not considering this as dependent upon post-mortem change. So far as the exudation was concerned in experimental cases in guinea-pigs, it might briefly be said that as early as one hour after intrapleural injection of diphtheria toxin there was an enormous output of finely granular oxyphilic (polynuclear, neutrophil) cells, fully charged with granules. Later the granules disappeared and the cells broke up. Ultimately a few finely granular oxyphilic cells, but numbers of desquamated endothelial cells and large cells unprovided with granules, were present in the exudation; the origin of the latter variety of cell is doubtful.

[The paper was illustrated by an interesting series of lantern slides and microscopic specimens.]

DISCUSSION.

Professor Greenfield said that Dr. Barlow's paper did not readily lend itself to discussion, as it embraced too wide a range of subjects, and included practically all the fundamental processes in general pathology. He thought that these processes would be more profitably studied if they were considered separately. It was important in the study of such changes to bear in mind the different effects produced by different irritants and at different periods of time. He remarked that for the last twenty years he had been accustomed to teach some of the statements for which Dr. Barlow was now contending.

Dr. Woodhead quite agreed with Professor Greenfield that they had here to deal with a most difficult and complicated question. To begin with, it was impossible to ignore the fact that in different animals there were different types and structures of pleura, so that different pathological processes must manifest different appearances, especially when irritants of different kinds are used. In the specimens exhibited evidence of this was very marked. Neumann's paper had been accepted by many, especially by those who had much experience in the examination of specimens as introducing a new light on the question of pleurisy, but many of the points raised had already been settled. It was useful to have such matters examined in fresh light. The one criticism he would make was that the pleurisy differed widely in character and could not be generally grouped, and that the "young" fibrinous tissue exhibited was really well-formed fibrinous tissue of some standing. He recognised that fibrin could be found in the lymph spaces, and that swollen connective tissue strands could be found in the pleura, but these were not hyaline fibrinous substance.

Professor McFadyean said that he had listened with special interest to Dr. Barlow's demonstration, because he had recently examined a series of naturally occurring pleurisies in the horse. He thought that it was not reasonable to expect a common type of pleurisy which naturally varied according to the cause, just as much as dermatitis or gastritis. According to his own observations, there was a remarkable constancy between the nature of the changes and the irritant determining them. One could not expect identical changes in experimental pleurisies induced by the injection of a chemical irritant such as diphtheria toxin, and natural pleurisies which were almost all due to bacteria. These bacteria were often present most abundantly in the deeper parts of the pleura, and thus differences arose as compared with pleurisies due to surface irritation.

Dr. Muir observed that in the results brought forward the nature of the irritant should be kept in view, as the agent was...
a cell poison, and many of the minor changes might thus be produced, such as necrosis of the muscle fibres in guinea-pig's pleura. The position of the endothelium might be affected by various circumstances. So far as his observations went, the endothelium in the human subject was not found above the exudation, but its cells degenerated and disappeared in the exudation. At an early stage swollen and endothelial cells might be seen at places still attached underneath the exudation. He doubted the advisability of making distinct varieties, as so much depended upon the stage of the process and the organs in which the proliferation has begun.

Dr. Welsh thought that the changes in the connective tissue of the pleura should be kept distinct from the changes in the exudation, as the two processes were essentially different. He deprecated the use of the term "fibrinoid" as applied to changes in the fibrous tissue. In some cases in which the irritant was very intense, the fibrous tissue of the pleura did undoubtedly undergo necrotic changes, and become swollen and hyaline; but the resemblance to the fibrin proper was only superficial, and could not be affirmed without confusing the true nature of the change.

THE PATHOLOGICAL EFFECTS OF BREATHING OXYGEN AT A HIGH TENSION.

By J. LORRAIN SMITH, M.D.,
Lecturer on Pathology, Queen's College, Belfast.

[Abstract.]

It has been noticed by Bert and other observers that, before oxygen has been raised to a tension which is fatal to animals, various symptoms develop which indicate profound disturbance in the tissues. Bert has in particular defined the effects on the nervous system, which he described as resembling those of tetanus poison.

The experiments now recorded deal with the effect of increased oxygen tension on the lungs. The results show that oxygen at a tension of about 130 per cent. of an atmosphere produces pneumonia in the lungs of mice in about 60 hours. If the tension be raised to 150 per cent. of atmosphere, further, it is found that tetanic symptoms do not arise in mice till the atmosphere to which they are exposed contains oxygen at this tension of 450 per cent. The fact that birds with damaged lungs and normal mice have similar power of actively absorbing oxygen indicates that the onset of tetanic symptoms at a given oxygen tension depends on the integrity of the active power of absorbing oxygen on the part of the lung.

That the effect depends on the tension, and not on the quantity, of oxygen in the blood may be further proved by exposing an animal to an atmosphere containing carbonic oxide and oxygen at a high tension. The tetanic symptoms then develop at the same tension as before, though a large percentage of the haemoglobin is saturated with carbonic oxide. The experiments show that oxygen tension at moderate height produces pneumonia, and at a considerably higher tension produces the tetanic effect described by Bert.

A DEMONSTRATION OF THE GRANULES PRECIPITATED IN THE BLOOD BY CHLORIDE OF AMMONIUM.

By ALEXANDER HAG, M.A., M.D. Oxon., F.R.C.P.,
Physician to the Metropolitan Hospital, etc.

The method is that proposed by Mr. Barker-Smith,1 as modified and adapted to quantitative purposes by the author. The granules are pale, more or less spherical bodies of one-sixth to one-third the size of a red corpuscle.

Procedure.—Draw a minute drop of blood, touch it with a microscope slide; mix with an equal quantity of 10 per cent. solution of sodium carbonate, and then with a similar quantity of 20 per cent. solution of chloride of ammonium. After mixing, put on a cover glass and let it stand for 30 minutes, preventing evaporation. The granules slowly increase in number; the longer the slide stands; it is therefore necessary to examine all specimens at about the same time after mixing.

To Examine.—Place under a microscope with a 1/2 inch objective glass and with a good light; choose a field about the centre of the cover glass, and count all the granules in the field; then count all the red cells, and divide the former into the latter. Counting is facilitated by somewhat diluting the blood with the solutions, so as to diminish the number of cells in a field, and by using a micrometer eye-piece.

The following are common relations of granules and red cells:

In Physiological Conditions.—1-10 in morning; 1-20 in evening, but more in children than adults.

Pathological Conditions.—1-1 to 1-5 in Bright's disease and chronic gout; 1-50 to 1-40 in fever.

Any of the above quantities can be reproduced by the action of drugs. Under all conditions the number of granules varies with the urine acid passing in the urine, and a diagram was shown to illustrate this point. A specimen of blood from Bright's disease was shown in contrast with a normal blood.

Reference.
1 Medical Times and Hospital Gazette, September, 1896.

MALFORMATION OF THE KIDNEY AND DISPLACEMENTS WITHOUT MOBILITY, WITH ILLUSTRATIVE CASES AND SPECIMENS.

By DAVID NEWMAN, M.D., F.F.P.S.G.,
Surgeon, Glasgow Royal Infirmary.

Anomalies of the kidney have until recently been looked upon simply as pathological or anatomical curiosities; but now that many of the diseases of the kidney come to be placed under the surgeon for treatment by operation, all departures from the normal, whether in respect of number, form, size, or situation, must be considered of moment to those who have frequently to operate upon the renal organs.

If we simply study the cases recorded it will be found that they group themselves together and may be naturally classified under the following anomalies.

A. Displacements without Mobility.
1. Congenital displacement without deformity.
2. Congenital displacement with deformity.
3. Acquired displacements.

B. Malformations of the Kidney.
1. Variations in number.
   (a) Supernumerary kidney.
   (b) Double kidney.
   (c) Congenital absence of one kidney.
2. Variations in form and size.
   (a) General variation in form, lobulation, etc.
   (b) Hypertrophy of one kidney.
3. Fusion of two kidneys.
   (a) Horseshoe kidney.
   (b) Sigmoid kidney.
   (c) Disc-shaped kidney.

C. Variations in Pelvis, Ureters, and Blood Vessels.

A.—Displacements without Mobility.

I. Congenital displacement without deformity of the organ is by no means uncommon.

Case I.—Fixed displacement of the right kidney above Poupart's liga-
ment simulating a periphtletic abscess; operation.1 The patient was
admitted complaining of pain in the right iliac region. There was a
slight fullness of the abdomen in the right iliac and lower lumbar re-
gions, and a rounded swelling was felt passing upwards and backwards.
The swelling was cut down upon, when it was found to have a rounded
outline, with a distinct hilum towards the inner and upper aspect, and
being semi-elastic but firm immediately suggested a displaced kidney.

Case II.—Left kidney displaced forwards and backwards in a pa-
tient upon whom lumbar colotomy was performed. On making an incision
from the lower border and tip of the last rib on the left side to a point
half an inch behind the centre of the ilium, the upper
border of the left kidney presented itself at the lowest limit of the
incision.
CASE III.—Right kidney displaced downwards and rotated on its antero-posterior axis, shortened ureter entering upper aspect of bladder. At the post-mortem examination the right kidney was found to be displaced and firmly fixed; the pelvis of the kidney looked upwards, inwards, and forwards, while the convex aspect of the organ rested upon the brim of the pelvis.

In the three cases above described, where the kidneys occupied abnormal positions, the fixed misplacements were not associated with any deformity of the organs.

II. CONGENITAL DEFORMATION WITH DEFORMITY.

CASE 4.—Right kidney at the brim of the pelvis, anomalous distribution of blood vessels; right kidney displaced into a perinephric abscess. The kidney was discovered with its convexity looking upwards and lying close to the diaphragm, while the pelvis was turned downwards.

