

successful conclusion at the Charité in Berlin. His material was obtained from a typical case of the disease, in which an afebrile ascending flaccid paralysis led in a few days to death from medullary involvement. By special staining methods Dr. Leschke claims to have discovered certain almost ultramicroscopic bodies both in fresh preparations from the spinal cord and in sections. Emulsions of the cord were injected intraspinally and intraperitoneally into rabbits and guinea-pigs, but it was only in monkeys that positive results and consecutive inoculability were proved. The period of incubation varied between seven and twenty-three days, and the minute bodies above described for man were found, *post mortem*, also in the nerve ganglion cells of the ape. Cultivation experiments in ascitic fluid and ascitic bouillon were not successful.

Friedmann has not suffered the recent criticisms of his remedy in silence. He has published (in the *Deut. med. Woch.*) a vigorous criticism of the Rabinowitsch results. It will be remembered that the latter ascribed the frequent abscess formation after inoculation to impurities in the emulsion, but Friedmann maintains that they are due invariably to a specific hypersusceptibility of the patients, and could have been avoided in every case if his precepts had been followed, and an intercurrent intravenous injection given at the proper time. To Rabinowitsch's statement that a distinction must be drawn between a Friedmann culture and a Friedmann emulsion, he retorts that the two are identical, and combats energetically the indictment that his bacilli were pathogenic to mammals. The tubercles found by Rabinowitsch in the organs of an injected guinea-pig¹ were, he maintains, really quite harmless, non-progressive, and non-pathogenic formations, and claims to prove the innocuous nature of the emulsion by the results of his own series of animal experiments. He denies absolutely the possibility of his inoculated non-virulent bacilli assuming pathogenic properties at some future date, and offers in proof the fact that every one of the children of tuberculous families prophylactically inoculated by him two and a half years ago had since developed surprisingly well, and the von Pirquet reaction had remained continuously negative. Frau Rabinowitsch answered these assertions immediately, and called to witness the impurities actually demonstrated by Vulpius and Brauer,² and the fact that the patients who had developed abscesses had suffered from their effects for months. She complained also that Friedmann was still concealing his culture methods, and had refrained from publishing in detail the animal experiments which had led up to his inoculations in man. She reiterated her statement that the Friedmann culture and the curative emulsion are not identical, and also that the tubercles she had found in the guinea-pig which had died three months after inoculation were of a true caseating tuberculous nature, and had originated from the point injected. She concludes with the emphatic expression of the hope that the State will immediately interfere to prevent further prophylactic inoculation of the children of tuberculous parents.

Correspondence.

DEATHS AFTER SALVARSAN.

The scientific interest and practical importance of the subject discussed in the article published under this head in the JOURNAL of May 2nd, p. 982, led us to send a copy of that article, and such other information as was in our possession, to Professor Ehrlich. We are indebted to him for the following interesting letter:

[TRANSLATION.]

Dear Sir,—I am very much obliged to you for your kind letter and the details which you give with regard to the fatal case which has recently occurred. Since I do not know the exact symptoms of the patient who died in Guy's Hospital, I will not discuss this case, but I would not neglect the opportunity to explain here in a few lines the views at which I have arrived as to the origin of the nervous phenomena after salvarsan injection, and in particular encephalitis haemorrhagica.

The phenomena mentioned are indeed happily rare, but their origin is extraordinarily complex. In my address at the London International Congress I explained in detail that I associate these cerebral symptoms with syphilitic processes (especially the presence of spirochaetes in the meninges, that is, in the capillaries of the brain), and believe that through the dissolution of the spirochaetes and the escape of the endotoxins certain alterations occur, which only find expression after an incubation of several days.

The essential point in haemorrhagic encephalitis is a colossal dilatation of the vessels in the affected part of the brain, which may lead later to oedema of the brain and to perivascular bleeding. The dilatation of the vessels is, in my opinion, in close connexion with the salvarsan injection. I believe that the vascular system, altered by the endotoxin, is not indeed oversensitive to salvarsan as such, for otherwise the condition would appear immediately after the second injection (and the illness occurs especially upon the second injection of salvarsan), whilst it generally shows itself two days later.

This delay indicates that here a derivative of salvarsan has come into action, and I have previously expressed the view that this is an oxidation product, paraminophenyl-arsenoxide, to the irritative properties of which I have from the first directed attention. The formation of paraminoarsenoxide is favoured by all forces which cause a delay in salvarsan excretion, such as an overdose or presence of kidney disease. Under these conditions larger quantities of salvarsan than usual may remain behind in the organism, and succumb later to oxidation, forming the dangerous oxide.

But from the latest occurrences it seems probable that yet a third factor enters into the matter, which is perhaps the most significant.

