NON - SPECIFIC THERAPY IN THE TREATMENT OF NEUROSYPHILIS.

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by

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INTRODUCTION. In deciding to adopt some form of pyrexial therapy for the treatment of neurosyphilis, I was much influenced by the gratifying results obtained by others and reported in the various medical journals from time to time. Most of such literature, it is true, dealt with the subject from one aspect only - namely, the induction of pyrexia by inoculation of the patient with the virus of malaria, but in view of the small number of cases to whom such treatment could be applied and the advanced stage of the disease in most of these, besides the fact that the hospital is situated on marshy ground and is infested by mosquitoes in the summer months, I was unwilling to institute a therapy which requires a specially protected room and which would seem to demand a greater stamina than most of our patients were thought to possess.

As an alternative, I wished to employ a treatment, which although apparently operating in the same manner as the malarial method, would appear to be less rigorous in its action, give a more controllable pyrexia, lend itself to spacing of the intervals between/

between the bouts of fever, and would involve no risk of infection to others.

And so a series of 12 cases of neurosyphilis, most of them general paralytics, was treated by a non-specific protein therapy in which the pyrexia was induced by the intravenous administration of small graduated doses of an antityphoid-paratyphoid vaccine. These cases were not specially selected, but represented the total number of neurosyphilitics available, excluding those in a stage of apparent remission and those who were actually moribund.

Eight of these cases were bedridden, a few showed signs of early dissolution, and so it was with some trepidation that treatment was attempted. But, as Dr. G. Bosch so succinctly has said " To contemplate with arms folded, a patient with general paralysis, is to enter into a compact with Death ".

HISTORY. It is only within comparatively recent times that pyrexial therapy in the treatment of general paralysis and other forms of neurosyphilis has come into prominence, but for many years physicians have recognised the favourable effects of intercurrent fevers in these diseases. As far back as 1848 Koster knew, and wrote on, the beneficial influence of malaria in insanity, and artificial abcesses were used to produce fever in cases of paralysis, by Jacobi in 1854, and Meyer in 1877.

In 1887 Wagner v. Jauregg suggested the use of malaria in the treatment of general paralysis, but it was not until 1917 that he actually introduced this fever as a therapeutic agent. Tuberculin and Besredka's typhus vaccine had been tried previously by him, as well as typhoid and staphylococcal vaccines and nuclein preparations, but seemingly he was convinced that more beneficial results might be expected from the action of an active virus and he chose malaria as the weapon for his attack on what hitherto had been regarded as an incurable and rapidly fatal malady. It would appear that he selected malaria merely because he considered it the most convenient and easily controllable fever available.

A few cases of general paralysis were inoculated with the blood of a soldier who was at the time suffering from benign tertiary malaria, and from these, other patients were infected, three being in an advanced stage of the disease, and the remainder more recent. In all, nine cases were treated/

treated, and a favourable result was obtained in six of these. This experience led to the treatment of further cases in 1919, since when, this method of artificially inducing pyrexia has been more and more universally adopted.

It was not until 1922 however, that the malarial therapy was introduced into England. On the 21st of July of that year, a male patient, the first to be so treated, was inoculated with benign tertiary malaria by Dr. Clark in the Whittingham Mental Hospital. Others followed this lead, and in 1923, eleven mental hospitals were applying the treatment. During the next few years, the successes claimed for this form of therapy induced many more to adopt it, and the number of patients treated in England and Wales, rose from eight in 1922 to five hundred and seventeen freshly inoculated cases in 1927. While this clinical exploitation of malaria was steadily gaining ground and adding fresh recruits yearly to the number who were applying it, until today it is the most generally accepted form of treatment for neurosyphilis, other means of artificially inducing pyrexia were being tried. Plaut and Steiner in 1919, shortly after Von Jauregg introduced the use of malaria, were inoculating their paralytic cases with the Spirochaeta duttoni, with the idea that a better effect might be obtained from the use of an actual spirochaete, than from the action of an organism/

organism such as the plasmodium of malaria, which is biologically unrelated to the Treponema pallidum.
Yet another means, by inoculation with the Spirochaeta morsus-muris, the organism of rat-bite fever, has been tried, but its inception was considerably later than that of the other two microbic methods.
The above treatments are all based on the introduction of aliving organism into the patient's blood stream, but dead cultures in the form of the various vaccines have also been employed. Typhoid, typhus, Staphylococcal, and coli vaccines, and tuberculin have been advocated, and various chemical substances such as sodium nucleinate, hetol, and a suspension of sulphur in olive oil have been of service. Lastly peptone, sterile milk, histamine, and the agents of autohaemotherapy, whole blood and serum, have their place among the pyrogenic bodies which have been used in the non-specific treatment of neurosyphilis.

The Pyrexial Treatment of Neurosyphilis.

The agents used in the different forms of pyrexial therapy can be classified roughly into two groups (a) the microbic and (b) the non-microbic.

Of the first group the principal member is malaria. A benign tertiary strain of the parasite is usually used and two methods of inoculation are employed - the first by mosquito-bite, and the second by blood inoculation from patient to patient. Clinicians are not agreed on which should be favoured, but Von Jauregg and others have pointed out the infrequency of malarial relapse in the blood-borne method. James (1929) reports 60% of mosquito relapses and prefers the alternative route for this reason. Nicol (1929) however, favours the mosquito-borne infection as a more certain way of getting a pure strain of the benign tertian parasite. He does not consider mosquito infection difficult to control and thinks that it gives better results than blood inoculation. In inoculated malaria, Grant and Silverston (1926) report less than 3% of relapses, and Davidson (1925) only 3.3%, although in mosquito - infection Davidson had 56.5% of relapses, and Yorke and Macfie, 57%. McAlister (1925) states that in inoculated malaria, the passage of the parasite through a long series of hosts tends to increase the virulence of the organism/

organism and therefore the risks of the treatment. In addition the results obtained by using such strains were not comparable with those obtained by direct inoculation. The resultant anaemia was more profound and splenic enlargement was found in 50% of the cases.

Lilly (1925) also, reports that the strain used in the Hanwell Mental Hospital seemed to increase in potency as it passed through successive hosts. The same strain, however, used elsewhere, became attenuated through time. Malarial relapses may occur from a few days to many months after treatment.

In using inoculated malaria, the incubation period varies with the route of administration. Davidson found that the average times for intravenous, intramuscular, and subcutaneous methods were respectively 7, 16 and 20 days. By mosquito-bite the average was fourteen days. Dunne (1926) found that the incubation period varied with the amount of blood injected. It was much shorter with 4cc. than with 2cc.

A previous attack of malaria would appear to induce a partial immunity. Davidson reports three cases which failed to develop pyrexia although the parasite appeared in the blood, and according to Reese and Peter, about 5% do not develop malaria even after repeated inoculation. Grant and Silverston consider that a patient undergoing a second course of/

of malaria tends to develop an auto-immunization after two or three rigors. Kirschbaum, where an immunity has been developed to benign tertiary malaria, has surmounted the difficulty by inducing quartan malaria. He states that this treatment is easier on the patient, as the rigors are less severe and the fever occurs only every fourth day. Anaemia is not so marked and he considers that quartan malaria is more suitable for debilitated patients than is the benign tertiary strain. He claims 50% of remissions by this method.

Eight or more rigors are generally permitted unless the patient shows signs of cardiac or other complications when the fever may be arrested, usually by small doses of quinine, or by the intravenous injection of salvarsan. Some clinicians allow as many as sixteen rigors but Grant and Silverston consider that a patient who is going to improve, will do so as readily with five rigors as with fifteen, and in their cases they found that a reduction in the average number of rigors was not followed by a drop in the rate of recovery or improvement. Theyallow no fewer than five, and no more than ten rigors, and the average female patient is allowed only $\frac{2}{3}$ the number of rigors permitted in the average male. On the whole, the fever is usually easily controlled. Davidson in some cases, found that 2, 3 and 4 rigors occurred after quinine had been given to terminate the infection, and Grant and Silverston report that quinine does not always prevent/

prevent the next succeeding paroxysm, although it nearly always delays the onset, and diminishes its severity. Spontaneous auto-immunization with disappearance of the fever and parasites took place, generally between the 5th and 10th paroxysms, in some patients inoculated for the first time, but this feature was more common in reinoculated cases, where according to Graham (1925), it often occurred after the 2nd or 3rd rigor. Rudolf (1929), found that the amount of quinine required to cut short the fever, varied with the different strains of the malarial parasite. Pyrexial therapy is now generally combined with some form of arsenical treatment. This does not seem to have much influence on the number of remissions, but it materially reduces the death rate. Fribourg-Blanc using malaria only, found that 46% remitted, of which number 22% died later. When malaria was combined with antisyphilitic drugs however, 66% remitted and only 6.7% died later. Meagher (1929) recommends reinforcing the malaria by some arsenical such as tryparsamide, and reports that in most continental clinics some such supplemental treatment is being given. Von Jauregg advises the use of salvarsan after the course of fever but Bamford (1928) advocates a course of tryparsamide before the rigors, as he considers that the loss of weight can be counteracted by this drug. It acts as an anti-syphilitic tonic and alterative, and a course given previously allows the maximum therapeutic effect to be obtained/

obtained from the malaria. Poole (1929) also recommends the use of tryparsamide as a general physical tonic, although he believes that malaria alone is as effective in producing a remission, Malaria, in some cases where optic atrophy has been present, has caused a rapid deterioration of vision, and when additional treatment with tryparsamide is considered, the fact that this preparation has in itself a detrimental effect on the optic nerve should not be forgotten.

On comparing the results obtained by malaria with those of untreated cases, there can be no doubt of the efficacy of the treatment. Meagher, in an investigation covering the general paralytics admitted to 55 mental hospitals where malarial treatment was not practiced, found that in 1927, of 624 patients who had been admitted in 1923, 90% had died, and of the surviving 10% less than 2% had been discharged. Nearly 68% had died within two years of admission. Of the 12 surviving discharged cases, not one was able to earn a living and all were mentally abnormal. The figures given for 1924 are no less appalling. From evidence gained in tracing discharged cases, and from details gleaned from hospital reports, he concludes that a complete remission of a year's duration is extremely rarely met with, and improvement such as to justify the discharge

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of the patient may occur in only 2 -3% of cases. No case came under notice in which a complete recovery from general paralysis was satisfactorily established.

In marked contrast to these are the results obtained by treatment with malaria. In 1927, of the cases treated in 1923, only 46% had died, and almost 25% had been discharged - that is 54% survived against 10% of untreated cases. The majority of the discharges were employed or capable of being so. Of the total treated in 1924, 58% were still alive in 1927, and about 24% had been discharged. Enquiries revealed that of the 67 discharged patients, only 5 showed progressive physical and mental deterioration, and most of the remainder were employed.

On analysing the total deaths in 5 years, he found that 40% of these occurred in the two months following inoculation, and he concludes that in the majority of these deaths, malaria hastened the end.

Brown (1929) reporting on 62 cases treated in Scotland, up to the beginning of 1929, found that 14 achieved a full remission, 12 were greatly improved and 11 showed slight improvement. In 5 the condition was apparently arrested and in 8 it progressed. There were 12 deaths.

Bunker and Kirby (1926) obtained a full remission in 34.9% of treated patients, moderate improvement in 12.3% and slight/

slight improvement in 7.5%. No improvement occurred in 24.5%, and 20.8% died. Of the 20.8% deaths, 6.5% died during the course of the malaria; 5.6%, 1 - 6 weeks after the malaria; and the remaining 8.5%, 2 - 11 months after. Bunker (1929) in reviewing 2460 cases treated with malaria found a remission rate of about 27%.
De Asis (1929) in 101 selected cases, obtained 33% discharges

In a mixed series of cases treated with malaria alone, it would appear that roughly one third may be expected to show remissions, and rather less than one third may be expected to die. Where the malaria is reinforced with arsenical treatment, the death rate should be reduced. Von Jauregg believes that if only early cases were treated, a cure could practically be promised with malaria.
In tabes also, the use of malaria would seem to be justified. Costa and Pires (1928) treated 12 cases with good results. The lightning pains and vertigo were at first increased but later passed off. Ataxia and incontenence were greatly modified, and in 30% of the cases, optic atrophy was arrested.

Though changes occur in the serological reactions after treatment with malaria, most observers are agreed that these are not constant. Reese and Peter find that there is no parallelism/

parallelism between clinical improvement and serological findings. Gerstmann states that the spinal fluid findings are modified gradually and only become definite after a considerable lapse of time. Graham reports a decreased cell count and diminished globulin content. The Wassermann reaction was improved in 3 out of 13 cases, and the gold sol test showed an ill-marked alteration in the curve in 9 cases. These cases however were all tested within 4 months of the termination of treatment. Bunker and Kirby found a considerable modification in the strength of the Wassermann reaction in 32% of cases, and a less marked but still definite change in another 26% De Asis found in practically all cases, a normal cell count but little change in the globulin, after treatment. In 16% of cases the Wassermann reaction became negative but the colloidal gold curve was only slightly affected. Wilson found that the fluid tended to approach normal 3 - 5 months after treatment, but that between 6 and 9 months the reactions became positive again.