B. MALFORMATIONS OF THE KIDNEY.

1. Supernumerary Kidney.—Supernumerary kidney is extremely rare. We have only seen one instance of this anomaly; lying close to the upper margin of the left kidney, there was a small pear-shaped body, supplied by a branch of the renal artery, and having a distinct ureter which passed into the upper ureter half an inch below the pelvis of the left kidney.

2. Single Kidney.—A careful distinction must be drawn between "single kidney" due to congenital defect of development of the opposite organ, and those instances in which one kidney has become wasted and functionally useless as a consequence of disease, while its neighbour has undergone compensatory hypertrophy.

CASE 5.—Complete absence of the left kidney, ureter, and vessels, compensatory hypertrophy of right kidney. The right kidney was normal in its position, but the whole organ was greatly enlarged, weighing 192 ounces, and measuring 4 inches in length and 4 inches in breadth. No trace was found of the left kidney or of its vessels and ureter, and no opening into the bladder could be discovered corresponding to the entrance of the ureter.

CASE 6.—Congenital absence of the left kidney, vessels, and ureter. The preparation showed with the right kidney, the bladder, and the right ureter. A most careful search at the time of the post-mortem examination failed to find the body of the left kidney or of its ureter.

The following cases show how one kidney may atrophy or become functionally inactive, either as a consequence of want of growth, or from disease in early life.

CASE 7.—Atrophy of the left kidney, with double pelvis but single ureter. I have no details of the post-mortem examination in this case. The kidney tissue is almost completely destroyed, and the whole organ is about the size of a walnut. The pelvis is branched, and there is no hilum; the upper limb of the pelvis springs from the inner and upper aspect of the atrophied organ, while the lower limb arises from the lower border of the kidney.

CASE 8.—Atrophied kidney, the renal tissue being almost entirely replaced by fat. The right kidney was 10 ounces; the left kidney weighed half an ounce; very little renal tissue could be found in the mass, and what remained was completely embedded in firm fat.

CASE 9.—Atrophy of the right kidney with compensatory hypertrophy of the left kidney; disease of the suprarenal capsules. The right only weighed 1 ounce.

II. VARIATIONS IN FORM AND SIZE.

1. General Variation in Form, Lobeation, etc.—Slight changes in shape from the typical normal kidney are by no means uncommon, and in more marked instances the organ may be elongated so as to become sausage-shaped, or it may be increased in the form and globular in form, resembling the shape of the kidney in the fetus. In a few cases the kidney has been found to assume the discoid shape.

2. Hypertrophy of one Kidney.—Hypertrophy of one kidney is not often met with independent of some condition which has produced a functional weakness of its fellow, inwards and forwards.

CASE 10.—Simple hypertrophy of the left kidney only; right kidney normal in size and appearance. The right kidney was normal in weight, 65 ounces, which weighed relatively low, while that of the left kidney was 120 ounces.

3. Fusion of Two Kidneys.—The amount of fusion that takes place between two kidneys varies greatly,

(c) Horseshoe kidney is the most common form of fusion. The two organs are joined at their lower ends, sometimes by a simple band of tissue.

CASE 11.—Horseshoe kidney united by an isthmus of fibrous tissue at the level of the bifurcation of the renal artery; ureteral form well retained.

CASE 12.—Horseshoe kidney with lobulation and complete fusion of both kidneys; malformation of pelvis and anomalous distribution of blood vessels. Both kidneys were joined to some extent to their renal form, and united at their lower ends by a distinct isthmus, which is marked off by two deep grooves.

CASE 13.—Horseshoe kidney, with complete incorporation of the two organs; lobulation of both segments, the ureters deformed, and anomalous distribution of blood vessels. The two kidneys are completely united at their lower ends, and the whole renal mass, although lobulated, is roughly speaking, uniform in diameter, and in this respect contrasts with the other horseshoe kidneys.

(b) Sigmoid Kidney.—Sigmoid kidney is an end-to-end fusion of the two organs. In this anomaly both kidneys occupy one side of the body, but the statistical materials furnished by the weekly returns of the Registrar-General, in so far as they are concerned with the prevalence of fatal diphtheria in the metropolis. My last communication to the Association was made two years ago; and since that time so much of interest has happened in regard to the present prevalence of London diphtheria, that I venture to think hardly any apology to be needed for once more introducing the subject. The points to which I have given special attention are (1) the general return of diphtheria in London; (2) its seasonal relations; (3) the important question of the influence of school-attendance on the spread of diphtheria; (4) the relation of diphtheria to so-called "croup"; (5) the effect of the treatment by antitoxic serum. In examining the statistics I have been careful to follow these and similar questions, and for confirming or modifying conclusions previously reached, it may be well for me to state that I have no preconceived views to uphold, my only object being to extract from the available evidence such information as it seems fairly capable of affording. Nor do I wish, on the present occasion, to propose remedies, my only business just now being to draw attention to facts.

One word I may be allowed to add on the special usefulness of these weekly returns. This seems to me to consist largely in these two points: (1) That by their means we are enabled to study the seasonal relations of fatal diseases and the immediate as well as remote effects of varying meteorological conditions; and (2) that we are able to bring our results more exactly up-to-date than if we had to wait for the publication of annual reports, which necessarily occupy much time in their preparation.


At two previous meetings of the British Medical Association, I have attempted to deal with the statistical materials furnished by the weekly returns of the Registrar-General, in so far as they are concerned with the prevalence of fatal diphtheria in the metropolis. My last communication to the Association was made two years ago; and since that time so much of interest has happened in regard to the present prevalence of London diphtheria, that I venture to think hardly any apology to be needed for once more introducing the subject. The points to which I have given special attention are (1) the general return of diphtheria in London; (2) its seasonal relations; (3) the important question of the influence of school-attendance on the spread of diphtheria; (4) the relation of diphtheria to so-called "croup"; (5) the effect of the treatment by antitoxic serum. In examining the statistics I have been careful to follow these and similar questions, and for confirming or modifying conclusions previously reached, it may be well for me to state that I have no preconceived views to uphold, my only object being to extract from the available evidence such information as it seems fairly capable of affording. Nor do I wish, on the present occasion, to propose remedies, my only business just now being to draw attention to facts.

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some diminution, though the notification figures were still well above the average of the last four years, including the fatal year 1893. During the present year the tendency on the whole has been a downward one.

The following table (Table L) gives the London mortality week by week since the beginning of 1896, according to the Registrar-General's returns. The corrected ten-yearly means for the corresponding weeks are also added for comparison. With regard to the last-named figures, it should be remembered that they are to be used with caution—not from any suspicion as to their substantial accuracy, but because the average results for a period of years in the case of a disease which varies in its incidence so much as diphtheria are somewhat artificial if considered as an index of its normal prevalence. Nevertheless, if studied with due regard to the actual circumstances, these weekly ten-year averages are not without their interest and value, even in the case of a disease like diphtheria.

<table>
<thead>
<tr>
<th>Week</th>
<th>Deaths</th>
<th>Corrected Mean (to Years)</th>
<th>Deaths</th>
<th>Corrected Mean (to Years)</th>
<th>Weeks</th>
<th>Deaths</th>
<th>Corrected Mean (to Years)</th>
<th>Deaths</th>
<th>Corrected Mean (to Years)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>66</td>
<td>35.8</td>
<td>July 28</td>
<td>47</td>
<td>34.4</td>
<td>36</td>
<td>36.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan. 2</td>
<td>59</td>
<td>35.6</td>
<td>Aug. 28</td>
<td>43</td>
<td>36.0</td>
<td>36.7</td>
<td>36.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan. 3</td>
<td>63</td>
<td>35.9</td>
<td>Sept. 28</td>
<td>46</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 3</td>
<td>63</td>
<td>35.9</td>
<td>Oct. 28</td>
<td>49</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 4</td>
<td>59</td>
<td>35.9</td>
<td>Nov. 28</td>
<td>48</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 5</td>
<td>63</td>
<td>35.9</td>
<td>Dec. 28</td>
<td>50</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar. 3</td>
<td>48</td>
<td>31.7</td>
<td>Jan. 28</td>
<td>48</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar. 4</td>
<td>53</td>
<td>31.7</td>
<td>Feb. 28</td>
<td>49</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar. 5</td>
<td>48</td>
<td>31.7</td>
<td>Mar. 28</td>
<td>49</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 2</td>
<td>42</td>
<td>31.0</td>
<td>Apr. 28</td>
<td>45</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 3</td>
<td>42</td>
<td>31.0</td>
<td>May 28</td>
<td>44</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 4</td>
<td>42</td>
<td>31.0</td>
<td>June 28</td>
<td>45</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May 2</td>
<td>42</td>
<td>31.0</td>
<td>July 28</td>
<td>45</td>
<td>38.9</td>
<td>39.6</td>
<td>39.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The same facts are shown in graphic form by the diagrams (exhibited), in one set of which is represented the actual number of deaths returned week by week, while in another the conspicuous inequalities of the curve are removed by the use of Mr. Bloxam's method.

2. SEASONAL RELATIONS OF DIPHTHERIA.

There is nothing exceptional about the seasonal prevalence of diphtheria, except a very slight decrease in the third quarter of the year, and the curve maintained its elevation for a longer period. The usual autumnal rise was better marked in 1896 than in the preceding year, and the curve maintained its elevation for a longer period. The gradual rise that took place throughout the spring and summer of 1895 was an unusual feature that has not been repeated.