The irritated vessels only undergo dilatation of so colossal a character under the influence of the arsenical substance, when the normal regulator of the vascular system, adrenalin, is present in insufficient quantities in the blood, as is the case in Addison's disease, and in hypoplastic processes occurring in the suprarenals (status thymolympathicus).

Milian (Paris) has done a great service by discovering the significance of adrenalin in a number of salvarsan accidents. He showed that the accidents described by Hoffman and Jaffé and Meirowsky, which developed immediately after the injection of salvarsan, and were characterized by blue-red swelling of the face, lips, and eye borders, by dyspnoea, etc., may be completely avoided if adrenalin be injected before the salvarsan injection. He showed, further, that severe diarrhoea and suppression of urine, threatening life, which occurred after salvarsan injection, were cured by an injection of adrenalin. Supported by these observations Milian has, by means of energetic adrenalin treatment, saved an otherwise hopeless case of encephalitis haemorrhagica, in which on the second salvarsan injection the deepest coma ensued.

A further favourable result has been obtained by Privat-dozent Dr. F. Pinkus in Berlin, in a case not quite so severe, and recently Dr. Milian informed me that Professor Fiocco, of Venice, had obtained still another success; in a case dangerously ill after salvarsan the coma disappeared after four injections of adrenalin, but after twenty-four hours it returned, and it was only after further treatment with adrenalin that the patient recovered. This case is, in my opinion, absolutely conclusive, since after the favourable result of the second course of adrenalin injections, it is to be taken as certain that the relapse of the coma was only due to excretion of the adrenalin between the first and second courses of injections of adrenalin.

I draw from these observations the hope that it will be possible, through a vigorous adrenalin treatment, to overcome this scourge of the salvarsan therapy in, it is to be hoped, a very large percentage of the cases.

You will see from the above remarks that I am absolutely against the view that the brain swelling (*Hirnschwellung*) signifies a simple arsenic intoxication, as has in several quarters been supposed. I believe, on the contrary, that we have to do here with a very complex process, consisting of at least three links, the details of which are now known to us, so that we can now avoid it, or, should it appear, combat it successfully in most instances.

¹ BRITISH MEDICAL JOURNAL, pp. 934-5.

² BRITISH MEDICAL JOURNAL, p. 993.

The patients specially threatened with encephalitis haemorrhagica are, as is known, those in whom the brain in the early secondary period of syphilis is flooded with spirochaetes. I have, during recent years, over and over again insisted that in these conditions we must not attack the disease with a bludgeon (*mit Hammerschlägen*) in the form of large doses, but must gradually steal in and get rid of the parasites gradually. For this purpose, in such cases—as is done, for instance, by Jennerich—a thorough course of mercury should precede the salvarsan treatment, and the dose chosen for the first injection of salvarsan should not be high. My views on this point are summarized in the book of Meirowsky and Kretzmer, from which I forward an abstract of the part which bears on the present matter.

When all the above-mentioned precautions are followed we may cherish the certain hope that the number of cases of encephalitis will no longer give occasion for hesitation. But should a threatening condition, in spite of all, ensue, the observation of Milian gives us a means whereby even here, through energetic and systematic treatment with adrenalin, it is possible to save the patient. A single injection is, in such conditions, naturally not enough; we must give the adrenalin treatment as strongly as possible and as long as is necessary to obtain the desired result.

It follows from what has been said that the demonstration by chemical examination of arsenic in the organs can offer no explanation at all of the etiology of this form of illness, for it is obvious that a few days after a salvarsan injection arsenic must be present in the organism. Such an examination would be of value only if it were possible to decide in what form arsenic was present in the organism, whether as unchanged salvarsan, or in the form of the poisonous oxide or—which does not seem to me probable—in the form of split-up arsenious acid. But a solution of this problem is, at the moment, not possible.

I shall be very pleased to give you any further information.—I am, etc.,

Frankfurt a/M., May 2nd.

P. EHRLICH.

[Extract from Drs. Meirowsky and Kretzmer's *Die Salvarsan-therapie der Syphilis*. (The Salvarsan Treatment of Syphilis, with its Practical Results in Skin and Genital Diseases.) Third Year. Wiesbaden: Bergmann. 1914. Pp. 609-10.]

With this increase of the reaction a number of unfavourable influences are frequently associated: first, a decrease in the quantity of urine (*Wasserfehler*); second, traumatic influences (such as long journeys, over-exertion); next, constitutional causes (such as Addison's disease, status thymolymphaticus), diminished excretion of salvarsan in nephritis, conditions causing exhaustion (alcoholism), and a status nervosus due to other affections; fourthly, imperfect preparation of the solution, formation of arsenoxide; and, fifthly, the important part played by the number of spirochaetes present in the focus—the richer in spirochaetes this is, the greater the destruction of spirochaetes. Ehrlich therefore advises that smaller doses should be given for the first injection, especially when nervous disturbances—for example, headache, disturbance of sleep, spinal pain, rheumatic pains, general malaise, alterations in psychic behaviour, giddiness, nausea, vomiting, swimming before the eyes, tinnitus, and other symptoms which point to a more marked participation of the brain—are present. When, after the first injection symptoms arise, the second injection must also be a small one, and the treatment must be carried through with calomel. On the other hand, the treatment should be continued energetically, with increasing doses up to the maximum. Begin low, end high!