Opinions are divided on the question of whether malaria actually cures the syphilis. In the opinion of Balado and Esteves (1929), it does not, and in support of this view they quote Claude, Targowla, Cenac and Prieur. They consider that in addition, antisyphilitic treatment is imperative, and they use preparations of bismuth and mercury, as/

as arsenicals had to be abandoned owing to optic and liver complications.

Many object to the use of malaria on the ground that an actual living organism is used, and it cannot be disputed that the introduction of a virus capable of multiplying in the body of the individual until there is no possibility of estimating the dose to which he has been subjected, is not desirable. But the resultant fever is usually cut short easily, and the actual bouts of pyrexia can be modified when necessary by small doses of quinine. Another objection which may be raised is the danger of infection to others. Gerstmann states that after repeated passages through human hosts, the malarial parasite changes in such a way that it can no longer be infective to the mosquito Anophelis maculipennis, or be transmitted by it to man. Vivaldi and Klauders also consider that inoculated malaria is not transmissible by anopheles. Sexual forms (gametes) are almost entirely absent from the blood of inoculated patients. They attempted to transmit by anopheles but failed, although the same patients were inoculated by the direct method afterwards. They conclude that there is little danger of spreading infection by this treatment. Grant and Silverston however, found that the strain of malaria which they used had undergone no change in pathogenicity during the direct passage from man to man through 60 generations. Anopheline mosquitoes/

mosquitoes were successfuly infected in the 12th and 16th passages of the strain.

In any case there is little danger of accidental spread of infection where proper precautions are taken.

One disadvantage of the treatment is the anaemia which follows its use. In many cases the destruction of red cells is extreme, and the patient is left in a condition of profound secondary anaemia. This however, is quickly remedied and Rudolf (1926) states that recovery usually occurs within 21 days.

A second and more serious complication of the treatment is the derangement of hepatic function which it causes. Williams (1927) carried out a series of tests on general paralytics undergoing malaria. A pure benign tertiary strain of the parasite was used. Laevulose tolerance curves were done at various times and untreated controls were examined. He found that in every malarial case, before the end of the treatment, the curves indicated some hepatic insufficiency. In many cases the curves became abnormal after the first and second rigors. In a few cases the insufficiency was apparently extreme and these patients remained critically ill for some days after the malaria had been stopped. In one such case, which died, acute yellow atrophy of the liver was found at autopsy. He also reports/

reports two previously fatal cases of this condition. In most cases the curves became normal soon after the fever had been arrested, but in a few the return was much slower. Conjunctival icterus was seen in almost every case, while several showed appreciable jaundice.

Tests were carried out in patients treated with relapsing fever, and in three cases of pneumonia and one of septicaemia. In none of these was the liver so severely affected. Graham (1925) found that jaundice was more apt to occur during malarial treatment, when the patient was on a liberal diet, and that it tended to disappear when the diet was reduced. In two cases of severe jaundice, both gave a history of alcoholism. Grant and Silverston in 78 cases treated, observed jaundice in four, and one case passed on to a fatal issue the day after the jaundice appeared. Muehlens and Kirschbaum in 72 cases, observed it in twelve.

Other complications occur. Hermann reports cases of marasmus, haemorrhagic cystopyelitis, pachymeningitis haemorrhagica, cardiac weakness and sepsis, and oedema of the face. Redlich observed such symptons as delirium, stupor, trigeminal neuralgia, spinal paraplegia, and epilepsy. Necrosis of the phalanges has also been noted. McIntyre remarks on the tendency to develop pyogenic infections/

infections, and reports cases of uraemia, circulatory collapse, acute bulbar palsy, and convulsions.
It has been suggested that malaria has some effect in causing aortitis or at least aggravating any such condition already existing. Castex and Beretervide, from their investigations into this condition, conclude that there is little to sustain such an assumption. They point out that aortitis is not especially prevalent in malaria zones, and when it occurs is merely a casual coincidence.

The other two microbic agents have not been used to nearly the same extent as malaria. Of the two, relapsing fever has the wider application. Blood from infected mice may be used to convey the infection, and on the third or fourth day the first paroxysm occurs. The pyrexial periods and inter-pyrexial periods are in most cases of five days duration, and abortive attacks are common. Schröter (1926) reports on 140 cases of general paralysis treated with the Sp. duttoni and claims results as good as those obtained by malaria. The previous treatment, age, or type of paralysis seemed to matter little, and the fever which was less vigorous than in malaria, needed no treatment as it became spontaneously arrested. Silverston (1924) treated three cases by this means. In two the inoculation failed, and in the third a mild/

mild attack consisting of one paroxysm, one relapse and spontaneous cure, occurred. The infection was conveyed by infected ticks. There was an incubation period of four days, pyrexia lasting six days, an apyrexial period of two days, and then relapse, after which there was spontaneous cure. The maximum temperature obtained was 101.2°F. A remission occurred but only lasted a few months. The spirochaete appeared in the blood at the commencement of the fever and multiplied rapidly, but arm-to-arm inoculation, when attempted, failed. Eddison (1929) found that although the blood of the mice teemed with organisms, these were sometimes scanty in that of the patient. Muehlens and Kirschbaum consider that recurrent fever is of value in the treatment of neurosyphilis because of the close relationship between the spirochaetes of relapsing fever and syphilis. Petrie (1929) however is of the opinion that although relapsing fever gives figures which are comparable with those of malaria, the results are not so good, and the fever is at times even more dangerous, and not so easily controlled. Horn (1928) reports on 66 cases treated in V. Jauregg's clinic. One half were given relapsing fever and the other half, malaria. The clinical results and the spinal fluid findings were decidedly in favour of malaria which proved the safer method. Eddison (1930) also, found that in none of his cases did relapsing /

relapsing fever produce any change in the intensity of the Wassermann reaction. Horn mentions the ease of keeping the infection alive in mice, against the inconvenience of using human hosts.

The third member of the microbic group, rat-bite fever, has not been used to any great extent. As in relapsing fever, the organism is a spirochaete, the strain of which can be kept going indefinitely in laboratory animals such as mice and guinea-pigs. Inoculation can be carried out by the intravenous or intradermal routes, but the former is preferable as it avoids the inconvenience of a primary sore and subsequent lymphangitis. An intermittent fever of 104-105° F is produced every one or two days. It can be readily controlled by salvarsan. Some writers claim for this form of treatment possibilities equal to those of malaria.

In the second group, the non-microbic, the agents are as numerous as they are diverse in constitution, but with the exception of the vaccines, of which the commonest in use is T.A.B., and a preparation of sulphur in olive oil, (sulphosin), they are not widely advocated. Mackenzie (1927) treated 13 patients with pyrexia induced by the intravenous administration of T.A.B. vaccine. This treatment was reinforced with injections of N.A.B. Temperatures up to 106° F were obtained and the average compared /

compared well with the pyrexia of malaria. Considerable mental and physical gain occurred in patients who were not too far advanced, and there were no permanent ill-effects, and no cahexia. No constant changes were found in the Wassermann reaction of the blood or spinal fluid, and although negative results were sometimes returned, these usually gave a positive reaction later. The gold sol, globulin content, and cell count shewed no constant change. Kunde, Hall, and Gerty treated 49 cases of general paralysis with typhoid vaccine, and obtained satisfactory results in 21 of these. They contrast the physical condition of the patient between the paroxysms with that of the patient treated by malaria. Petrie (1929) in comparing treatment by T.A.B. with that by malaria, stated that the results obtained by typhoid vaccine were good, but that remissions were not equal to these obtained by malaria, and this is more or less the view held by most observers. Sulphosin, a preparation of sulphur in olive oil, is a comparatively recent addition to the number of agents which are used in the pyrexial treatment of neurosyphilis. Schroeder (1929) claims that it has the same therapeutic effects as malaria without the drawbacks. Using sulphosin, he obtained 58% of discharges, including 33% apparently cured who had recovered their capacity for work. He states that the treatment is innocuous, and that the fever is easily controllable /

controllable and can be regulated by the size of the injections. It can be used anywhere and is applicable to patients in infancy and old age. The injection is given intramuscularly and the temperature attains its maximum 8 - 12 hours later, and returns to normal in about 24-48 hours. There is often some local tenderness experienced at the site of injection. He thinks that the sharp rise and slow fall are desirable and considers that the sulphur may have some specific action. The serological findings are no more parallel with the clinical results than they are in malaria. In 4 cases the Wassermann reaction became negative and there was a marked fall in the cell count. His patients received general antiluetic treatment in addition, but he reports very good results in patients treated by sulphosin alone. He concludes that when given in the proper way, sulphosin is a harmless remedy which can be used in serious renal and cardiac lesions. Even pregancy and pulmonary tuberculosis are not absolute contra-indications. He recommends that antisyphilitic treatment should be given in addition.

Winkler (1928) used sulphosin in five cases where optic atrophy was present after obtaining unfortunate results in this condition with malaria. The results were encouraging, especially in one case where central colour vision/

vision was recovered. Harris (1930) gives a good report on this method and advocates its use before the patient is certified in order to obtain earlier treatment. Sodium nucleinate, used in a 2% solution has been employed. The temperature rises to its maximum in about eight hours, but the injection is often painful and is sometimes followed by abcess. Donath, using this agent, obtained ten complete remissions out of twentyone cases of general paralysis. The white cell count on one occasion attained 61,000, and the temperature rose to 101 or 102°F. and remained above normal for three to five days. Shand (1929) however, using sodium nucleinate, reports no improvement in any of his cases. Templeton (1924) points out that this method depends not on temperature, although this may be obtained, but on the resulting neutrophil leucocytosis which is the most prominent feature of the reaction. Weisz (1928) gives a course of 10-12 intravenous injections of blood from a patient suffering from general paralysis, in whom the disease has become arrested. The results are good and the treatment is suited to patients who are too weak to undergo malaria. Robb (1930) used the patient's own blood serum in treating neurosyphilis amongst other conditions. The injection was given subcutaneously. There was some mental improvement with a transient reduction /

reduction in the intensity of the Wassermann reaction. Mehrtens and Pouppirt (1929) used prolonged hot baths in the treatment of the patients. They claim that the results in neurosyphilis compare well with those obtained by malarial therapy. Sterile milk is an agent which has been employed for a number of years. Given into the buttock, it can produce a fair degree of temperature, but the reaction in comparison with malaria is mild. Ahlswede considers that the introduction of a foreign protein is a more practical and effective method of treatment than malaria which has many objections. He uses an albumen - milk solution, given into the buttock and claims that it produces a suitable reaction which can be completely controlled.

Lastly, diathermy and other high frequency apparatus has been used to produce pyrexia in the treatment of general paralysis.

THE MECHANISM OF THE "SHOCK" REACTION.

Although within recent years much work has been done and a great mass of literature has accumulated dealing with the administration of non-specific agents, little is known regarding the action of these and their use still remains to a great extent empirical.

Numerous agents are used, but many of them, according to Kolmer, can be classified together as acting by virtue of the introduction of a foreign protein into the tissues. Such agents as the various vaccines, split proteins, cows' milk and peptone can be grouped as truly foreign proteins. The products of tissue excitation and destruction as produced by the injection of turpentine, hypertonic saline, etc., may cause a mild non-specific reaction due to the production and absorption of homologous proteins altered sufficiently to be capable of acting as foreign proteins.

He considers that the agents of autohaemotherapy, whole blood and serum, are changed by very slight manipulation to be capable of acting upon reinjection as non-specific stimulants, and that probably the effects of the intravenous injection of water and hypotonic saline are due, in part, to the products of haemolysis acting as foreign agents.

In 1885 Golgi observed that in malaria the paroxysm of fever coincided with the segmentation of a group of the parasites. When the merozoite bursts into the blood stream, the corpuscle

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is ruptured, and I think it is not unreasonable to suggest that part at least of the beneficial results obtained by the clinical use of malaria may be due to this ruptured corpuscle substance acting as a foreign protein and causing what may be termed an "auto-protein shock".

If this then is true that the foreign protein is supplied from the patient's own blood elements, it may seem a costly method of producing the "shock" reaction , but I hold the view that, as a body protein already tainted with the luetic infection is used - Adami has pointed out that the antigen must enter into chemical combination with the body cell - some slight specific antibody production may be stimulated, and this may in part explain the superiority of malaria to the other agents used.

The introduction of the foreign protein, whether it is endogenous or exogenous, seems to derange the balance of the metabolic processes in such a way that the resistance of the host to the organism is raised. Whether this raising of the body forces actually kills the organism or leaves it still active but inhibited for a time is doubtful, but the fact that remissions are caused in some cases only to be followed by relapse, although in others the benefit is apparently permanent, would seem to indicate that the difference is only one of degree, and that the effects could include an absolute cure of the disease.