3. DIPHTHERIA AND SCHOOL ATTENDANCE.

Connected with the subject of personal prevalence comes a question of practical importance: that of the influence on the spread of diphtheria of infection contracted at school. It is hardly necessary to point out this is a matter on which there still exists much difference of opinion. For recent discussions of the point I would refer to Dr. Newsholme's work just published, and my own conclusion is fully to Mr. Shirley Murphy's 'Report of the Medical Officer of Health for the Administrative County of London,' p. 35, with Appendices I, II, and III. I have before stated my conviction that Mr. Shirley Murphy's views are fully justified by the available evidence, and I would draw attention to the fact that in both of the years 1895-96 now under review the drop in the number of fatal cases corresponding with the period of summer holidays is again perfectly apparent even in the curve for "All Ages." As some of my readers may be aware, I am inclined to think that the Christmas holidays can also be shown to have their influence on the curve of fatal cases, though this, as might be expected, is of a less pronounced character. No doubt in any given year the operation of this school-attendance factor tends to be obscured by other circumstances; but when several years are taken together, the other influences are found to counteract each other, and the holiday fall with its succeeding rise comes more clearly into view. An examination of the successive ten-year averages will show that the general prevalence of the disease is increased or maintained, the "holiday drop" exhibited by the ten-year means becomes more and more distinguished the year by year, and the explanation of these special and temporary depressions in the course of the regular curve is most often to be found (as shown by the ten-year mean) in the third and thirty-fifth weeks of the year respectively. Thus in the eight years from 1891 to 1898, the bottom of the first or January curve was reached four times in the third week, twice in the fourth; while on two more occasions it was deferred until the sixth. In the seven years from 1891 to 1897 the second or August depression reached its lowest point in the fourth week and the thirty-fifth week. In the thirty-sixth, and once in the thirty-fourth. Looking at the facts as a whole, I do not see any way of escaping the inference that there is a factor at work, distinct from ordinary seasonal conditions, which is sufficiently powerful to induce a fairly regular disturbance of the course of fatal diphtheria in two definite times of the year, these times corresponding with the usual holiday periods of schools. If this conclusion should appear to be well grounded, those responsible for action in the matter will doubtless not be content with a mere abstract acquiescence in its probable truth.

4. DIPHTHERIA AND "CROUP."

It is now, I think, admitted on all hands that in former years in many cases of fatal diphtheria have appeared in the Registrar-General's returns under the heading of "croup."
Nor is there much doubt that, although cases of true diphtheria are tending more and more to be referred to their proper category, the register of "croup" still contains cases that have escaped transference. The preceding table (Table II)—which contains data for "croup" corresponding to those of Table I for diphtheria—demonstrates for the period since 1895 now under discussion that the gradual shrinkage of the "croup" returns which began many years ago is still continuing, while the comparison given below of the annual number of deaths recorded under the two headings since 1893 shows that even the present reduced mortality from "croup" sufficiently reflects that from diphtheria to suggest the inclusion of a common element in both.

**Table III.** London, 1893-97: Annual Total of Deaths from Diphtheria and "Croup."

<table>
<thead>
<tr>
<th>Year</th>
<th>Diphtheria</th>
<th>&quot;Croup&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1893</td>
<td>3,264</td>
<td>217</td>
</tr>
<tr>
<td>1894</td>
<td>2,674</td>
<td>166</td>
</tr>
<tr>
<td>1895</td>
<td>2,316</td>
<td>144</td>
</tr>
<tr>
<td>1896</td>
<td>2,684</td>
<td>147</td>
</tr>
<tr>
<td>1897</td>
<td>2,261</td>
<td>72</td>
</tr>
</tbody>
</table>

In 1896 I published a table showing that the decline in the mortality from "croup" had on the whole affected the winter period rather than the spring; which is what might be expected if Dr. Whitelegge's opinion is correct that the old winter and spring maxima of "croup" were due to different causes—the former more especially owing its existence to the inclusion of cases of true diphtheria. I am now able to present the table in a more complete form by the addition of the years 1896-97, and it will, I think, be seen that the new evidence points in the same direction as the old. Putting together the seven years from 1891 to 1897, and comparing them with the ten years from 1881 to 1890, we find that the average number of March deaths from "croup" has fallen from 70 to 21; that is to say, the March fatality has fallen 65 per cent., but the December fatality as much as 74 per cent. This is all in favour of Dr. Whitelegge's contention.

**Table IV.** London: Average Number of Deaths from "Croup" in March and December for the Periods 1881-90 and 1891-97, together with the Actual Number of Deaths during the same Months in each of the latter Seven Years.

<table>
<thead>
<tr>
<th>Months</th>
<th>1881-90</th>
<th>1891</th>
<th>1892</th>
<th>1893</th>
<th>1894</th>
<th>1895</th>
<th>1896</th>
<th>1897</th>
</tr>
</thead>
<tbody>
<tr>
<td>March</td>
<td>70.5</td>
<td>57</td>
<td>37</td>
<td>17</td>
<td>17</td>
<td>16</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>December</td>
<td>80.5</td>
<td>36</td>
<td>27</td>
<td>29</td>
<td>17</td>
<td>16</td>
<td>18</td>
<td>21.3</td>
</tr>
<tr>
<td>Excess in March</td>
<td>—</td>
<td>21</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>7</td>
<td>3.1</td>
</tr>
<tr>
<td>Excess in Dec.</td>
<td>10.0</td>
<td>—</td>
<td>12</td>
<td>0</td>
<td>4</td>
<td>—</td>
<td>—</td>
<td>1</td>
</tr>
</tbody>
</table>

* Mean of 10 years. † Mean of 7 years.

N.B.—The months here are not calendar months, but periods of 5 weeks corresponding to March and December respectively.

5. **Effect of the Antitoxin Treatment.**

It is a fact admitting of no dispute, that whatever the cause, the case-mortality of diphtheria in the metropolis has undergone a steady diminution since 1894, the year of the introduction of the serum treatment. In a paper to which I have already referred, read at the Carlisle meeting of the British Medical Association in 1896, I anticipated that by the end of that year the case-mortality for the twelve months would for the first time on record have sunk below 20 per cent. This expectation, based on the course events were then taking, was quite borne out by the result, the proportion of deaths to notifications for 1896 being, as will be seen by reference to Mr. Shirley Murphy's report, lately published, only 19.3 per cent. in 1896, as against 20.4 per cent. in 1895 and 23.6 per cent. in 1894. Since the date of the materials dealt with in that report the figures for 1897 have become available, and I am satisfied that the diminution in case-mortality still continues, the percentage of cases to notifications for last year having sunk to the comparatively low figure of 17.7. The following table (Table V), the data for which are derived partly from Mr. Shirley Murphy's report, partly from the Registrar-General's weekly returns, and partly from the monthly list of notifications published in the columns of the Lancet, shows that this diminution in case-mortality has progressed in spite of fluctuations in the number of both cases and deaths.

**Table V.** London, 1893-97: Annual Deaths from Diphtheria, with Notifications and Percentage Case-mortality.

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths</th>
<th>Notifications</th>
<th>Case-mortality per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1893</td>
<td>3,264</td>
<td>17,654</td>
<td>19.3</td>
</tr>
<tr>
<td>1894</td>
<td>2,674</td>
<td>11,190</td>
<td>23.9</td>
</tr>
<tr>
<td>1895</td>
<td>2,316</td>
<td>11,299</td>
<td>20.6</td>
</tr>
<tr>
<td>1896</td>
<td>2,684</td>
<td>13,668</td>
<td>16.7</td>
</tr>
<tr>
<td>1897</td>
<td>2,261</td>
<td>12,827</td>
<td>17.7</td>
</tr>
</tbody>
</table>

N.B.—The figures in this table, being in some instances derived from returns which have not undergone their final revision, show some slight differences from those given in the text above. There is, however, no material discrepancy.

It may be added that the experience of 1898, so far as it has gone, makes it probable that a still further reduction in relative fatality may be looked for. If anyone doubts that this improvement in the case-mortality of diphtheria is due to the introduction of the serum treatment, I think he may fairly be called upon to say what other factor can have been at work since 1894 capable of producing the present result. The fact of the diminution in case-mortality cannot be disputed, and of this the more or less general adoption of the antitoxin treatment would seem to supply the most feasible interpretation.

The conclusions arrived at in the present paper may be briefly summarised as follows:

1. The amount of diphtheria present in London is still high, but is now diminishing after a temporary exacerbation in 1896.

2. The experience of the last two years has disclosed nothing exceptional with regard to the seasonal relations of diphtheria.

3. The interruption to the usual course of diphtheria mortality coincident with the two chief school holiday periods is again apparent in both 1896 and 1897. The new evidence, like the old, tends to show that school infection is an important, though not the sole factor, in the spread of diphtheria.

4. A considerable, but yearly diminishing, number of cases of true diphtheria are still returned as "croup."

5. A marked diminution in the case-mortality of diphtheria set in at the end of 1894, and has continued up to the present time. This diminution is coincident with the employment of the treatment by antitoxin serum.

In remarking on Dr. Dixey's paper Dr. F. J. Allan (Strand) pointed out that he had drawn attention in his annual report for 1896 to the point that the Christmas and Easter holidays afforded better evidence of school influence than did the longer holidays in the summer, when so many children were away at the seaside or in the country. Moreover, the summer holidays in the London schools did not all begin simultaneously, whereas those at Easter and Christmas did so.

1 See British Medical Journal, August 31st, 1895, and August 29th, 1896. 2 This objection has been well stated with reference to yearly averages by Dr. Newsholme in his valuable work lately published on Epidemic Diphtheria (London, 1898).
THE ETIOLOGY OF "RETURN CASES" OF SCARLET FEVER.

By C. Killick Millard, M.D., D.Sc.(Public Health), Medical Superintendent, City Hospital, Birmingham.

Or all the more than usual return cases in isolation hospitals, it is so difficult to pronounce with certainty as to the condition of a patient with regard to his freedom from infection, or the reverse, as in the case of scarlet fever; and it is not surprising, therefore, that with this disease the discharge of patients from hospitals is not determined with the conveyance of infection to others, and the resulting so-called "return case" than with any other disease.