To quote Ehrlich's views: He does not ascribe the unpleasant occurrences after the use of salvarsan to a toxic property of the remedy—leaving aside those cases which have died with symptoms of acute yellow atrophy of the liver—but seeks their cause in the patients themselves, in the swamping of the organism, and especially the brain, with spirochaetes, by whose destruction Herxheimer's reaction is produced and leads to alarming symptoms. Ehrlich's words on dosage should be especially laid to heart. He repudiates large doses in the beginning, especially when nervous symptoms are present, and advises that the second injection should also be a small one should the first not be well borne.

THE WORK OF THE ASSOCIATION.

SIR,—Those of us who are interested practically in the work of the Association must appreciate the great debt of gratitude we owe to the members of the Council for their zeal in watching the interests of the profession.

To only two points shall I refer: Arrears of subscription £1,480, an enormous sum, representing 1,184 members, of course. Doubtless there are many men who are chronic offenders in this respect, but the figure I mention brings the matter home to us. Personally, I cannot help thinking

that six months is a sufficient length of time to allow any member to be in arrear with his subscription.

The second point refers to membership of the Association: Resignations in 1913, 2,675. This mainly represents, I suppose, the malcontents. Now, I have ascertained the grievances of some of these gentlemen, not only in my own Division but in others. What are these grievances? (1) The Association "let us down" over the Insurance Bill; and (2) the Association has plenty of money and need not have raised the subscription.

1. As I have repeatedly pointed out, the Council was "let down" by us. The Council had a definite plan, and asked us, Do you agree with it? With an overwhelming majority we replied, Yes. Then the Council asked for subscriptions to the Central Defence Fund, as for a fight there must be ammunition. The response was, to say the least, disheartening. However, the Association went on with the campaign, harassed indeed by lack of adequate financial support. Then a pledge was prepared. We signed it, and forthwith broke it. Therefore, we are entirely to blame for any lack of success of our resistance scheme.

2. Men are saying that the Association has plenty of funds. This shows how carelessly the Annual Report of the Council is read. Others prophesy a still more serious fight with the Government in the near future and advise the Association to be prepared for the contest, and yet leave the Association as soon as the subscription is raised. I suppose we shall have a number rejoining at this time who having got all they can out of the Association will forthwith resign; and yet there are members of the profession who assert that we are united.—I am, etc.,

Bedford, May 3rd.

S. J. ROSS.

THE SPECIAL FUND: TRADE UNION OR TRUST?

SIR,—I have read with interest the objections raised in the Minority Report of the Council in Subappendix II¹ to the proposal that the suggested special fund should be administered by a trade union, and as a small amount of practical knowledge is worth a volume of theory, I believe it will be of service if I give some details showing that in actual working many of the objections which have been raised to a trade union of members of the medical profession are found to be without foundation.

I have the honour to be the chairman of the Union of Medical Practitioners—a trade union formed to protect the interests of the medical practitioners of Leicestershire and Rutland—and although the idea of a trade union for professional men was considered at first in some quarters to be a proposal of a very revolutionary character, yet we now find that within less than eighteen months after its formation no less than 212 are members of the union, being over 98 per cent. of those engaged in general practice in the two counties. This fact should, I think, effectually dispose of the theory expressed in Clause 2 of the Subappendix, as to the antipathy existing against a trade union, particularly when it is remembered that when our union was formed it was an entirely new idea, and the way for its reception had not been paved by the discussion which has since taken place, and which has tended to familiarize the profession with the idea.

Clauses 3 and 4 of the Subappendix do not attempt to suggest that the points raised in such clauses can be better met by a trust, and, taken at their highest estimate, are mere opinions that too much optimism has been expressed regarding the advantages of a trade union for securing cohesion among the profession. These opinions may or may not be found to be correct in practice, but, if a trade union failed to secure cohesion, a trust would be in precisely the same position.

Clause 5 of the Subappendix is also concerned with a theoretical objection to a trade union, which even if proved to be well founded could not be guarded against by a trust. The contention is that each member of the community considers merely his own interest in reference to the medical profession, and that no pressure could be brought to bear on the community who are the employers of the medical "blackleg." A practical knowledge of the working of a union shows that this is a most unfortunate argument to bring forward, as this is the case of all others which most aptly illustrates the advantage of a union. It

¹ BRITISH MEDICAL JOURNAL SUPPLEMENT, May 2nd, page 320.