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In the general reaction induced by the administration of a non-specific body, two definite responses are included - (a)/

(a) a rise in temperature and (b) a leucocytosis.

The majority of investigators suppose that the various fever-producing agents act by virtue of the lethal effect of high temperatures on the Treponema pallidum. In this respect the experiments of Schamberg and Rule (1927) are of interest. An emulsion of spirochaetes after being heated for one hour at 104° F. failed when injected into rabbits to produce syphilis despite the fact that when examined under the dark-ground illumination, it showed numerous motile spirochaetes at the time. The organisms seemed to be biologically injured by the action of the temperature and, when the heating process was continued for six hours at 106° F. , motion ceased and they began to disintegrate. In a series of experiments carried out to determine the curative effect of hot baths on chancres, these authors inoculated three rabbits in the scrotum with an emulsion of spirochaetes, originally of human origin, but which had passed through many generations of rabbits. Well-marked chancres were present thirty days after inoculation. Two of the animals were given baths at 113° F. for fifteen minutes daily, sublingual rises of 5.2 - 5.8° F. being obtained and the third animal was kept as a control.

Eight days after the institution of the baths, spirochaetes had practically disappeared from the serum of the chancres, which in two weeks time were entirely healed. The popliteal and inguinal glands were removed 75 days after inoculation, emulsified and injected into the testes of other rabbits. These remained free from infection although kept under observation for/

for 83 days.

Meanwhile the chancre on the control animal had increased in size and 75 days after inoculation was still present and showed numerous spirochaetes.

In a previous study (1926) the same authors demonstrated that in rabbits inoculated intratesticularly four days previously, eleven hot baths given on consecutive days and producing an average rise of temperature in the rabbit of 4°F. prevented the development of syphilis.

In the experiments of Weichbrodt and Jahnel (1919) an incubator was used instead of baths and the chancres were healed in from 3 - 5 weeks. The rabbits were subjected to a temperature of 41° C. for half-an-hour twice daily, their rectal temperatures being raised from 42 - 44° C.

Frazier (1927), in his experiments with hot baths given for 10 - 20 minutes, treated three animals from the fourth day of incubation. One rabbit, in which the temperature had been raised to 106 - 110.6° F.,developed a latent syphilis with a doubtful Wassermann reaction. Two normal rabbits were infected from its gland and testes material.

Six rabbits treated from the third day of inoculation with temperatures not above 106.5° F. developed syphilis, although the incubation period was slightly longer than in untreated animals.

Five animals with syphilitic orchitis, in which the maximum temperature obtained was 106.7° F., showed no effect.

From these experiments, it would appear that a temperature applied/

applied externally has at least an inhibitive, if not a lethal, effect on the spirochaete. The organism in vivo can survive a temperature of 106.7° F. although it is apparently inhibited as is shown by the prolongation of the incubation period. Temperatures between 106° and 110° F. seem nearer its lethal point.

On the foregoing lines is the therapy employed by Mehrtens and Pouppirt (1929) on various neuro-psychiatric conditions including neurosyphilis, in which the patients are given prolonged hot baths. To obtain clinical results, it was found necessary to raise the mouth temperature to at least 104° F. and sometimes to 107° F.. The Wassermann reaction of the cerebro-spinal fluid was often diminished in intensity, and the Colloidal Gold reaction frequently changed from a paretic to a luetic curve. The patients gained in weight and showed an increase in haemoglobin and reticulocytes. The authors considered that the results in neurosyphilis compare favourably with those obtained by using malaria.

The change from a paretic to a luetic curve is of interest in view of the opinions of Sträussler and Koskinas, who consider that the diffuse inflammation of the brain and meninges found in general paralysis, is converted by pyrexial treatment into a more localised gummatous type resembling cerebro-spinal syphilitic meningitis.

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The second very definite response to the stimulus of a foreign protein is shown in the increased activity of the haematopoietic tissues/

tissues, producing a rise in the number of leucocytes.
Eddison (1929 and 1930) found in general paralysis an impaired function of the leucoblastic tissues in the bone marrow, with a diminution of the leucocyte reserve. The functions were depressed in proportion to the stage of the disease and he found that when leucocytosis was stimulated, the intensity of the neutrophilic reaction varied inversely with the stage to which the general paralysis had progressed.
In early cases of untreated general paralysis, I found that the total and differential counts showed little variation from the normal, and any change which was present affected the polymorphs, which sometimes had a slightly higher percentage than usual.
The Schilling index, that is, the number of metamyelocytes calculated as a percentage of the total number of leucocytes, was not affected, being about 4% the figure given by Schilling himself and Piney as the normal.
The polynuclear count however, a modification of the Arneth index described by Cooke and Ponder (1927) gave a weighted mean (W.M.) of between 2 and 2.5, that is to say a "shift to the left". The change was mostly due to an increase in the number of cells in class I. at the expense of those in class III. Classes II. and IV. were little affected although class V., which according to the authors should contain about 4 cells, was generally below normal.
In the more advanced stages of the disease, the blood picture was not constant. In most cases, generally where a leucopenia was/

was present, the percentage of polymorphs was reduced, but in others there was a slight increase, the variation in the percentage of neutrophils being compensated by a swing in the number of lymphocytes and, to a less degree, in the number of monocytes. The percentage of eosinophils and basophils did not vary much, but was usually smaller than normal. Eddison found that in the periodic rises of temperature, characteristic of the later stages of the disease, the total count was slightly raised, the increase being due to a rise in the number of neutrophils, which brought the differential count to within normal bounds.

The Schilling index generally showed a rise in the later stages to above 10% and the polynuclear count a further shift to the left, the W.M. being about two or lower. The change was now due to an increase in the cells of classes I. and II. at the expense of the others.

The total count usually showed a leucopenia, but occasionally a mild leucocytosis was found. In these cases which were advanced and showed a neutrophil leucocytosis, a secondary infection, possibly focal, was suspected to co-exist with the syphilitic state.

The red cell-count in the early stages was not affected, but anaemia occurred in the more advanced cases. Hoppe-Seyler has pointed out that the severe anaemias met with in the later stages of syphilis are often associated with syphilitic involvement of the liver. (Piney)

In/

In treatment with T.A.B. vaccine it was found that a leucocytosis occurred about one hour after the rise in temperature and followed the temperature curve very closely. The degree of leucocytosis was largely dependent on the height of the pyrexia, but towards the end of the course of shocks, when the patient had developed some tolerance for the vaccine, it was found that although the temperature could be forced up by using massive doses of the vaccine, a proportionate rise in the number of leucocytes could not be obtained. In the earlier shocks a mild degree of fever usually co-incided with a well-marked leucocytosis. This is a point in favour of spacing the intervals between the bouts of fever in order that tissue exhaustion might be avoided.

After the injection was made, but before the rigor took place, a leucopenia constantly occurred. This was caused by an absolute and relative reduction in the number of neutrophils with a relative increase in the number of lymphocytes. The percentage of mononuclears was also reduced. This leucopenia generally co-incided with a drop in temperature.

During the rigor the temperature started to rise and mounted rapidly to reach its maximum in about one hour. It was followed by an increase in the white cell-count and the circulation was flooded with an enormous number of young neutrophils, their percentage of the total count sometimes reaching as high as 94%.

The total count, on occasion, rose to 26,000, but usually did not go beyond 17,000 or 18,000.

The/

The Schilling index and the polynuclear count did not vary much during the rigor, but thereafter the first rose steadily and the W.M. of the Cooke index was progressively deviated further to the left. In an early case which was treated, the Schilling index did not rise much above 20%, but in the later cases it mounted higher, although it never attained 60%, the level observed by Eddison in some of his advanced cases treated by relapsing fever therapy.

On one occasion, the W.M. of the polynuclear count reached as low as 1.18. The following is the count obtained on that occasion :-

I.	II.	III.	IV.	V. W.M.= 1.18.
84	14	2	0	0

This indicates a great preponderance of young and immature forms of neutrophils. It is of course an extreme example and usually the W.M. was higher and the older classes better represented.

As the pyrexia subsided, the total count slowly followed it, and reached its usual level within a few hours. The percentage of neutrophils fell and there was a slight relative lymphocytosis.

The Schilling index was slowly reduced, but usually remained slightly higher than before, unless a lengthy interval occurred before the next shock was given.

The polynuclear count recovered to some extent, but did not regain its former level during the course of the treatment.

The erythocyte count usually showed a slight increase after the/

the injection and rose with the pyrexia, a gain of over 500,000 sometimes occurring. The numbers had fallen by the next morning, but the rise occurred after each injection and at the end of treatment, the count did not show much change. No evidence of the protein cahexia mentioned by Petersen was seen.

During the erythrocytosis no nucleated forms were seen and there was no poikilocytosis, but occasional polychromasia occurred.

Pijper and Russel (1924) found that a subcutaneous injection of 0.5cc. - 10cc. of blood containing benign tertiary malarial parasites was quickly followed by a rise in the red cell-count amounting to 10 - 30%, which lasted several days and was followed by a fall. All cases showed this rise and a control injected with malaria-free blood showed no change at all.

Rudolf and Ramsay (1925) found an erythrocytosis preceding the anaemia of malaria, which was of the secondary type with a colour index at times becoming as low as 0.5.

Eddison (1929 and 1930) found in using relapsing fever therapy that the total white-count rose to about 13,000 during a paroxysm and fell to 5,000 during the afebrile periods. Neutrophilia was almost entirely responsible for the increase. The leucocytosis tended to become less marked after the third or fourth paroxysm. The Schilling index rose, especially in the more advanced cases, but dropped again to 5% during the afebrile periods. A favourable case seldom rose above 30% but/

but less favourable cases sometimes reached 60%.
Using malaria he reports a mild leucocytosis associated with a rise in the Schilling index. The leucocytosis was due to an increase in the number of neutrophils, the subsequent withdrawal of which led to a leucopenia.
In untreated general paralysis, he found little change in the numbers and characters of the red cells in early cases, but where the disease was advanced the numbers fell as low as 3 - 4 million with a colour index of 0.8. The size and shape of the red cells showed no appreciable change.
Eddison considers that the intensification of the Wassermann reaction which sometimes occurs during malarial treatment, should be regarded as a sign that the tissue concerned with the production of resistance and immunity, namely, the reticulo-endothelial system, is showing increased activity, since the Wassermann reaction may be looked upon as a phenomenon of resistance to infection. This latter statement, however, is open to question as to whether he is not misled by the common error of confusing the syphilitic antibodies with those lipoidophilic substances, which, according to Stitt (1923), are responsible for the Wassermann reaction, which I consider is more an indication of the intensity of the infection than of the degree of resistance. I would suggest that the malarial infection itself may be responsible for the increase in intensity, as it is common knowledge that in non-syphilitic subjects, this fever may produce a mildly positive Wassermann for a time.

Eddison/

Eddison suggests also that the reticulo-endothelial system plays a part in the production and control of pyrexia. Although in the charts showing the relationship of pyrexia to leucocytosis, the leucocytosis follows the temperature, it must be remembered that some time must elapse before any stimulus can show by the presence of an increased number of cells in the blood stream, and I think that the various factors such as pyrexia, leucocytosis, are dependent, the one on the other, rather than that one is the master which calls the pace the others must follow, and that the stimulation of one implies the stimulation of all. This view is supported by the experiments of Mehrtens and Pouppirt, where a temperature applied externally produced a rise in reticulocytes and haemoglobin, and I consider that any clinical improvement obtained by this treatment is not due to temperature alone, but to the activity of all these body functions which are associated with a rise in temperature.

The introduction of a foreign protein into the blood stream, therefore, produces a rise in the white cell-count, the change, as shown by a rise in the Schilling index and a shift to the left of the polynuclear count, being due to an increased number of young and vigorous neutrophils. The leucocytosis, however, is transient and is not maintained for more than a few hours, unless there is some further stimulation, and the tendency is for the response to become less to the stimulus as this is repeated.