The importance of this subject from an administrative point of view was more forcibly impressed upon me than would otherwise have been the case in consequence of an action brought against the Corporation of Birmingham some three years ago by the parents of a child who was discharged from the Birmingham City Hospital shortly before my appointment as Medical Superintendent. This case—Keegan v. the Corporation of Birmingham—was, I believe, unique, and attracted a good deal of attention. Certainly the verdict came as a great surprise. The jury before whom the case was tried found in infection of scarlet fever had been carried home by a child discharged from the City Hospital, with the result that another child had contracted the disease and died, and they awarded the plaintiff damages to the extent of £50, although adding a rider to their verdict acquitting the hospital officials of any negligence or misconduct, insisting that such a verdict would have been upheld. Did it really represent the law on the subject, the position of those responsible for the management of isolation hospitals would be a most unenviable one. It is certainly, however, most desirable in the interests of the precedent created by the above case should be overruled as soon as possible.

Amongst those writers—and they are not very numerous—who have approached this subject during the past few years, few, if any, have attempted to systematize cases in such a way as to give statistics which would form some reliable basis for comparison and deduction. This appeared to me to be desirable, and I have therefore been endeavouring for the past two and a half years to collect the material for my present paper.

The tables are based on an analysis of 4,810 cases of scarlet fever discharged from the Birmingham City Hospital during the above period. The exact condition of these patients at the time of their discharge, and other details, were recorded in a register specially kept for that purpose.

DEFINITION OF TERMS.

Before going further it will, perhaps, be advisable for me to define exactly the meaning of the special terms I propose to use in connexion with my subject.

I count as a "return case" any patient coming to the hospital with scarlet fever from a house to which a patient discharged from hospital has recently returned.1 The latter, called by some writers the "original case," I shall speak of as the "infecting case." The period elapsing between the return home of the "infecting case" and the onset of the first symptoms in the "return case" is the "interval." The time from the onset of illness in the infecting case to the time it finally leaves hospital is the "period of isolation." Where, as sometimes happens, patients are not admitted until some little time after the onset of their illness, as in the case of patients coming directly from hospitals, it becomes important to distinguish this from merely "time in hospital," as spoken of by some writers. The time from the onset of the illness in the infecting case to the onset of illness in the return case, deducting four days for incubation period, is the "duration of infection." It is not infrequently happens that an infecting case is followed by disease usually treated in isolation, in which case, if any of the other members of the family, who might be likely to take it, after a few days or a week, or perhaps after the full fortnight-enjoyed, this precaution is relaxed, and if inquiry is directed to this point it will often be found that this accounts for many of the later infecting cases. Indeed, the return case is sent away for a time after leaving hospital to be followed by a return case immediately upon his return home.

1. DOMESTIC ISOLATION.

In many cases the parents make an attempt, more or less conscientiously, in compliance with the instructions received from the Medical Officer of Health, to keep the return case from any contact with other members of the family, who might be likely to take it. After a few days or a week, or perhaps after the full fortnight-enjoyed, this precaution is relaxed, and if inquiry is directed to this point it will often be found that this accounts for many of the later infecting cases.
2. **Recrudescence of Infectivity.**

There is no doubt that many cases which appear free from infection at the time they leave hospital really are so then, as far as their power of infecting others goes, but suffer from a sort of recrudescence at varying periods after their return and they may become infectious. This is frequently manifested by the recurrence, or even primary development of a nasal or ear discharge.

3. **Slight Degree of Infectivity.**

Some cases are probably so slightly infectious that they require to be brought into the closest possible contact, and that repeatedly, before the infection "takes," so to speak.

4. **Varying Susceptibility of Individuals.**

It is a well-known fact that patients admitted to a scarlet fever ward on an erroneous diagnosis may develop the disease at any period during their stay in hospital. They by no means always develop it during the first week. Probably this reason is the strongest of all.

**"Period of Isolation" of the Infecting Cases.**

This is a very important point, because the occurrence of a return case is often, rightly or wrongly, held to be an indication of premature discharge, and undoubtedly the period of isolation must exercise an important influence on the occurrence. The exact relationship between the duration of the period of isolation and the number of return cases is not, however, so clear. The average period of isolation of "all cases" discharged during the time over which my inquiry extends was slightly longer than this, and the average period of isolation of my infecting cases was 8 or 9 weeks.

**Table II.** —Showing "Period of Isolation" of "Infecting Cases" as Compared with "All Cases."

<table>
<thead>
<tr>
<th>Period of Isolation in Weeks</th>
<th>Under 9 weeks</th>
<th>9-10 weeks</th>
<th>10-11 weeks</th>
<th>11-12 weeks</th>
<th>12-13 weeks</th>
<th>Over 13 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Infecting Cases</td>
<td>5</td>
<td>30</td>
<td>30</td>
<td>27</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Percentage of Infecting Cases</td>
<td>3.9%</td>
<td>20.5%</td>
<td>25.5%</td>
<td>17.5%</td>
<td>4.5%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Percentage of All Cases</td>
<td>5.5%</td>
<td>16.0%</td>
<td>21.0%</td>
<td>16.2%</td>
<td>11.2%</td>
<td>8.7%</td>
</tr>
</tbody>
</table>

Average period of isolation of infecting cases, 8.3 weeks.

One anticipated that an undue large proportion of the infecting cases would be found to be patients who had been discharged after the minimum period of isolation, and that the average would have been equalised by a few cases that had been detained exceptionally long. As a matter of fact, however, the table shows that no such generalisation can be accepted, for whilst the proportion of infecting cases is about the same as that of "all cases" in the first three columns, it becomes distinctly greater in the 8 and 9 weeks' columns, and then very much smaller in the remaining columns, until in the last one, over 13 weeks, the percentage is only 2.6% as against 10.4% of "all cases."

The explanation I would give is this: The patients discharged after the shorter periods of isolation, that is, under 8 weeks, are principally the simple complicated cases, whereas the complicated cases—more especially those complicated with otorrhea or rhinorrhea—that is, the cases most calculated to carry infection, are always detained longer. With this discrimination we see that the period of isolation becomes a very important factor, and that after a certain point the risk of infection becomes exceedingly small. The safety induced by such prolonged isolation is probably greater than appears merely from the table, because the cases leaving hospital after 12 weeks include those chronic and incurable

ones which have to be sent out at last in desperation. At the same time, whilst taking 12 or 13 weeks as a fairly safe maximum period of isolation, I believe that infection may be carried in rare cases after as long as 15 or even 16 weeks.

In Table III I have classed the infecting cases into two groups—one showing the percentage of cases under the other over those.

**Table III.** —Showing proportion of Infecting Cases and All Cases Isolated under 9 weeks and over 9 weeks respectively.

<table>
<thead>
<tr>
<th>Period of Isolation</th>
<th>Under 9 weeks</th>
<th>Over 9 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of Infecting Cases</td>
<td>6.0%</td>
<td>31.0%</td>
</tr>
<tr>
<td>Percentage of All Cases</td>
<td>5.0%</td>
<td>41.0%</td>
</tr>
</tbody>
</table>

This brings out the fact that the proportion of infecting cases after less than 9 weeks is unduly large, whilst, conversely, the proportion after over 9 weeks is unduly great. Taking this fact together with Table II, I conclude that, independently of a patient's apparent fitness for discharge, the risk of his carrying infection begins to fall after 9 weeks.

**Age Distribution of "Infecting Cases."**

In Table IV the infecting cases are grouped into age periods, and the figures are also given as percentages, with the corresponding percentages of "all cases" for comparison.

**Table IV.** —Showing Age Distribution of Infecting Cases.

<table>
<thead>
<tr>
<th>Age Period in Years</th>
<th>0-5</th>
<th>5-10</th>
<th>10-15</th>
<th>15-20</th>
<th>20 and upwards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infecting Cases</td>
<td>27</td>
<td>56</td>
<td>20</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Percentage of Cases</td>
<td>24.3</td>
<td>45.6</td>
<td>18.0</td>
<td>7.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Percentage of All Cases</td>
<td>25.7</td>
<td>41.4</td>
<td>19.6</td>
<td>6.9</td>
<td>3.2</td>
</tr>
</tbody>
</table>

I had thought it possible that an undue proportion of infecting cases would have occurred at some particular age-period—for example, amongst children under 5. The age distribution, however, being almost exactly proportionate to that of "all cases," we can only conclude that age has no influence on the tendency to carry infection.

**Sex.**

Of my infecting cases 88 were females, and only 69 were males. This excess of females may possibly be accidental, but it is quite conceivable that a difference in the domestic habits and relationships of the two sexes may account for it. Thus a girl would probably be more kissed on her return home by other members of her family.

I have also found that infection is more frequently conveyed by one sex to the same sex than to the opposite sex. Thus 87 of the infecting cases were of the same sex as the returning cases, they gave rise to, and only 64 of the opposite sex. This, again, is no doubt due to domestic relationships, some attempt at grouping the sexes in their sleeping arrangements being made even in the most primitive households.

**Seasons.**

Boobbey, of Nottingham, in a paper on the subject which he contributed to Public Health in June, 1896, stated his opinion that return cases of scarlet fever were more prevalent, that is that the percentage was greater during the autumn months of the year, and he attributed this to the accommodation in fever hospitals being generally strained at that season, so that there would be a tendency to reduce the period of isolation. My experience as yet has been of too short duration to enable me to speak as to this. In November and December, 1896, we did certainly have a very marked increase of return cases, but it was not repeated the following year. Nor was it due to any reduction in the period of isolation, the mean duration of the latter being equal to the average for other months.

**Type of Return Cases.**

It has been found by several writers that the type of the disease in return cases is somewhat more severe on an average, and therefore they are more fatal than when contracted in an ordinary manner. My experience corroborates this, for out of the 171 return cases 13 were fatal, or a case of
mortality of 7.6 per cent. as against 4.8 per cent. for "all cases" during the same periods. As time is an important factor in relation to the vitality of the patient, it might have been expected that it would reduce virulence also. It must be remembered, however, that the patients who carry infection out of hospital are, so to speak, selected cases; for it is just because the infection in the infecting case is active and resistant that the infection is carried out.

**Type of Infecting Cases.**

It is not possible to consider the seventy of infecting cases by the simple but accurate method of comparing their case-mortality with that of "all cases," for the obvious reason that it is necessarily only those patients who recover who can become infecting cases. I do not, however, think that the cases which carry infection are much more severe than the average, and certainly some cases are of the very mildest. I do, however, think that complications, more especially certain complications, are more common.

**Condition of Infecting Cases on Discharge and Subsequent Health.**

I will first briefly mention the routine method adopted at the Birmingham City Hospital before patients are allowed to return home. All cases are detained for a period of six weeks, counting from the onset of their illness, not from the day they come to hospital. A special register is kept in each pavilion, in which is entered the name and number of the patient, and the fact of the period of isolation, the number of children at home (if any) who have not had the disease, and any special remarks. If the case has been previously examined, the condition then noted is also included. The patient is minutely examined in the best light available, and the bed chart consulted to ascertain the type and course of the attack, complications, etc. The patient's exact condition at the time of examination is then recorded, whether it is decided to "pass" her to go home or not. In the former, a printed notice is sent to the parents or friends asking them to bring the necessary clothing two days later. At the appointed time the patients going home are taken to the "bathing-out" pavilion, which is of the approved type, and consists of a double suite of rooms for males and females, each containing waiting-room, undressing room, bathroom, dressing-room, and opening into a common "finishing" room. A special staff of nurses is told off on discharging days for the duty of "bathing-out" the patients, and the following special rules have to be observed:

1. The bath is to be commenced immediately upon receipt of the patient's clothes, and to be performed as quickly as possible compatible with thoroughness and care.
2. If insufficient clothing is brought, or if the nurse considers it unfit for wear, she must inform the Matron.
3. The patient's own clothes to be kept carefully separated from the infected ones worn in hospital.
4. Each patient to have a clean bath sheet.
5. The bathing-out nurse to wear clean apron and sleeves.
6. "Isal" to be added to the water until it becomes distinctly milky.
7. Carbolic soap to be used and the patient washed all over with it.
8. The head of each child to be rubbed with carbolic oil after the bath.
9. The hair of each child must, after the usual washing, be dipped in 1 in 1,000 formalin; in the case of women this should be done and the hair dried before the bath is given.
10. The nose and ears to be syringed out, if this has not already been done in the wards, with 1 in 1,000 formalin.
11. No patient to be handed over to friends until the hair is quite dry.
12. Every patient to be seen by the medical officer on duty after bathing.
13. The nurse to report anything about a patient which she may discover and which is not noted in the Discharge Register.
14. Every patient to have a hot drink and something to eat before being handed over to the friends.

By order of the Medical Superintendent.

The final disinfecting bath having been given, the patients are again examined before being handed over to the friends. This second examination I prefer should not be done by myself, but by one of my colleagues, the condition already noted by me being checked in the register. I strongly believe in this dual examination. In the first place, it not very frequently happens that in the interval since the patient was first examined some fresh development occurs which may render it desirable to detain the case for a longer period. In ensures that the process of bathing, drying, and dressing have been properly performed by the nurses. It leaves a record of the patient's exact condition at the actual time of leaving the hospital, and it gives an opportunity for the medical officer to interview the friends, who are in a waiting-room in the same block, and to give them any instructions or advice. Lastly, it is a check on the primary examination, and ensures that it will be carefully and minutely made.

On examining convalescent scarlet fever patients at the end of six or seven weeks various lesions or traces of the disease may be discovered—for example, desquamation, usually on the hands or feet, inflamed throats, enlarged glands in the neck, sores, cracks, excoriations, etc., albuminuria, otorrhoea, and rhinitis. Patients manifesting any of these conditions are usually detained for a longer period of isolation, and in the majority of cases it is possible to get them perfectly clear before sending them out. This is not, however, always feasible. Sometimes the lesions referred to are exceedingly unyielding and persistent; often the parents decline, not unnaturally, to have their children indefinitely detained, occasionally it is desirable for the patient's own sake that he should be sent out. In practice, then, a certain number of cases are sent home after varying intervals with one or other of these conditions present. It has been one of my chief objects in this inquiry to endeavour to ascertain in what degree, if at all, these different lesions are likely to be associated with the carrying out of infection, and I have prepared a table (No. 5) with this in view. It would obviously have been of little use merely to have tabulated the number of the different conditions noted at the time of discharge, the "infecting cases" only. It was essential for such figures to be of real value that we should also know in what proportion the same lesions existed amongst "all cases" discharge. This, fortunately, I have been able to obtain from our registers.

In preparing this table it was necessary to guard against certain possible errors. In the first place it not infrequently happens that when a patient is an only child, or is returning to a house where there are not susceptible individuals, he is allowed out with lesions still present which otherwise would be the case. Obviously it is highly improbable, if not impossible, that such patients will give rise to return cases, and therefore they must be excluded. Secondly, I have already shown that the risk of a patient conveying infection after thirteen weeks' isolation is very small indeed, no matter what his condition may be, and therefore all cases discharged beyond that period must, in fairness, also be excluded.

**Table V.—Showing Condition on Discharge of "Infecting Cases" as compared with All Cases.**

<table>
<thead>
<tr>
<th>Condition on Discharge</th>
<th>Desquamation</th>
<th>Fauces Abnormalis</th>
<th>Abdominales</th>
<th>Nervos and Mucous Membranes</th>
<th>Skin Eruptions</th>
<th>Albuminuria</th>
<th>Otorrhoea</th>
<th>Rhinitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection Cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>11</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>8</td>
<td>36</td>
<td>92</td>
</tr>
<tr>
<td>Percentage</td>
<td>7.0</td>
<td>3.7</td>
<td>2.1</td>
<td>3.1</td>
<td>0.6</td>
<td>2.2</td>
<td>22.9</td>
<td>52.2</td>
</tr>
</tbody>
</table>

| All Cases              |              |                  |             |                             |               |            |          |         |
| No.                    | 205          | 137              | 59          | 55                          | 16            | 13         | 151      | 1815    |
| Percentage             | 8.7          | 5.4              | 2.3         | 8.2                         | 1.0           | 0.5        | 6.0       | 72.6    |

* Applies almost exclusively to late desquamation on the feet only.
† Based on records of 4,900 cases discharged, and not on the total 4,800 cases amongst which the "infecting cases" occurred.

Some explanation is also necessary as to the meaning attached to the headings of the different columns. "Desquamation" refers almost exclusively to desquamation on the feet and hands; the term "Fauces Abnormalis" includes generally, and on the hands, is nearly always completed within the minimum period of isolation, and in any case is seldom prolonged much beyond it. "Fauces Abnormalis" includes
enlarged tonsils as well as congested mucous membrane.

Sores and exorciations includes cracks, abrasions, and raw areas other than those in or about the nostrils. "Adenitis" means hypertrophied cervical glands. "Skin eruptions" includes all forms of eruption liable to occur during convalescence. "Albuminuria" includes chiefly chronic nephritis. "Otorrhoea" means purulent discharge from the middle ear. "Rhinitis" is meant to include all cases, however slight, where there was any reason to suspect the nasal cavity, whether there was actual discharge from the nostrils or not. It frequently happens that after a rhinorrhea has ceased, or even when there is little or no purulent discharge, an unhealthy condition may still be detected at the nostrils. There may be redness or actual exorciation, or crusts may be found just inside them. Sometimes no discharge may be seen until the nose is syringed, when thick, dried-up, purulent discharge may be found in the return lotion. Frequently there is a thin, watery mucus ooze from one nostril, scarcely distinguishable from normal nasal secretion.

**Rhinitis.**

I have for some time believed in the special infecting power of any discharge from the nose following scarlet fever, but I was scarcely prepared for such a striking confirmation of my belief when I took the table of cases under consideration. It will be seen on contrasting the percentage of lesions in infecting cases with those of "all cases" that in almost all the columns, except that for rhinitis and otorrhoea, the percentages are fairly uniform, and in the columns for "desquamated" and "adenitis"

are almost entirely accounted for by the fact that desquamation in this region not only may not begin until the process has been entirely completed elsewhere, and the cuticle take much longer in separating, but it is more liable than elsewhere to be shed by the second or even the third time. Whether the desquamating cuticle of a scarlet fever patient is specifically infectious—that is, more than would be accounted for by its close contiguity to an infectious body, or in other words, whether it contains the germs of the disease in itself or only carries them as any fomites might do, is a debated question. At first sight the distinction I have indicated may not appear of much practical importance, but, nevertheless, it is so, because if the shed epithelium only obtains its infection as fomites, it can no longer be regarded as a criterion of infectivity as it was until now, and probably still is by a majority of the profession. We all admit, of course, that a patient desquamating about the body or hands is almost certainly infectious, because we know that the state of infection is usually last longer than the process of general desquamation, and therefore it is a good practical rule to regard a desquamating patient as still infectious. At the same time there are certain considerations which rather point, I think, against the scientific correctness of the old and accepted view.

1. The infection certainly persists in very many cases for weeks and months after all trace of desquamation has disappeared. There is obviously then no end of infectiousness of scarlet fever, and a great centre of infection to its neighbour, and, moreover, if the reverse is the case, though the scales of epithelium must float away with every breeze to be deposited in the surrounding houses.

On the other hand we can scarcely say that it has yet been proved that the old and classic view is not correct, even though Klein has failed to find its special organism in the desquamating cuticle. Moreover the process is essentially a specific one, and it may reasonably be held that its very existence is an indication that the disease is still present. For myself I consider that the question has not yet been settled, and prefer to withhold my judgment.