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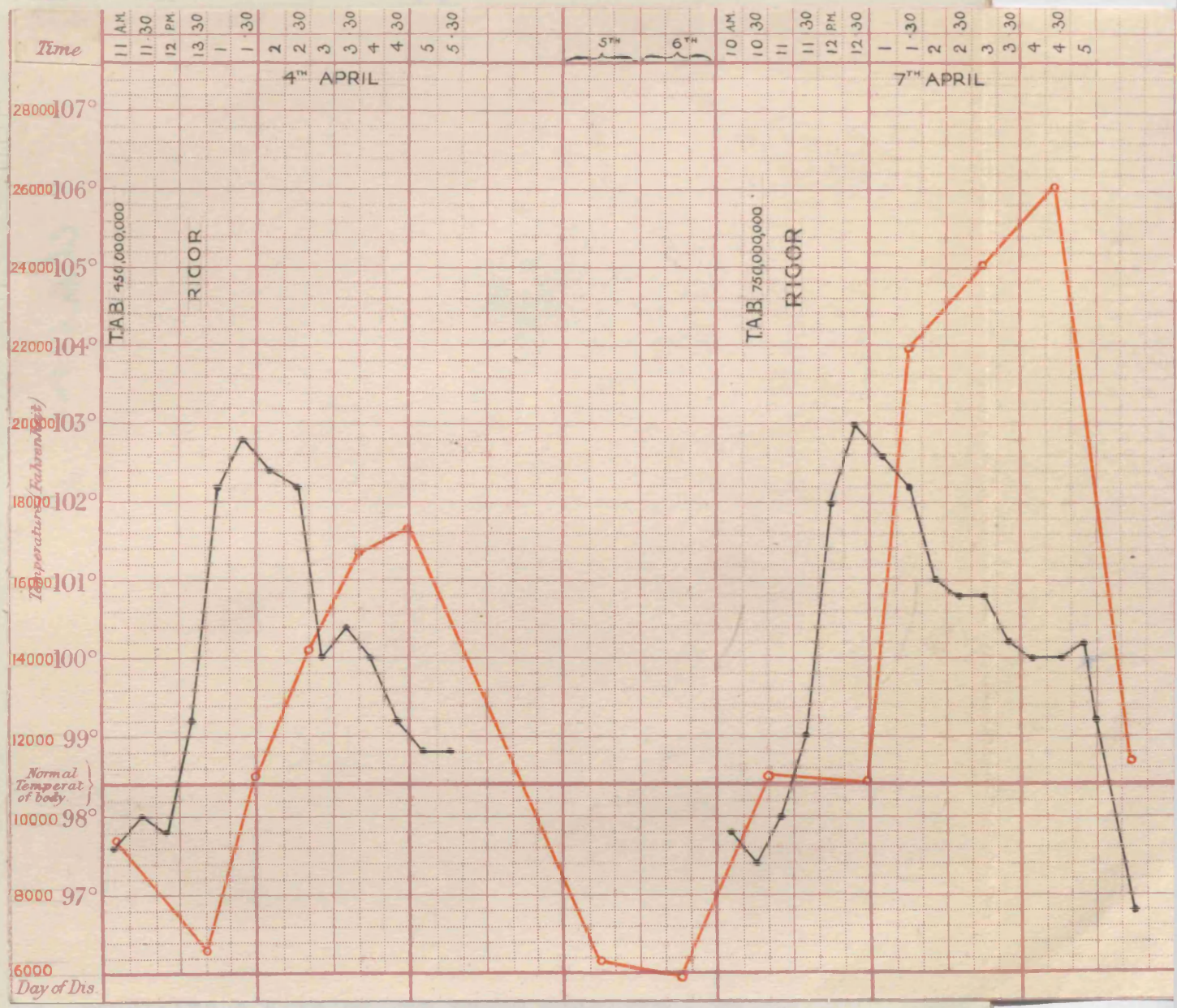
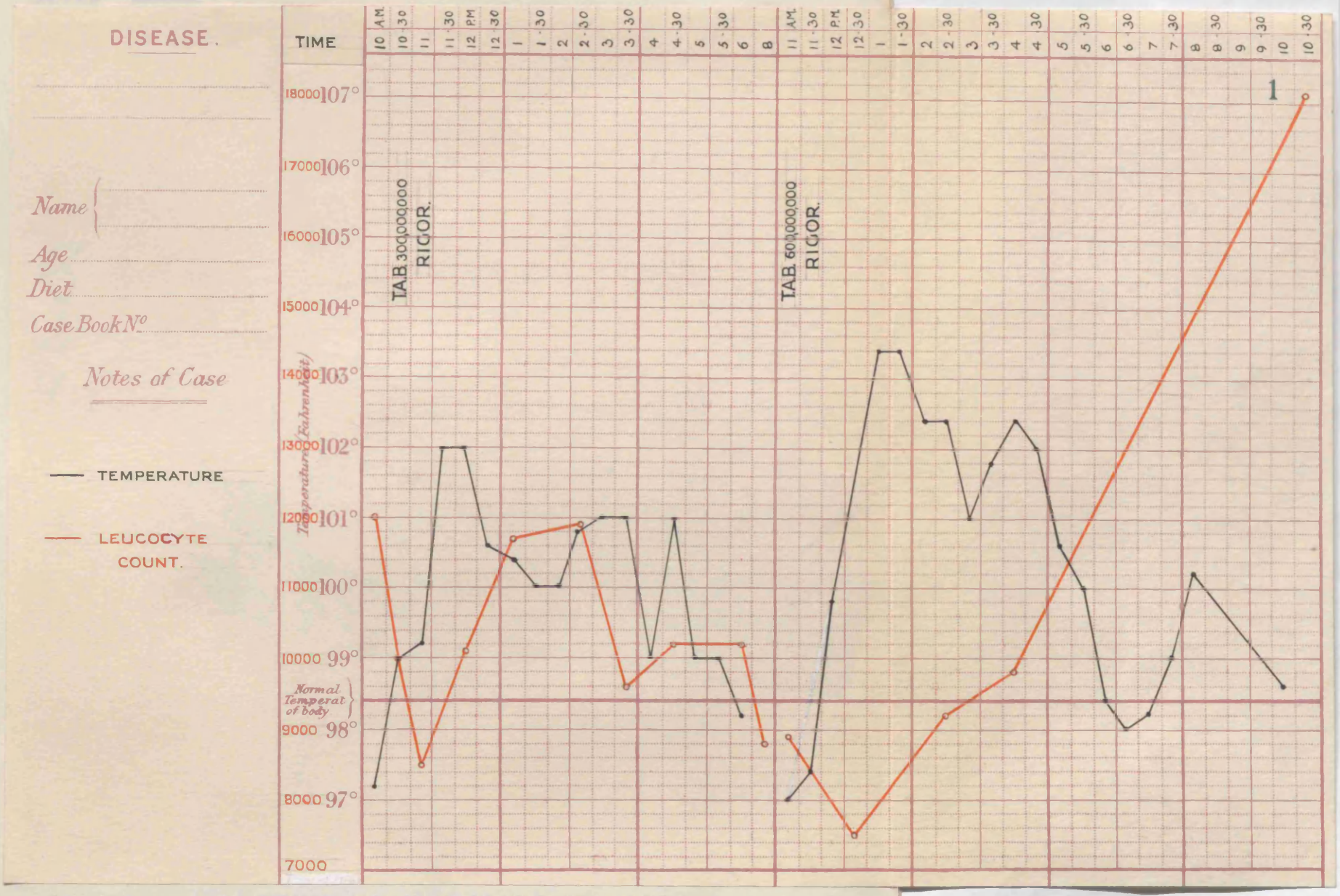
CHART ONE.



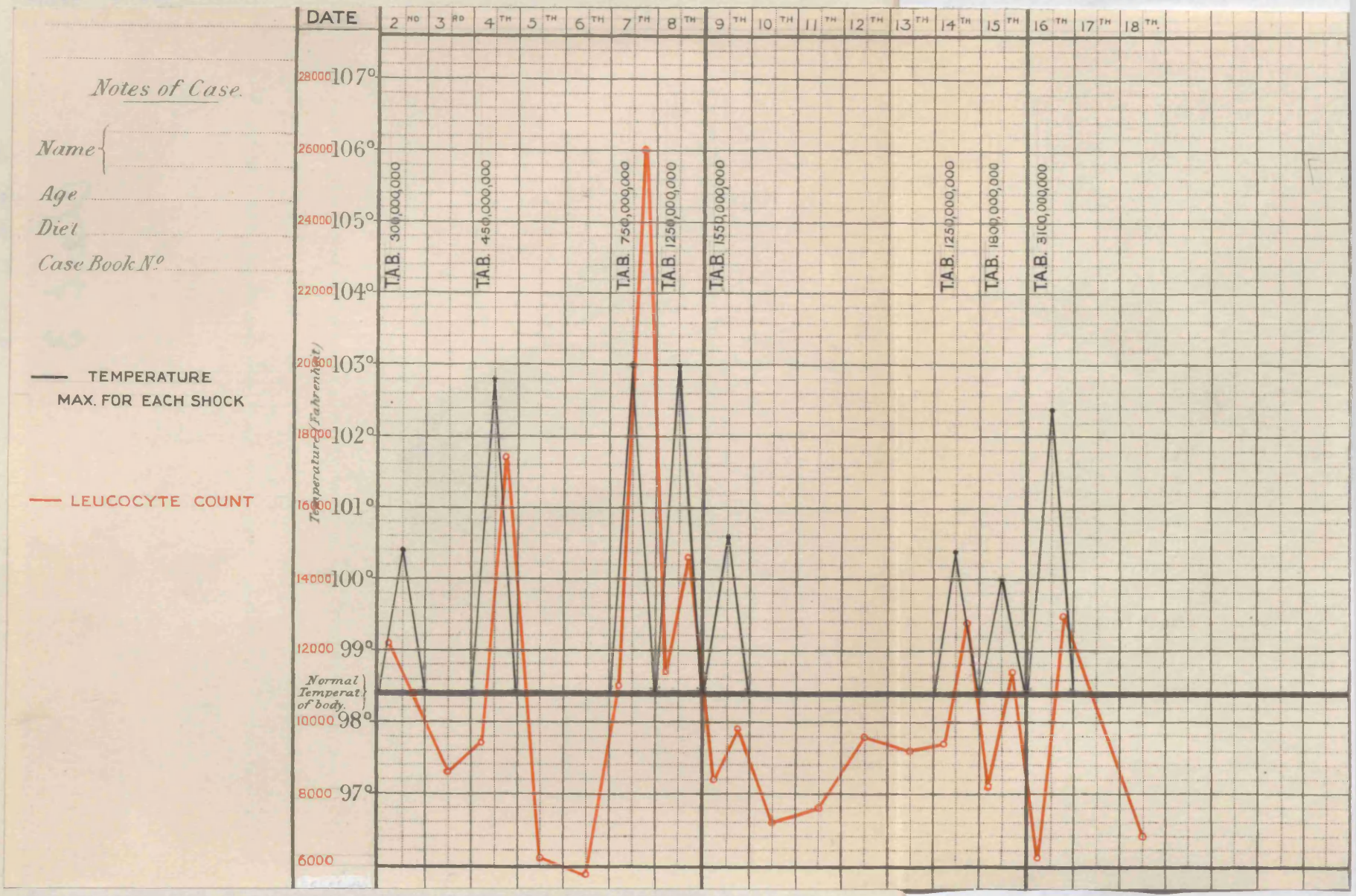
Charts one and two demonstrate the relationship between the rise of temperature and the leucocytosis following the shocks. It will be seen that the rise in the white cell count is to some extent dependent on the height of the temperature induced, and that both curves follow a fairly parallel course.

CHART TWO



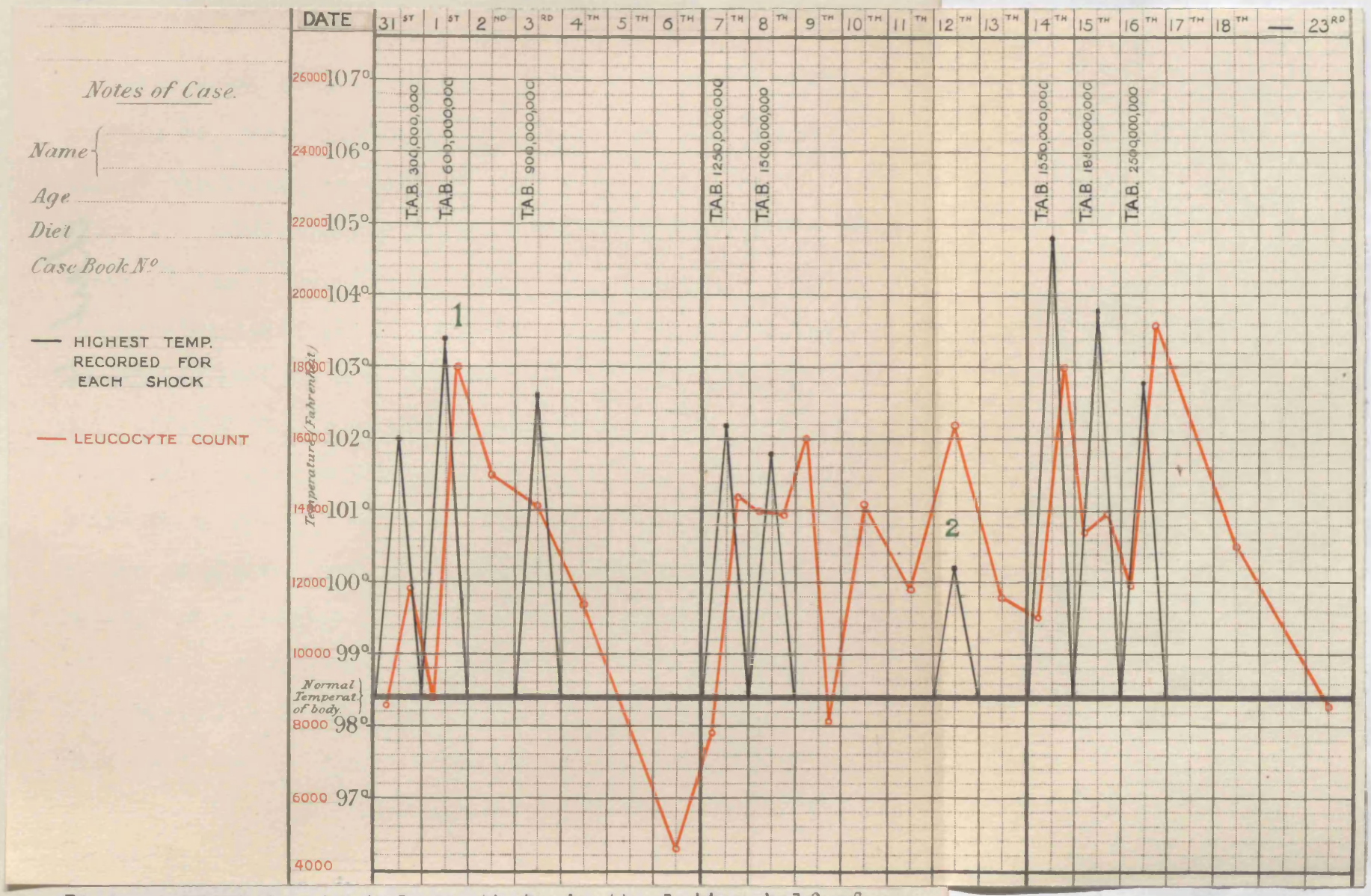
1 signifies a rise in the white cell count which coincided with the onset of acute confusion in the patient - probably the exacerbation of the meningo-encephalitis which subsequently proved fatal.