**Otorrhoea.**

This complication differs in one respect from rhinitis in that it is more definite both in its onset and termination; at least as regards its external manifestations. Consequently an indication that the disease is still present can in no given case. This is the reason why it has played but a small part in the causation of our return cases. Being firmly convinced of its highly infectious nature, I make a routine practice of detaining all cases for at least two weeks isolating. Beyond this period I believe the risk of its carrying infection is very slight. The longest duration of infection amongst my cases, counting from the onset of the illness in the infecting case to the onset of the return case, with a few exceptions of from four to fifteen days, or approximately seven to thirteen weeks. The next two or three weeks, and the remainder a shorter period. As a precaution, however, I usually supply the parents of all children returning home with otorrhoea, though the proportion not cured in hospital is very small indeed, with a syringe and other materials for continuing antiseptic treatment at home.

**Subsequent Health.**

I have already referred to the possibility of patients undergoing a recrudescence of infectivity. I think all will agree with me that this does undoubtedly occur. The following case is a good example:

W. D. (Reg. No. 56), aged 5, was discharged from hospital early in the present year after eight weeks' isolation. He had had a simple attack without complications, and was apparently in good health. He returned home and mixed with the other members of the family without bad effects. Three weeks later, however, his nose began to discharge, and a week later his sister, aged 10, began to stick with the disease.

This case is by no means exceptional. I have made special inquiries in my last 60 infecting cases, with the result that I find that out of 33 of them who went home apparently quite well, two subsequently developed otorrhoea, and no fewer than 10 suffered from a discharge from the nose (sufficiently marked to obstruct the nostrils or to require the use of the syringe), without bad effects.

**Conclusion.**

In conclusion, I would say that I think that attempts to explain away return cases, as is often done, as being due to other causes than an infectious condition of the patient returning home are much to be deprecated. Other causes of discharge from the nose, even though it may possibly operate to vary occasions, is but a part of the process which has preceded in the process of general desquamation, and therefore it is a good practical rule to regard a desquamating patient as still infectious. At the same time there are certain considerations which rather point, I think, against the scientific correctness of the old and accepted view.

1. The infection certainly persists in very many cases for weeks and months after all trace of desquamation has disappeared. There is obviously then no end of infectiousness of scarlet fever, and a great centre of infection to its neighbour, and, moreover, if the reverse is the case, though the scales of epithelium must float away with every breeze to be deposited in the surrounding houses.

2. Although there is abundant evidence to prove that desquamating patients are infectious, as others have shown, I am aware, in the absence of demonstrable evidence to show that the desquamation is itself the special source of infection, that it is an extraction of the difficulties of the case, there is evidence, gradually accumulating from fever hospitals, that late desquamation, more especially secondary desquamation, is not a source of infection. My own figures point to this.

4. From the physical character of dry epithelial scales rendering them specially liable to be disseminated by currents of air, we should have expected to find that the striking distance of scarlet fever to have been a long one, and a scarlet fever hospital to be a great centre of infection to its neighbour, and, moreover, if the reverse is the case, though the scales of epithelium must float away with every breeze to be deposited in the surrounding houses.

On the other hand we can scarcely say that it has yet been proved that the old and classic view is not correct, even though Klein has failed to find its special organism in the desquamating cuticle. Moreover the process is essentially a specific one, and it may reasonably be held that its very existence is an indication that the disease is still present. For myself I consider that the question has not yet been settled, and prefer to withhold my judgment.

**Otorrhoea.**

This complication differs in one respect from rhinitis in that it is more definite both in its onset and termination; at least as regards its external manifestations. Consequently an indication that the disease is still present can in no given case. This is the reason why it has played but a small part in the causation of our return cases. Being firmly convinced of its highly infectious nature, I make a routine practice of detaining all cases for at least two weeks isolating. Beyond this period I believe the risk of its carrying infection is very slight. The longest duration of infection amongst my cases, counting from the onset of the illness in the infecting case to the onset of the return case, with a few exceptions of from four to fifteen days, or approximately seven to thirteen weeks. The next two or three weeks, and the remainder a shorter period. As a precaution, however, I usually supply the parents of all children returning home with otorrhoea, though the proportion not cured in hospital is very small indeed, with a syringe and other materials for continuing antiseptic treatment at home.

**Subsequent Health.**

I have already referred to the possibility of patients undergoing a recrudescence of infectivity. I think all will agree with me that this does undoubtedly occur. The following case is a good example:

W. D. (Reg. No. 56), aged 5, was discharged from hospital early in the present year after eight weeks' isolation. He had had a simple attack without complications, and was apparently in good health. He returned home and mixed with the other members of the family without bad effects. Three weeks later, however, his nose began to discharge, and a week later his sister, aged 10, began to stick with the disease.

This case is by no means exceptional. I have made special inquiries in my last 60 infecting cases, with the result that I find that out of 33 of them who went home apparently quite well, two subsequently developed otorrhoea, and no fewer than 10 suffered from a discharge from the nose (sufficiently marked to obstruct the nostrils or to require the use of the syringe), without bad effects.

**Conclusion.**

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Officers of Health in March 1896, for as long as six months. In this disease, however, bacteriology comes to our aid, and it is in the direction of the latter science that we must look in the future for assistance in scarlet fever also. I think it very probable we shall find that it is really in the nasal cavity that the organism of scarlet fever most readily finds a lodgment in those cases where the infection is unduly prolonged. In the meantime it is to the condition of this cavity that we must pay most attention in examining patients with a view to pronouncing them free from infection.

Certain resolutions were adopted at the conclusion of the business of the Section will be found on page 363 of the British Medical Journal of August 6th.

THE SECTION OF OBSTETRICS AND DISEASES OF WOMEN.

Professor A. R. Simpson, M.D., President.

CLAMP AND LIGATION IN VAGINAL HYSTERECTOMY FOR MALIGNANT DISEASE OF THE UTERUS.

By F. J. McCann, M.D., C.M., Physician to Outpatients, St Pancras Hospital, London.

My purpose in this short paper is to elicit opinion as to the relative merits of the clamp and ligature, or a combination of both in vaginal hysterectomy for malignant disease of the uterus. In my first cases I used the ligature alone, following the method which I first saw employed by Professor Leopold of Dresden.

A larger experience of malignant cases convinced me that recurrence was best prevented by a free excision of the broad ligaments, and for this purpose clamps are undoubtedly more serviceable. Ligatures cannot be applied close to the pelvic walls, as there is great difficulty in tying the knot deep in the pelvic cavity. The ligature is most suitable as a means of temporarily arresting the hemorrhage from the growth—where the cervix is involved—by securing the uterine arteries in the bases of the broad ligaments. The objection to the use of clamps for this purpose is that they occupy more space, and thereby hinder the further steps of the operation.

In operating for malignant disease of the body of the uterus, this preliminary ligature of the uterine arteries is most important. The great desideratum is to prevent the patient losing blood; for most of the unfortunate sufferers are already affected with anemia. Doyen and others advocate traction on the broad ligament in cases of arrest of hemorrhage. In many cases where the disease is well marked the uterus cannot be pulled down, and, moreover, ineffectual attempts at traction are frequently the cause of considerable hemorrhage. When the base of the broad ligament is secured on each side it may be divided between the ligature and the uterus, thus permitting the latter to be pulled downwards. A sufficient separation of the bladder anteriorly and the vaginal wall posteriorly for that purpose can be effected without the necessity of drawing down the uterus. Much blood is frequently lost where the growth is scraped away by the fingers or curette. It is much better to secure the uterine arteries before this is done.

I am firmly convinced that the less the malignant growth is scraped or cut the better for the patient. Such a procedure may favour dissemination. For this reason I am opposed to the method of splitting the anterior wall of the uterus, and still more to morellement. If the uterus be small, splitting the anterior wall is unnecessary; if large it can be easily removed by separation of one broad ligament previously ligatured from below upwards. The uterus can then be pulled downwards and outwards, and the remaining broad ligament clamped from above. The cut end of the other broad ligament should be ligatured before being removed. As the uterus is much enlarged should be treated by abdominal total extirpation.

The following method of operation is the one which I find most satisfactory. After the preliminary cleansing and disinfection of the vagina and vulva, the cervix is fixed by a suitable instrument (tenaculum, or some of its modifications). As the anterior lip of the cervix is so frequently involved in the disease, the tenaculum is placed on the anterior lip. Where the growth resembles the so-called cauliflower excrecence, it may be absolutely necessary to remove a portion of the disease in order to obtain a hold with the tenaculum.

I then make the posterior incision first (the posterior cervical lip being previously drawn forwards), because if the anterior incision is made first the hemorrhage tends to obscure the view. It is also a good plan to prolong the incision into the lateral fornices. A little separation of the bladder anteriorly, and especially laterally, in order to lift the ureters forwards, the posterior vaginal wall is separated. The ligatures should then be applied to the uterine arteries, in order to arrest the hemorrhage from the growth. Before any great traction efforts are made on the uterus, the pouch of Douglas should be opened in order to investigate the presence or absence of cysts, fibroids, or tubal swellings which may complicate the operation. I have found this precaution very advantageous when operating on complicated cases.

In one where a large cervical sarcoma was complicated with fibroid outgrowths into the blood ligaments, I found on examination with the finger in Douglas's pouch that, on the left side of the uterus the fibroid outgrowth was smaller, and accordingly the left broad ligament was pulled out, and divided, thus permitting the uterine and right broad ligament to be pulled downwards. In this case traction on the uterus did not pull that organ downwards, on account of the size of the fibroid outgrowths. If cysts are found they should be punctured.

The bladder should now be completely separated, and the utero-vesical pouch of peritoneum opened by grasping the peritoneum with forceps and snipping with scissors. The opening may then be enlarged. The broad ligament should now be grasped by a strong tenaculum as near the fundus as possible and pulled outwards. A long clamp can then be applied from above downwards to each broad ligament, including as much of the ligament as possible. If the ovaries are to be removed, the clamp should be applied externally to each ovary. The uterus is cut away, and the vagina cleansed. Gauze is packed into the vagina between and around the forceps in long strips.

The gauze should be changed when the clamps are removed at the end of forty-eight hours. There is so much oozing of blood and serum after vaginal hysterectomy that it is too great a strain on the antiseptic of the gauze to leave it in situ longer than forty-eight hours. Moreover, the patient is rendered more comfortable when the operation is finished.

I found the convalescence following after vaginal hysterectomy, as it is dangerous should the peritoneum not be completely shut off. Swabbing out the vagina daily with pledgets of wool steeped in corrosive sublimate is much more efficient. It has been stated that operation by means of the clamp is more rapid than by the use of the ligature. Much, however, depends on the skill of the operator and the nature of the case.

In cases of early cancer of the cervix, where the uterus is small and freely movable, the operation can be done by the foregoing method. It is doubtful if there is any great difference in rapidity when the two methods are employed by a skilled operator.

The great advantage of the clamp is that a larger amount of the broad ligament on each side can be removed. This cannot be done equally well by the ligature alone, and unless the broad ligaments are freely excised in cases of cancer of the cervix, I fail to see the advantage of total extirpation over supra-vaginal amputation. It is further stated that in this disease the convalescence is prolonged the longer the operation is done by the operation described.

From my own experience I have not found the convalescence delayed, nor have I found the large amount of sloughing after the operation which some authors describe. Much depends on the degree of care in the use of antiseptic during the operation. I believe that gauze plucks left too long in the vagina may account for the increased sloughing.

As to the amount of pain after the operation, this varies considerably. Where violent traction has been employed,
more pain will be experienced, and here let me add that the shock of the operation is thereby much increased. Patients who suffer from cancer of the uterus do not, as a rule, stand prolonged traction on that organ. Perhaps there may be more pain after the use of the clamp, but from my own cases I have not observed a comparable difference.

There is no one method of operating applicable to all cases of malignant disease of the uterus treated by vaginal hysterectomy. I believe, however, that a judicious combination of clamp and ligature will ultimately become the usual method adopted. I hope, however, to have the advantage of hearing the opinion of those who have had a large experience of the operation under consideration, in order that we may be able to settle on the method most advantageous to our patients.

A TABLE OF CASES OF INDUCTION OF PREMATURE LABOUR.

BY JOHN MOIR, M.D., F.R.C.P.

Dr. Moir submitted the accompanying table, showing the result of his practice in the induction of premature labour in cases of malformed pelvis. He desired to point out the advantages of the practice, initiated by Professor Hamilton, of gradual dilatation of the os and cervix over the modern practice of forcible dilatation of these parts and accomplishing the whole process of delivery in a single day or less. He believed that the latter mode of practice was attended with great risk to the mother and danger of uterine damage—such as prolapsus and its consequent evils—and little chance of having a living child, which was the chief end and object of the operation. The table showed that 29 women who went to the full time were pregnant 42 times, and that not one of these 49 children was or could have been born alive. Premature labour was induced as above indicated in these 29 women, and the result was the birth of 66 living and healthy children; 17 only were stillborn or lived only a very short time. But for the induction of premature labour not one of these 66 children would have been born alive, whereas, to Dr. Moir's knowledge, many of them became strong and healthy and were themselves parents of families. For the details of the practice Dr. Moir referred to his paper on this subject published in the Transactions of the Edinburgh Obstetrical Society, 1897-98.

Table of Thirty-one Cases of Malformed Pelvis in which Premature Labour was Induced.

<table>
<thead>
<tr>
<th>TABLE I.</th>
<th>TABLE II.</th>
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| Labour at Full Time, or 9 Months. | Labour Induced after 7 Months. |

<table>
<thead>
<tr>
<th>Cases</th>
<th>Very severe.</th>
<th>Cases</th>
<th>Very easy. (8th month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>6</td>
<td>0</td>
<td>2</td>
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</tbody>
</table>

Remaining Twenty-nine Cases.

<table>
<thead>
<tr>
<th>Times.</th>
<th>One—embryotomy</th>
<th>0</th>
<th>9</th>
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<tr>
<td>1</td>
<td>Two</td>
<td>2</td>
<td>6</td>
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<tr>
<td>1</td>
<td>Three</td>
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<td>6</td>
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<td>1</td>
<td>Four</td>
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<td>3</td>
<td>Five</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>One—forcesps</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>One—version</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>31</td>
<td>*Twins in one case.</td>
<td>66</td>
<td>17</td>
</tr>
</tbody>
</table>

Maternal Mortality.

Accouchments | ... | ... | ... | ... | ... | ... |
Deaths | ... | ... | ... | ... | ... | ... |
Both deaths were from septic poisoning, one in her fifth, the other in her third premature confinement.

An exhibition of improved clothing for women and of women’s hygiene will be opened in Berlin during the next two weeks. It is organised by the Berlin branch of the Society for the Improvement of Women’s Clothing. It contains a special section for sick nurses and monthly nurses, which will contain in addition to clothes specimens of various objects of use in the sick room.

SECTION OF OPHTHALMOLOGY.

D. ARGYLL ROBERTSON, M.D., LL.D., President.

THE USE OF HOLOCAINE IN OPHTHALMIC PRACTICE.

By JAMES HINSHELWOOD, M.A., M.D., F.F.P.S.G., Surgeon to the Glasgow Eye Infirmary.

[Abstract.]

Of late several new drugs have been introduced into ophthalmic practice as substitutes for cocaine. Of these the most recently discovered, ho1ocaíne, has been the subject of considerable attention since its discovery by Tauber in the beginning of 1897. The first communication regarding it will be found in the Centralblatt für praktische Augenheilkunde, January, 1897, where Professor Hirschberg, of Berlin, gives a short note regarding his experiences with a new drug as a substitute for cocaine. This new drug had been given to him for trial by Dr. E. Tauber, Privat-dozent of Chemistry in the Technical High School of Berlin. Professor Hirschberg remarks in his note that a few drops of 1 per cent. solution of his drug rendered the eye insensitive in a few seconds, so that foreign bodies could be removed from the cornea without pain.

This communication was rapidly followed by others, chiefly by German and French ophthalmic surgeons, who gave their experiences in the use of ho1ocaíne, who have recorded their experience with ho1ocaíne, while differing in matters of detail, are agreed that the chlorohydrate of ho1ocaíne can be substituted with advantage for the chlorohydrate of cocaine as a local anaesthetic in ophthalmic practice by reason of certain decided advantages which it possesses over cocaine. I have thought it might prove interesting to the members of this Section who have not yet tried this new anaesthetic to hear the experience of one who has used it in a considerable number of cases.

Ho1ocaíne is a derivative of para-phenetidin, from which also are derived phenacetic and lactophenin. It is a strong base, insoluble in cold water but readily soluble in alcohol and ether. The chlorohydrate of ho1ocaíne, which Tauber proposed as a local anaesthetic for the eye, takes the form of white needles, slightly soluble in cold water, but more readily soluble in warm. Its aqueous solution is neutral, and undergoes no change on prolonged boiling.

Before using it for operative purposes or in the diseased eye, I made a large number of observations on the effect of the instillation of a few drops of a 1 per cent. solution of ho1ocaíne into the normal eye. The following is a brief summary of the facts observed:

1. There is complete anæsthesia of cornea and conjunctiva produced in from 15 to 30 seconds after instillation.
2. The anæsthesia produced lasts about 10 minutes.
3. There is immediately after instillation a slight feeling of burning, which rapidly passes off.
4. There is produced shortly after instillation a slight hyperemia of the bulbar and palpebral conjunctiva, which rapidly passes away.
5. There is no alteration in the size of the pupil.
6. There is no disturbance of accommodation.
7. There is no alteration in the tension of the eye.
8. The corneal epithelium is not changed in the slightest, but retains its normal appearance.

In short, to put it concisely, ho1ocaíne seems to have no other effect upon the eye than rendering it anaesthetic. Herein lies its advantage over cocaine, which causes a conjunctival anæmias by constriction of the vessels, dilates the pupil, and often causes a desication of the corneal epithelium. Another great advantage of ho1ocaíne as evidenced by these observations is the great rapidity of its action, producing complete anæsthesia in from 15 to 30 seconds.

My experiences of ho1ocaíne in ophthalmic practice may be divided into two groups.

I.—In Inflamed Eyes.

It was used in conjunctivitis, phlyctenular affections, cornitis, etc., to soothe the patient, to relieve pain and blepharospasm, and so admit of a more exact examination of the eye.
I have found holocaine particularly useful in hospital practice, where its rapidity of action leads to a very considerable saving of time. For examining inflamed eyes with photophobia and blepharospasm, a few drops of the 1 per cent. holocaine solution will enable these one within a very few seconds to get a good view of the cornea. I have used it also very frequently for little manipulations such as the application of nitrate of silver or sulphate of copper to diseased lids, when you are able to make your applications with but little discomfort to the patient within a few seconds of the instillation of the drops. It has been claimed for holocaine by some observers that where the conjunctiva is inflamed and the vessels enlarged, its anaesthetic effect is more profound than that of cocaine. My experience does not harmonise with such observations. I made a number of observations, putting per cent. holocaine in one eye and a 2 per cent. solution of cocaine in the other. I found that the anaesthetic effect of the cocaine in these inflamed eyes was quite as great as that of the holocaine, but that the cocaine was much slower in its action. I tested this also in several cases of hypopyon ulcer, where the anterior chamber had to be tapped several times in succession in the same patient by using holocaine and cocaine alternately. This I considered an excellent test for seeing if the same results whatever have been observed an anaesthetic effect to the cocaine. All the patients however agreed in saying that there was no appreciable difference in the amount of pain, whether the operation was performed with holocaine or cocaine. So far as my observations have gone in such cases, holocaine does not produce a more profound anaesthesia, but only acts much more rapidly.