CHART THREE



Charts three and four demonstrate the relationship between temperature and leucocytosis throughout a complete series of shocks. The highest and lowest counts only were recorded. It will be observed that although a fair degree of temperature can be induced at the end of the series, a proportionate rise of leucocytes is not obtained.

CHART FOUR



It is evident in chart four, that, in the latter half of the series another factor, apart from the shocks, is influencing the white cell count. The patient, who became very confused during the treatment, died a few days after the final shock.

1 as in Chart Two.

2 signifies a spontaneous rise in temperature.

As regards the stimulation of the production of specific antibodies, most observers are agreed that little if any change occurs in the blood in this direction.

McIntosh (1926) found a slight increase in the bactericidal power of the blood 18 hours after injection with B. typhosus, but he considers that no satisfactory evidence has been brought forward to show that non-specific therapy owes its main effects to the stimulation of antibodies, and that non-specific antigens have no measurable effect on the antibody titre.

Kolmer considers that it is not improbable that non-specific agents may stimulate the production or elaboration of specific antibodies, providing the antibody producing tissues have been previously sensitized by the specific antigen, and that part of the good effects observed clinically after the injection of non-specific agents may be due to this antibody production.

Bieling found that in rabbits immunized with typhoid bacilli, the subsequent injection of other non-specific substances, such as colon, dysentery and diphtheria bacilli, resulted in the production of specific typhoid agglutinin.

Dujardin and Targowla believe, however, that general paralysis is the outcome of an abnormal prolongation of the anallergic period of the primary and secondary stages of syphilis in which the tissues of the body have not yet become sensitized to/

to the virus, while in non-paretic syphilis, the tertiary stage is an allergic one of marked reaction to the antigen, in which the vascular changes, allowing greater permeability, permit the production and dissemination of antibodies.

McAlister (1924) thinks that where malaria is used, a biological influence - an antagonism between the causative organisms - is at work, but others base their ideas on the fact that in non-syphilitic subjects an attack of malaria often gives a mildly positive Wassermann reaction, and they assume that specific immunity reactions are renewed in the tissues of the paretic infected with malaria, which have a direct action against the spirochaete.

Lewis (1925) however, considers that malaria can have no specific reaction, otherwise several other infectious diseases and fevers would not produce a similar response.

Kolmer looks upon the exacerbation of the lightning pains of tabes and the epileptiform attacks and psychic symptoms of paresis after the injection of non-specific agents, as examples of non-specific focal stimulation, which he regards as both a specific and a non-specific reaction.

In the following series of cases treated with T.A.B. vaccine, this exacerbation of symptoms was frequently found and it was noticed that the most satisfactory results often followed its occurrence. Pilcz, using malaria, also regards the development of acute mental symptoms in the course of the fever as favourable.

I think it is reasonable to assume that at least in some cases treated/

treated by non-specific therapy, specific antibody production may occur.

There is no definite concensus of opinion among the various observers as to which factor is mainly responsible for the benefit which may be derived from non-specific therapy. McAlister considers that of the two factors supposed to be at work, namely temperature and leucocytosis, temperature appears to play a larger part than leucocytosis. In a series of cases, he proved that, although leucocytosis without temperature could be readily produced, the effect on general paralysis was negligible.

Lewis, however, holds that the fever alone is not responsible, as good remissions often follow slight rises of temperature, and Stewart (1928), in treating his cases by what he calls "apyrexial" malaria, in which the patient was inoculated and the rigor allowed, but the attack was cut short by means of quinine, found that the results compared to advantage with those obtained by the ordinary method in which the pyrexia was allowed to continue. The percentage of cured and improved cases was higher and the percentage of deaths lower.

Eddison suggests that the involvement of the reticulo-endothelial system by the syphilitic virus and the consequent depression in function are factors in the pathogenesis of general paralysis, and that the benefits of pyretotherapy are conferred through rectification of this depression as it stimulates the reticulo-endothelial system at a time when its function/

function is flagging under the influence of the syphilitic infection.

McIntosh, also, considers that the curative effect of non-specific antigen depends chiefly on the general tissue reaction and leucocytic response.

Jahnel, however, rejected leucocytosis as an explanation of the action after he found moving spirochaetes in the brain of a patient with suppurating meningitis accompanying the paralysis. He states that when such a severe cerebral suppuration as this had no influence on the spirochaete, we must give up all hope of therapeutically affecting paralysis by means of an artificial leucocytosis.

Graham (1925) also discounts the idea that leucocytosis is responsible for the beneficial effects obtained from the use of malaria. In several cases which he examined during and after the course of the fever, the leucocyte count did not rise above 10,000 and counts of 4,000 - 6,000 were mostly found.

Krundratitz, at a recent conference in Vienna, stated that in treating old cases of congenital syphilis with malaria, he had demonstrated the spirochaete in the blood in the seventh and eighth paroxysm. He considered that the attacks of fever acted by opening out nests of the spirochaetes, thus exposing them to attack.

Muellers believes that changes in the vascular tonus occur, vaso-dilatation leading to local hyperaemia and transudation accompanied by invasion of polymorphs and the escape of serum, and/

and Starkenstein has demonstrated an increased permeability of the endothelia of the capillaries, followed by a decreased permeability in non-specific protein medication.

This affords an explanation of the access of the defensive agents to the seat of the disease.

Lord (1929) suggests that the fact of improvement being obtained from the use of malaria in one general paralytic and not in another, may be due to the presence of toxaemia. In a case of paralysis he says, one knew that syphilis was present but there might be half-a-dozen toxaemias also operating on that case.

While admitting that toxaemias may be, and very often are, present in cases of general paralysis, and that their cure or amelioration would certainly improve the patient's condition, I might point out that the examination of the brains of treated general paralytics would suggest that the treatment actually has a lethal effect on the spirochaete itself.

Lewis, Hubbard and Dyer, in examining the brains of four paralytics, found no spirochaetes in two of these and only a few apparently damaged ones in the other two. There was also a greatly diminished plasma cell and lymphocytic infiltration of the perivascular spaces.

Jossman and Steenarts reported in 1923 that no spirochaetes had been found in eight brains examined by them, and Nicol reports that in a number of brains examined in the Maudsley Hospital, no spirochaetes had been found except in one - that of a juvenile paralytic.

From this maze of surmise and conjecture, little has emerged which can be accepted as an explanation of the mechanism of non-specific therapy as applied to neuro-syphilis, but opinions incline towards a biological explanation of the action.

It is a well-known fact that antibacterial substances require a sufficiency of complement for their bactericidal action, and assuming both antigen and immune-body to be present in sufficient amount in the blood of neurosyphilitics, I decided to investigate the complement content.

On comparing results previously obtained in our laboratory, it was found that in non-syphilitic cases the M.H.D. of free complement was usually contained in about 0.08cc of serum, but in general paralytics the complement content was much lower, from 0.4 - 2cc. of serum being required.

To ascertain what effect treatment with T.A.B. vaccine had on the balance of free complement in the blood, three cases were chosen and the complement content was estimated in each. The first patient was an epileptic, the second a case of dementia praecox and the third a case of toxic confusional insanity.

A course of treatment with T.A.B. vaccine was administered, the shocks being given every second day and the complement estimation being carried out on the alternate days.

In all three cases, it was found that a rise in the amount of free complement, of 100% or more, was obtained following the/

the injections. In two of these cases, this was preceded by a fall and in all, the rise did not occur until about a week after the first shock. In two cases it was maintained for about three weeks, but in the third it did not persist for more than one week. The amount of free complement, thereafter, tended to swing, great variations occurring in its level.

From estimates made at short intervals during the individual shocks, it was found that the level of complement did not vary during the pyrexia.

The increase in the amount of free complement coincided with some improvement in the clinical conditions of the patients. In the first, a severe acne of the face cleared up, and there was an increase in weight; in the second, the state of catatonic stupor became less profound; and in the third, mental symptoms were greatly relieved and about 14 lbs. in weight was rapidly gained.

It is known that the proportions of antigen, immune-body and complement have to be within certain limits for complete fixation to take place. If the amount of immune-body, for instance, be too great or too small, the reaction is incomplete. (Neisser-Wechsberg phenomenon.) This, of course, applies to reactions "in vitro", but assuming it to apply equally well to those "in vivo", it might be possible to bring the relative proportions of antigen, immune-body, and /

and complement, to within the optimum zone for complete fixation to take place, by altering the amount of one of these units, and I consider that it is probable that this point may be touched at some time during the swing in the complement level which seems to follow the initial rise. McIntosh found no change in the blood complement after the administration of vaccines, but he obtained a considerable diminution when colloidal silver was injected. I might point out again, that in my cases the rise in the level of free complement did not occur until about a week after the first injection.

Robb (1930) used the patient's own blood-serum as a therapeutic agent in the treatment of various forms of insanity. The serum, after separation, was kept on ice for five days before use, 0.04% of carbolic acid being added on the fourth day as a preservative.

The initial dose consisted of 2cc. followed in one hour by another 6cc. given into the abdominal wall. On the third day of treatment 12cc. were given, and on the fifth day, 25cc. This constituted a course of treatment. In 15 out of 16 cases so treated a rise in the level of free complement was obtained. In 9 cases recovery resulted, in four of these there was some improvement, and in two no change occurred. In these cases also the rise did not show until at/

at least one week after the first injection and very often three or four courses of treatment were necessary to bring it about. It was usually preceded also by an initial fall.

Robb suggests that the serum on standing for a few days and becoming "anticomplimentary", may absorb free complement in the blood on being injected into the tissues, and cause a physiological increase of fresh complement. He draws an analogy between this and the giving of an alkali to stimulate the secretion of Hcl in the stomach. He allows however that the treatment may be a mild form of protein shock. A rise in temperature was seldom obtained and was not desired, but in one or two cases a small rise did occur. The preliminary drop in temperature, also found in shocks elicited by the administration of T.A.B. vaccine, was common, and moreover the leucocytic curve corresponded to that found in the latter treatment, although it was less marked. I consider that this therapy is probably a mild form of protein medication in which the stimulus is insufficient usually to produce a rise in temperature.

In the general tissue reaction produced by the stimulation of a foreign protein in the blood stream, no one of the physiological and biological responses can be singled out as the factor mainly responsible for the ensuing clinical benefit.

benefit./

The temperatures obtained by the different forms of pyrexial therapy are rarely high enough to have more than an inhibitive effect on the spirochaete, and moreover it has been clearly proved that a high temperature is not essential to the production of results.

The leucocytosis stimulated, is transient and sometimes ill marked, and it is significant that in malaria, the treatment of election in neurosyphilis, the leucocytosis is relatively slight in comparison with that obtained by less effective agents.

The antibody response so far as increased production is concerned, is uncertain, although in some cases, especially where malaria is used, it probably does occur.