II.—In Operations.

I have used holocaine in 154 cases of operative interference on the unmindful eye. In the removal of foreign bodies from the cornea, holocaine is an excellent anaesthetic, enabling one to remove the foreign body within 15 or 20 seconds after the instillation of the drops. Only three or four drops of the solution are necessary for complete anaesthesia. In all the conjunctival operations the holocaine was used in an efficient manner and was found sufficient after 20 or 30 seconds to begin the operation, seemed to last longer than that of cocaine, so that the instillation was repeated only at rare intervals, and very little of the solution was used. In these operations was any holocaine injected under the conjunctiva, but after cutting through it, a few drops were let fall directly on the conjunctival opening. In the operations in which the globe was opened, the holocaine acted well. In the iridectomies it has the very great advantage of not altering the colour of pupill, and this will be of very special value in operating on cases of glaucoma. In the extractions and needling operations the only special advantages of the holocaine was that it enabled us to operate sooner than would have been possible with cocaine. No toxic or any disagreeable effects have ever been observed in any of these cases. Heinz has found by experiment on animals that holocaine is a poison producing convulsions and analogous to strychnine. He found its toxic action more intense than that of cocaine or any other anaesthetic. The reason for this is doubtless because such a very small quantity of the drug is required to produce a complete anaesthesia of cornea and conjunctiva, and herein lies one of its advantages.

Holocaine is therefore a most valuable agent for the production of anaesthesia of the eye. Its peculiar value lies in the fact that apart from the anaesthesia, it seems to have no further effect on the eye whatever. It seems to act simply by paralysis of the sensory nerve endings, and has no other action on the eye, leaving the pupil accommodation and tension quite unaffected. The rapid action of the drug is also a definite advantage, and in daily surgical practice where one is dealing with a large number of patients, leads to a considerable saving of time. According to Heinz a 1 per cent. solution of holocaine is powerfully antiseptic, as proved by experiments on the growth of bacteria, and therefore boiling the solution to sterilise it is not necessary. This is a further advantage that the solution is itself a powerful antiseptic.

Discussion.

Mr. Edgar Browne (Liverpool) said he had used holocaine for some time, and found it very satisfactory. It must be had from a first-class chemist, as it was very difficult to make up and did not keep long. The cornea never became fuscous under its use, as it did after cocaine. He had used it in all superficial operations, less in the deeper ones. He had not noticed that it penetrated more rapidly than cocaine, into a chalazion, for instance. It was not so good for the patients' own use as cocaine in painful ulceration of the cornea. It acted in 1 per cent. solution in about 15 seconds. In reply to Mr. Netteship, Mr. Edgar Browne said that he had not not used it in the form of an ointment.

Dr. Arygl Robertson said he had tried a 2 per cent. solution which had been made up by Messrs. Duncan and Flockhart; it was a clear solution. He had found it infinitely inferior to cocaine as a local anaesthetic.

Dr. Hinschwood, in his reply, laid great stress on the difficulty in getting even a 1 per cent. clear solution. It must be made up with fresh distilled water, as he believed all cases of failure to be due to badly-prepared solutions. He had a solution made up fresh every week, and found it would not keep longer than a fortnight.

CASE OF POLYPOLYD GROWTH FROM A MEIBOMIAN CYST.

By J. Fallows, L.R.C.S.Edin.,
Extramural House-Surgeon, Royal Ear Hospital, Soho Square.

The patient, a girl aged 19, presented a swollen appearance of the upper right eyelid. When the lid was everted a flat polyoid growth possessing a very narrow base springing apparently from the site of a Meibomian cyst, which had been opened surgically, was seen. This cyst was one of a series of five from which the patient had suffered within the space of three months. The cases of cysts themselves had apparently slowly developed after a patient suffered severe conjunctivitis for which treatment was given by Dr. Alfred Edmowes two years ago. She was cured in five weeks and had no relapse or further trouble so far as the skin was concerned. It was suggested by Dr. Eddowes that the infection of the follicles and formation of Meibomian cysts was a form of extension of the same infective process that had given rise to the acute attack of seborrhoeic eczema. From his own recent observations Mr. Fallows was disposed to think that there was a close connection between these cysts and eczema.

ON THE SURGICAL TREATMENT OF CATARACT.

By Ernnet F. Neve, M.D., F.R.C.S.Edin.,
Kensington.

Mr. Neve related the results of 730 operations for cataract. Of this number 677 were successful, 39 failed, and in 14 cases the patients left the hospital before the result was known. In the last 200 cases the percentage of failure had been reduced from 6 per cent. to 3½ per cent. Success in cataract operations was to be attributed to selection of cases and to antisepsis, but it was not right by the selection of only good cases to condemn many to hopeless blindness. The success of the operation was accepted by the patient, and the results were very satisfactory, in such cases the proportion of successes did not exceed 50 per cent. In glaucoma, also, the results were poor. With regard to the method of operating he recommended that the incision should not be too peripheral, and found that both iridectomy and capsulotomy were advantageous. With regard to inflammatory sequelae, he had met
with panophthalmitis in 5 cases, septic infiltration of the cornea in 3 cases, irido-cyclitis in 1, and glaucoma in 5. In 60 cases iritis occurred, ending in recovery in 41 cases, in occlusion in 13 cases, and in partial occlusion in 6 cases.

A CASE OF Cavernous Angioma of Orbit.

By C. H. Usher, M.B.,
Ophthalmonic Surgeon, Royal Infirmary, Aberdeen, etc.

G. C., aged 40, a farmer, came to the Aberdeen Royal Infirmary on October 12th, 1897.

History.—For about eighteen months he had noticed his left eye gradually "getting bigger" (some time later he stated that someone had noticed this for five or six years). It had never been painful, only slight irritation and watering caused by the wind. The sight of his left eye had been getting gradually worse; a year ago he could read large print with it. The eye had never been injured. For many years he had been subject to headaches, usually frontal and on the left side the pain was often very severe, keeping him awake at night.

State on Admission.—Left eye, V=pl.l., very great proptosis. The eyeball projects straight forwards, its movements are fairly free, they are limited mostly in an upward direction. The proptosis is not appreciably diminished on pressing the globe backwards, there is no tenderness, no pulsation, and no bruit. No growth can be felt in the orbit; cornea clear; pupils equal; left pupil acts sluggishly to light. Tension normal. Fundus imperfectly seen owing to vitreous opacities; optic disc is pale. Right eye appears normal, but V is only 4, no hypermetropia, vision not improved by lenses. Reads 1 J. at 5 ins. Field full.

Description of Growth.—The growth was situated within the muscular cone and was removed subsequent to enucleation of the globe. It had a dark blue smooth surface, studded with small nodules, and had considerable elasticity.

A DEMONSTRATION OF A NEW AND ORIGINAL METHOD OF MAKING CASTS.

Given before the Surgical Section of the British Medical Association at Edinburgh, July, 1898.

By Geo. A. Peters, M.B., F.R.C.S. Eng.,
Associate Professor of Surgery and Clinical Surgery, University of Toronto, Toronto, Canada.

It has long been desirable to have a better method of casting living objects, anatomical subjects, and pathological specimens than that which has hitherto been in vogue. Up to quite a recent period plaster of paris has been the material almost universally employed, and certainly many useful casts have been made by its use. Recently Cathcart and others have used gelatine, paper mâché, wax, etc., and for certain subjects these substances fulfill many desirable conditions.

Some six or seven years ago I began to work with paraffin wax in a molten state, and after considerable experimenting and many failures I have elaborated the apparatus which I am about to describe, and with which I gave several demonstrations at the recent meeting of the British Medical Association at Edinburgh, and subsequently in Dr. Sims Woodhead's laboratory at Examination Hall, London.

Paraffin wax possesses many qualities desirable in a material for making moulds. It is a clean, inert, homogeneous, workable substance, capable of taking a finer impression than almost any other material, and contracting but little in passing from a hot liquid state to a firm solid mass. It "works" easily, and can be used over and over again with but little deterioration in quality. Hard wax, with a melting point of about 85°C., is the quality which I have found most useful. Moreover, it possesses another quality which I find is appreciated to its full extent by those only who have had experience in the older method of casting from plaster-of-paris moulds, namely, the mould can be separated from the cast with the greatest possible facility simply by immersing the whole mass—cast and mould—in warm water until the wax becomes soft and plastic. In fact, in very delicate subjects the whole of the wax may be melted away, though this is rarely necessary. In this way the laborious process of chiselling away the waste mould, with the attendant anxiety for the safety from injury of the contained cast, is entirely got rid of, and the mould comes away with almost as much ease as one would lift a layer of gauze from the surface of the body, and with quite as little damage to the underlying surface.

One disadvantage of this process is that the apparatus is somewhat expensive and cumbersome, the principal expense being in connection with the "electric motor" and air pump. The place of this may be taken for ordinary work by a pump worked by hand or foot power, and connected to an air cylinder properly fitted with valves. It is necessary, however, to furnish oneself with a pressure of some 10 or 12 lbs. to the square inch, and this in considerable volume.

Briefly it may be stated that the process consists in spraying melted paraffin over the whole surface, cooling it by spraying ice-cold water at the same time, strengthening the mould with plaster-of-paris, and removing it in as many sections as the nature of the subject calls for.

The Apparatus.

Fig. 1.—A. The "jacketed" paraffin container, with "jacketed" tube leading to c. the paraffin ejector. b. Tank containing ice-cold water, with single tube leading to p, the cold-water ejector. d. The "pressure blower," or air pump, which forces air into the air cylinder f, which is provided with four exit pipes guarded by stopcocks. (The pressure may be regulated with great nicety by opening or closing a greater or lesser number of these). e. The electric motor.