I consider that although these factors probably play a part in bringing about the ultimate improvement in the patient's condition, they are not wholly responsible, and I think that the alteration in the balance of free complement brought about by non-specific treatment, is worthy of consideration, as complement is a factor which is essential to the complete fixation of specific antigen and immune body, although generally considered to be non-specific in itself, and which, as a non-specific factor, can be influenced by widely divergent agents.

Charts five, six, and seven, show the deranged balance of free complement in the blood during and after a course of protein shock.

CHART FIVE.

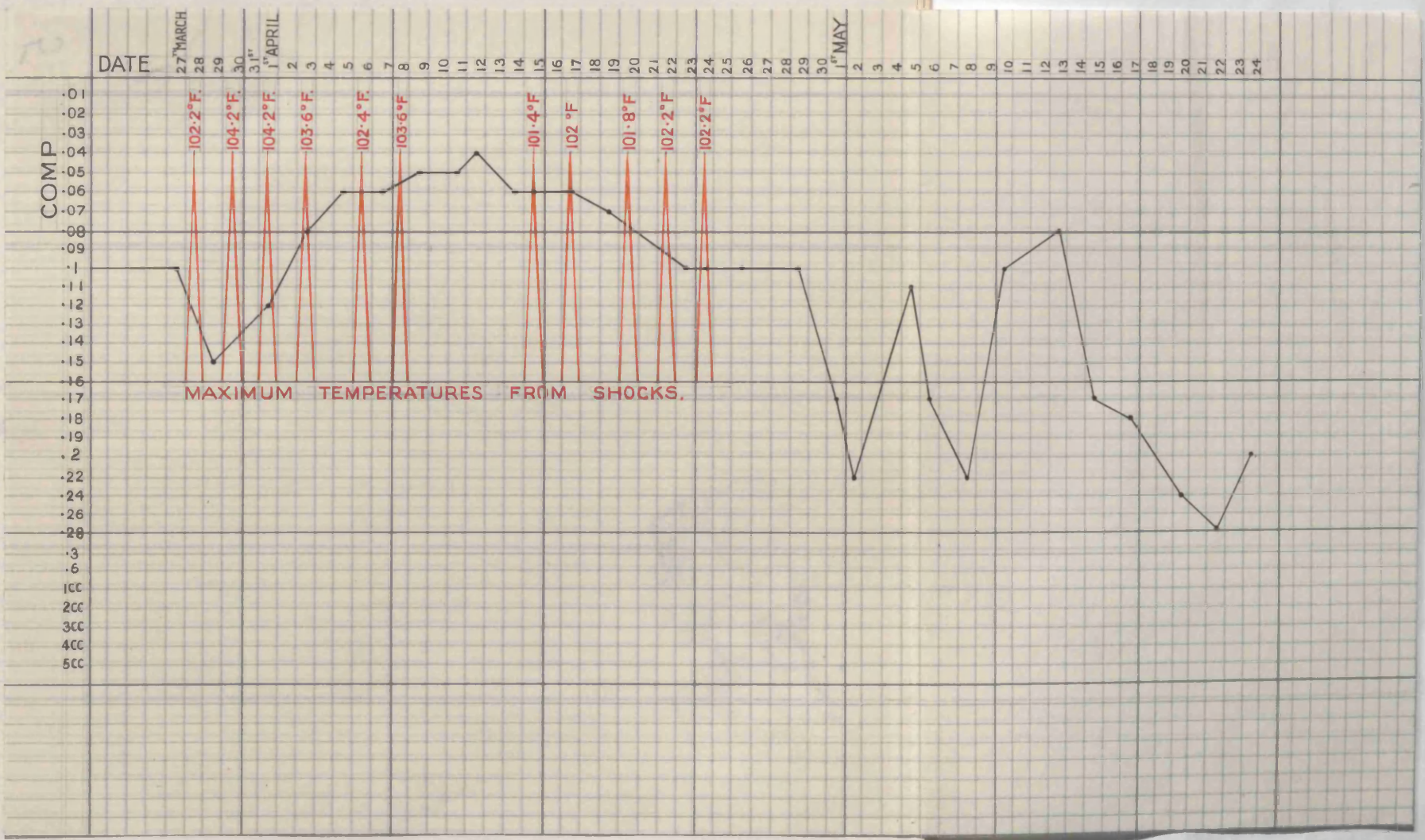


CHART SIX

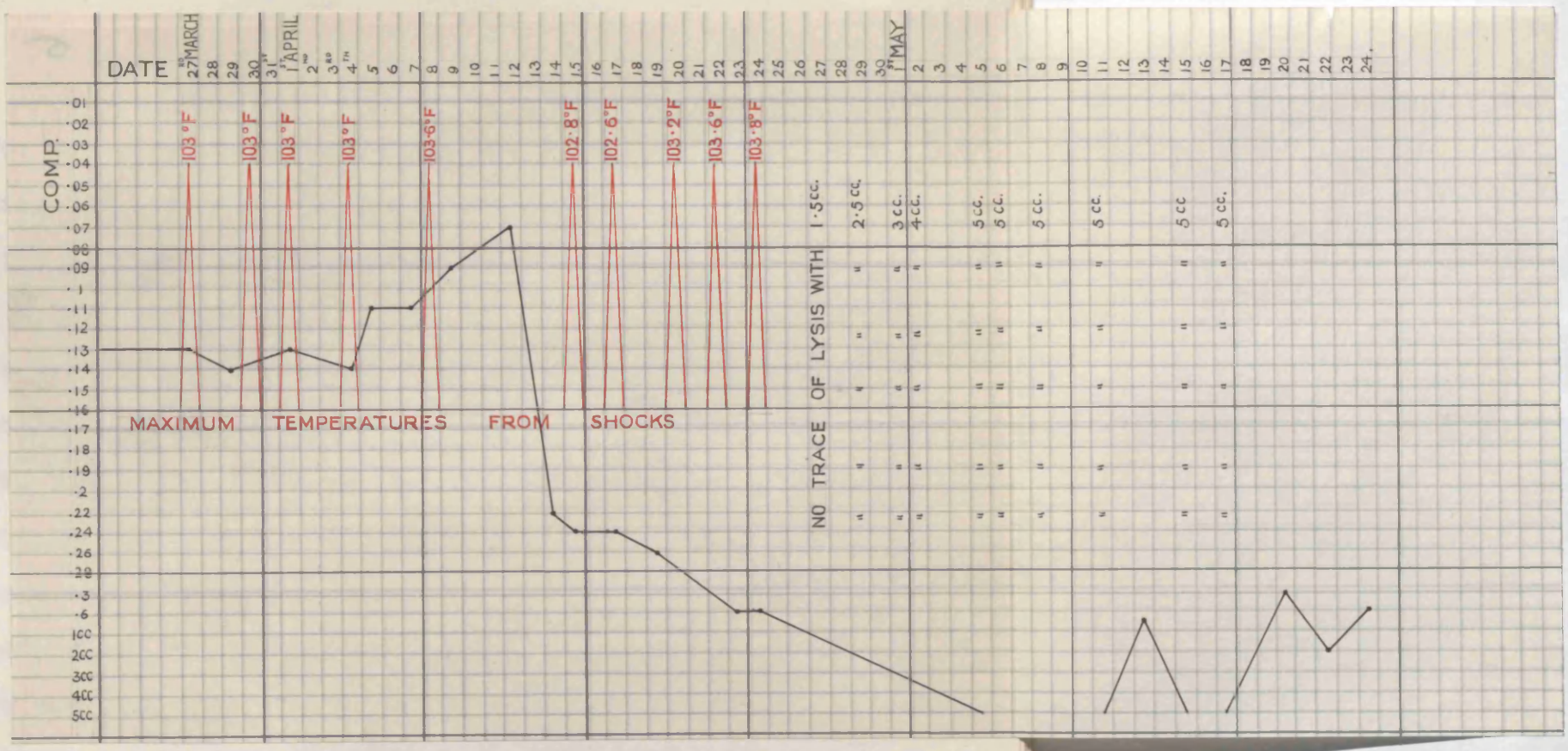
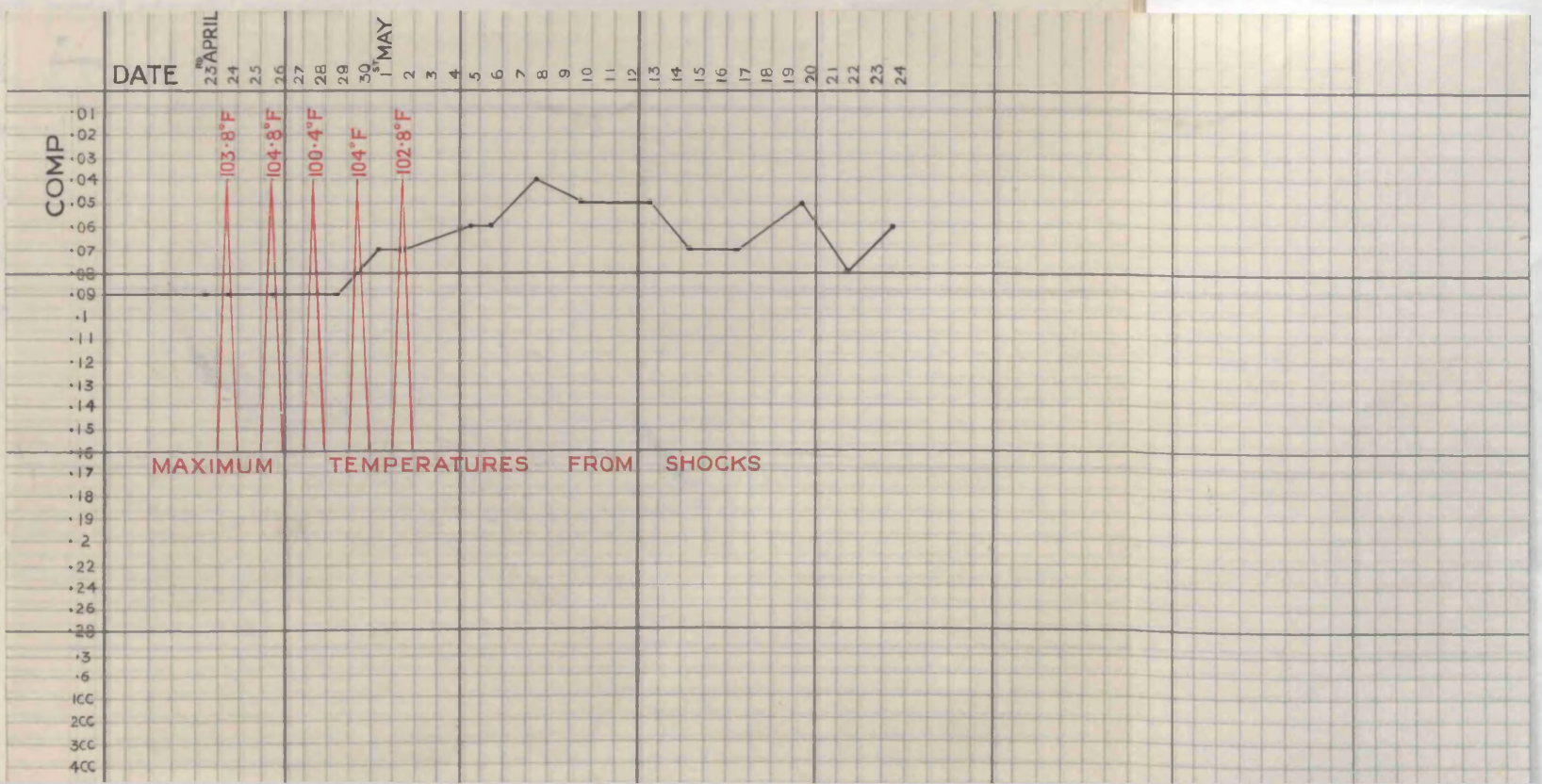


CHART SEVEN



For the complement estimation the haemolytic system was prepared according to Browning's method, and consisted of a 3% suspension of washed red blood corpuscles plus 5 M.H.D. of I.B.

It was allowed to stand for twenty minutes with occasional shaking before use.

The M.H.D. was taken as the smallest amount of complement which, at the end of one hour in a water bath at 37°C., produced just complete lysis of 1cc. of a suspension of sensitized red blood corpuscles.

To commence with, 20 tubes were put up containing increasing amounts of serum from 0.01 - 0.2cc., and 1cc., of sensitized corpuscles was added to each. A control with sensitized blood alone was used, and the results were read after one hour in a water bath at 37°C. Later in the tests a further number of tubes was found necessary to record changes accurately.

This technique was rigidly adhered to throughout the tests.

INTRODUCTION TO CASES. Although in the modern treatment of neurosyphilis it is customary to combine the non-specific with some form of specific therapy, in the following series of cases, arsenical and other spirochaetocidal preparations were deliberately withheld, in order that the results of treatment with T.A.B. vaccine alone, might be observed.

To produce the shock reaction, a stock antityphoid-paratyphoid vaccine (Burroughs Wellcome & Co.) containing 1250 million organisms in 1cc., was used, but at the end of a series of shocks, where a larger dosage was being employed, a more concentrated vaccine, containing 2500 million organisms in 1cc., was sometimes found to be more convenient.

The injection was made with a hypodermic needle and an all-glass syringe into a vein at the elbow, care being taken to ensure that the point of the needle was properly in the lumen of the vein. In most instances the same site was used throughout the series. No thrombosis or local manifestations of the injection were seen, and little difficulty was experienced in regard to inaccessible veins.

To elicit a temperature of 103° - 104° F. was the purpose in view, and the initial dose of vaccine given was 4m. - about 300 million. The dosage therafter was regulated and/

and increased according to each patient's individual requirements. Some cases quickly developed a tolerance for the vaccine and even with large and rapidly increasing doses did not react well. Usually however a progressive addition of 150 million per dose was found to be adequate. The general tendency in all patients was to respond less towards the end of the treatment

A course generally consisted of eight shocks which could be given as a daily series or on alternate days, but it was found best to give two or three shocks together with a few days interval between each group of injections. Smaller doses of vaccine were required and as the patient was permitted to have some solid food in the apyrexial periods, the loss of weight which occurred during treatment was lessened. A rigor, variable in duration and severity generally followed the injection of the vaccine in a-half to two hours. The temperature, rising during the rigor, climbed rapidly to attain its maximum about one hour later and was maintained at this level for 1 - 2 hours, thereafter falling gradually to reach normal about twelve hours after its onset. The pyrexia was easily controllable and could usually be reduced when necessary by tepid sponging. Sweating generally occurred when the temperature began to fall.

The/

The pulse was increased by 20 - 30 beats per minute, the increase coinciding with the rise of temperature. The rate of respiration was affected little.

During the treatment the patients were kept on a fluid diet. Herpes facialis was common, and albuminuria sometimes occurred, but this in all cases was only transitory and the urine became clear soon after the shocks had ceased.

The serological tests were carried out in the following manner.

The Wassermann reaction. As the end - reaction was done in each case, a constant quantity of complement was used and the patient's cerebrospinal fluid was varied to find the intensity of the reaction. In each tube, .5 cc antigen, with 4 M.H. doses of complement, were used with, .004, .006, .008, .01, .03 .05, .07, .09, .1, .2, .3, .4, .5, and .7cc of the patient's C.S.F.

After heating in the water-bath at 37°C. for an hour and a half, each tube received .5cc of the sensitised sheep red blood corpuscles, and was heated for another hour before the readings were taken.

Reagents were tested before use, and known positive and negative cerebrospinal fluids were used throughout the tests/

tests as controls.

In addition controls were used on antigen, corpuscles, corpuscles and complement, cerebrospinal fluid and haemolytic serum.

The antigen and haemolytic serum were supplied by Burroughs Wellcome and Co.

Colliodal Gold Test.

The reagents for this test were supplied by Merck of Germany.

All possible care was exercised in the preparation of the glass ware, which was treated with nitro-hydrochloric acid, and washed with tap water, distilled and triple distilled water before use.

The gold solution was prepared by the method advocated by Stitt (7th ed. p. 598).

By using a Jena flask in which good solutions had been made previously, no difficulty was experienced in preparing a clear red solution, free of any purplish tint.

The hydrogen-ion concentration was adjusted to pH6, and a standardised solution was obtained, which gave constant readings with negative and positive controls.

The cell counts were done in a Fuchs Rosenthal counting chamber.

CASE No. 1. A Male aged 34 years. Occupation - Tanner.

He was admitted to Gartloch on the 6th May 1929.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- The early history is unknown. He received anti-syphilitic treatment in the 51st General Hospital in France during the War. In February 1929 his behaviour became peculiar; he was grandoise in his manner, insisted that he was a rich man, swore frequently and, on several occasions, he attempted to strike his wife. This conduct continued for some weeks and culminated in his jumping from a one-storey window and spraining his ankle. There was a bad family history of tuberculosis, but no history of nervous or mental disease. The patient did not indulge in alcohol.

MENTAL CONDITION :- On admission he was noisy, restless, excited and was disorientated for time and place. He had delusions of grandeur, thought his income amounted to £1,080 per annum and talked of his motor car and other imaginary possessions. He was subject to violent outbursts of excitement, during which he was dangerous and difficult to control. He was argumentative, but his conversation was rambling and full of his delusions, and he was incapable of any sustained concentration. His mental condition showed no improvement from the time of admission, until the commencement of his treatment by Protein shock.

PHYSICAL CONDITION :- This deteriorated rapidly and before treatment, he was practically bed-ridden and could not walk without support. Nutrition was fairly good, but he had lost weight/

weight since admission. The heart and lungs were healthy and the urine contained no abnormal constituents.

The pupils were contracted, equal and regular. They reacted to accommodation but not to light.

Examination of the fundus revealed no abnormality.

The tendon jerks were exaggerated and sustained, more markedly so on the left side.

The superficial reflexes were brisk and swallowing was not impaired. The plantar reflex was extensor on both sides.

There was a well marked tremor of the tongue and speech was slurring and incoherent.

Rombergism was well marked and co-ordination of the arms was poor.

The gait was a combination of staggering and shuffling.

There was no apparent loss of muscular power and sensation appeared to be unaffected, but the patient's mental condition made a satisfactory examination in this respect impossible.

TREATMENT :- He received a series of eight shocks commencing on 18th June 1929. The final shock was given on 25th June 1929. The dosage of vaccine used increased from 300 - 2000 million. The highest temperatures reached in each shock were :- 102.4° 103.2°, 104.2°, 102.4°, 102.6°, 102.4°, 101.8°, 101.8° F.

COURSE.:- During the shocks he became more excited and noisy and his delusions, always very apparent, became more prominent and ludicrous. He was emotional and would burst into tears without apparent reason. He became unmanageable for female nurses and, after using violence towards one of them, he was/

was transferred to a ward under the care of male nurses.

One month after treatment, he was not so noisy and was rarely emotional, but his delusions were still well marked, although he did not express them so readily. He was more rational in his conversation and not so exalted. For the next two weeks improvement was rapid. He became disinclined to talk of his delusions, would preface his statement with a laugh, and seemed to have less confidence in himself.

Six weeks after treatment, he would not admit to any delusions. He was still exalted and easily upset, but his confusion had largely cleared and his memory was better.

Ten weeks after treatment, his delusions and exaltation had gone, his confusion had cleared completely, and he could converse rationally and appreciate a joke against himself. His memory was good and he could perform fairly intricate calculations correctly. This improvement in his mental condition was maintained until January 8th, 1930, when he was discharged to his home.

His physical condition had improved steadily; he began to put on weight soon after the shocks, during which time he had lost 4 lbs.

Two months after treatment, he showed less Rombergism, his gait was steadier and his speech was clearer. He was up all day.

Three months after treatment, he showed few signs of disease. He was an enthusiastic performer at the patients' weekly dances and employed his time helping in the ward.

Three and a half months after treatment, his physical condition/

condition was as follows :-

The heart and lungs were healthy and the urine contained no abnormal constituents.

The pupils were equal, regular in outline, and dilated, and reacted smartly to light and accommodation.

Examination of the fundus showed no abnormality.

The tendon reflexes showed no abnormality.

The plantar reflex was still extensor on both sides.

There was no tremor of the tongue and speech was clear and distinct.

Muscular co-ordination was good and there was no Rombergism.

The gait was smart and steady, although modified as the result of War wounds in both knees.

There was no disturbance of sensation.

His physical condition was maintained until his discharge on the 8th January.

He found employment and kept it for two months, but was re-admitted on the 12th March 1930, having relapsed suddenly a few days previously.

He was again delusional and this time most of his ideas had a sexual basis. He was noisy and boisterous, confused and extremely foolish. Memory and orientation were impaired; his physical health had not deteriorated to the same extent, but he had lost weight and his gait was unsteady. Rombergism was again present.

The pupils still reacted smartly to light and accommodation and the tendon jerks showed no abnormality, but there was a slight/

slight tremor of the tongue and speech was slurring.

He received a second series of shocks commencing on the 2nd April 1930, the final shock being given on the 10th April. He did not react well, although large doses of vaccine were used. (300 - 3000 Million).

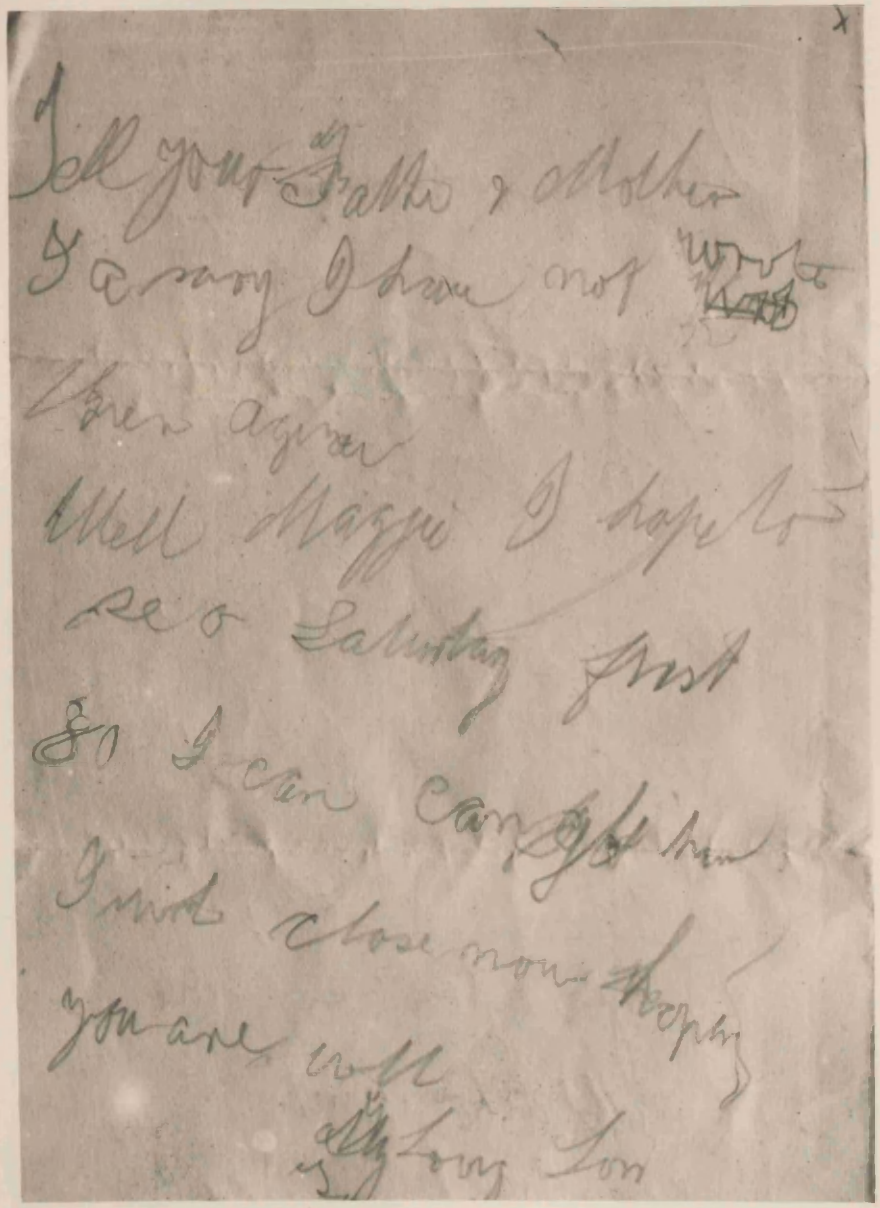
The highest temperatures recorded were :- 100.4°, 102.8°, 103°, 103°, 100.6°, 100.4°, 100°, 102.4°,F.

He lost 5 lbs. in weight during the treatment but recovered this within a week and gained steadily thereafter. At the end of May 1930, he was still foolish and confused, but was quieter and not so restless. He seldom required sedative. He had lost his sexual ideas entirely, and orientation and memory were better. His physical health had improved and he had gained 9 lbs. in weight since admission. His gait was steady, speech was much clearer and muscular co-ordination was good. He was capable of having a walk in the grounds every day.

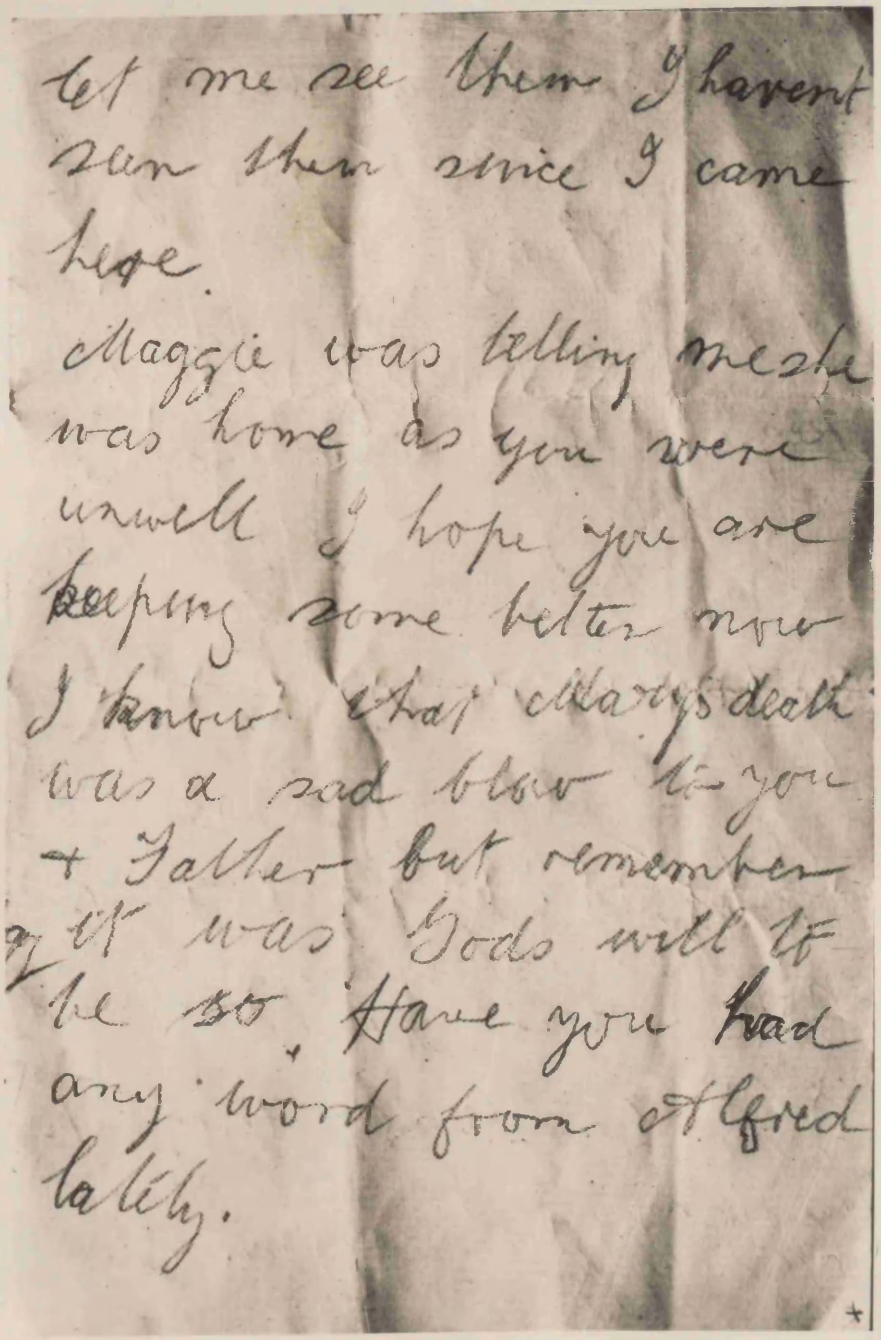
The serological reactions of the cerebro-spinal fluid were as follows :-

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count.
10/6/29.	+++++++++	55555555540	+	+	45.
10/9/29	+++++++++	55555555540	+	+	48.
29/5/30	++++++	55555554300	+	+	43.

A facsimile of the handwriting of Case No.1 before treatment. It shows the typical general paralytic caligraphy.



This shows the improvement in co-ordination which had occurred six weeks after the cessation of treatment.



let me see them I haven't seen them since I came here.
Maggie was telling me she was home as you were unwell I hope you are keeping some better now I know that Mary's death was a sad blow to you + Father but remember it was Gods will to be so. Have you had any word from Alfred lately.

This shows the improvement which was achieved four months after treatment.

2

do anything to make me ill again. I will write you sometimes and let you know how am keeping I will close now wishing you every success in your great calling

Yours Truly

CASE No. 2. A Male aged 48 years. Occupation - Engineer.

He was first admitted to Gartloch on the 21st July 1927, but was discharged "relieved by Minute of Council" on the 9th September 1927. He was readmitted on the 24th January 1929.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- The early history is unknown. He was a healthy man until April 1926 when he sustained a slight accident and was incapacitated for a few weeks. He lost his employment and was idle for nine months. When he did resume his occupation, it was found that he was unfit to carry out his duties efficiently. He made many mistakes and seemed to be incapable of performing any calculation correctly. His personality had changed and his behaviour led his employer to describe him as a "madman". His wife also noticed the change in him. His speech was thick and when he spoke his lips trembled. His conduct became more peculiar until he expressed delusions of grandeur, and, his physical condition having meantime deteriorated rapidly until he was quite unable to look after himself, he was admitted to Gartloch in July 1927. He was discharged after six weeks by Minute of Council, having gained slightly in health, but was readmitted on the 24th January 1929.

He has two children, both apparently healthy, and his wife has had no abortions.

MENTAL CONDITION :- On admission he was confused, simple and facile, and was quite unable to appreciate his condition. He was helpless and showed well marked physical signs of general/

general paralysis. He became progressively worse, more confused and restless, until he was demented and could not answer a simple question, or even understand what was said to him. His habits were faulty and he had to be fed. He was noisy at night and required a constant sedative.

PHYSICAL CONDITION :- This deteriorated rapidly after admission until, prior to his course of shocks, he was completely bedridden and helpless. The heart was greatly enlarged downwards and to the left, the left border being well outside the nipple line. There was a systolic-diastolic murmur in the aortic area and the mitral valve also showed signs of incompetence. The pulse was of the waterhammer variety, being full and bounding with a sharp rise and fall. There were signs present of an aortic aneurism and aneurisms of both brachial arteries were visible and palpable. The pulse in the neck could be seen clearly many feet away from the patient. The lungs were healthy and the urine contained no abnormal constituents.

CENTRAL NERVOUS SYSTEM :- The pupils were pin-point and did not react to light; they reacted sluggishly to accommodation. Examination of the fundus revealed no abnormality.

The tendon reflexes of the lower extremity were absent and those of the upper extremity gave a poor response.

The superficial reflexes were active and equal.

The plantar reflex was doubtful on the right and extensor on the left.

The tongue showed a marked tremor and there was a tremor of the/

the lips. Speech was slurring and incoherent.
Muscular co-ordination was poor and Rombergism was well marked.
There was little loss of muscular power.
The patient's mental condition precluded any examination of the sensory system.

TREATMENT :- He received a series of eight shocks commencing on the 18th July 1929. The final shock was administered on the 1st August 1929. The dosage of vaccine used increased gradually from 300 - 1250 million.

On several occasions after the pyrexia, the temperature dropped to subnormal with a pulse varying from 30 - 40 per minute, and he showed signs of collapse, but he was easily brought round with warmth and stimulation.

The highest temperatures recorded in each shock were as follows: 104.6°, 102.2°, 103°, 99°, 103°, 101.6°, 101.4°, 101°, F.

COURSE :- Immediately following treatment, he was quiet, but this, in a few days, was succeeded by a state in which he was restless, excited and noisy. For six weeks he settled slowly and by the middle of September, he was fairly quiet but still required a sedative at night. He was less confused and could answer a simple question correctly, and even frame a fairly long sentence himself. His physical health had improved and he was putting on weight. By the end of October (three months after treatment) he could voice a complaint when displeased and, although his speech was still very incoherent and articulation was defective, he showed more initiative in conversation. He could feed himself and his habits had improved until now he/

he was clean, provided that he was attended to regularly. He was quieter and about the middle of the next month, all sedative was withdrawn.

At the end of November, he was allowed up occasionally, but was unable to walk without support and assistance. He helped himself more and was an easier patient to nurse; he could see the point of a joke and even make one himself.

For the next six months, he maintained this improvement and some additional physical gain occurred.

At the end of May (10 months after treatment) he was quiet, still slightly confused, his memory was better and orientation had improved. He could let those in attendance know his requirements and could answer simple questions. His habits were clean and he fed himself. No sedative was required and he slept well at night.

The physical condition at the end of May 1920 was as follows :-

He spent most of his time in bed, but was fit to be up for part of the day.

His gait was steadier, but he still required assistance, although one person to guide him was now sufficient.

The Argyll-Robertson pupil persisted. Examination of the fundus showed no change.

The tendon and superficial reflexes were unchanged.

The tremor of the tongue was not so apparent and tremor of the lips was absent. The speech was clearer.

Muscular co-ordination was better and Rombergism not so marked.

He had put on weight.

The action of the heart was not so violent. The rythm was /

was regular and the pulse wave appeared to be more sustained. The brachial aneurisms were not apparent and the carotid pulse no longer could be seen.

The cerebro-spinal fluid showed the following changes:-

	Wassermann	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count
10/6/29	+++++++++	5555555540	+ +	+ +	53
13/3/30	+++++++	55555400000	+	+	53
29/5/30	+++++	55555543200	+	+	48

CASE No. 3. A Male aged 36 years. Occupation - Tinsmith.

He was admitted to Gartloch on the 22nd June 1927.

DIAGNOSIS :- Cerebro-spinal Syphilis.

HISTORY :- He had always been a quiet and reserved man and for five years before admission here, he had been unemployed. During that time he was restless and depressed, slept poorly and used to walk the streets constantly. In 1926 he was a patient in Stobhill Hospital suffering from pneumonia. While there he was transferred to the mental wards and later was admitted here. He did not indulge in alcohol and had no family history of mental disease.

MENTAL CONDITION:- On admission, he was depressed and apathetic, but occasionally resistive and outrageous. He usually lay with his head under the bed clothes, taking no interest in his surroundings. His condition did not improve at all and he at times exhibited suicidal tendencies and required constant observation. About one year after admission, he became delusional and stated that he was responsible for the condition of the other patients. He also manifested hallucinations of hearing. He tended to deteriorate mentally, but his bodily health was fairly well maintained. He was given a course of Kharsulphan with no improvement.

Immediately prior to his course of Protein shock, he was depressed and very delusional. He was apathetic and lay listlessly in bed all day, and would not even recognise his visitors/

visitors when they came to see him. On occasions he refused all food for days and he had rare outbursts, when he was noisy, obstreperous and difficult to control.

PHYSICAL CONDITION :- He was thin and poorly nourished; the heart and lungs were healthy and the urine showed no abnormal constituents. The pupils were contracted, equal and regular. They reacted to light and accommodation sluggishly.

Examination of the fundus showed a commencing optic atrophy.

The tendon reflexes were present, but gave poor responses.

The superficial reflexes were sluggish.

The plantar reflex was flexor on both sides, but difficult to elicit.

There was no tremor of the tongue or lips, but speech was slow and heavy.

Rombergism was present and this showed in his gait, which was otherwise unaffected.

Co-ordination of the arms was fairly good.

There was no apparent loss of muscular power and no disturbance of sensation.

TREATMENT:- He received a series of eight shocks commencing on October 22nd, 1929 and a second course of eleven shocks commencing of 27th January 1930. Reactions were on the whole poor and he was sick frequently during the rigors. The dosage of vaccine used during the first course increased from 300 - 2500 million and during the second course from 600 - 3600 million.

The highest temperatures recorded were :- 103.4°, 102°, 101°, 101.6°, 101.6°, 102.4°, 99.4°, 99.6°, F. and 102.6°, 101.6°, /

101.6°, 100°, 100.6°, 100°, 101.6°, 101.2°, 101.4°, 100.8°, 101.2°, 102.2°, F.

COURSE. :- For about a month after the first series of shocks there was little change in his condition. He regained some of the weight he had lost during the treatment, but he was still miserable, apathetic and delusional. He then began to take more interest in his surroundings and was less unwilling to converse. Six weeks after the last shock, when questioned on his delusions, he was not so sure of them and stated that he "thought so" where before he had been positive. He continued to improve slowly and for a few days denied his delusions, but they returned.

Two months after treatment, he was still dull and listless and lay in bed most of the day. He was induced to rise occasionally, but as this seemed to make him more miserable, he was ultimately allowed to please himself.

On January 27th 1930 the second series of shocks were begun. Thereafter improvement was more rapid and by the end of February he had brightened considerably. He was allowed up at his own request and did not again show any desire to return to his bed during the day. He did not express his delusions and, although still dull, he was not so foolish. He took his food well and occasionally assisted in the work of the ward. He was more militant than before and frequently asked when he was likely to be discharged. His gait was now steady and speech was clearer. He continued to improve slowly and by the end of May 1930 he took a fair amount of interest in the life of the ward and,

and, although reserved and inclined to avoid attention being drawn to himself, he could answer questions well if challenged. He was no longer subject to outbursts and did not, on any occasion, refuse his food. He was more sociable, made friends with other patients and asked permission to attend the amusements, which he seemed to appreciate. He did not express any delusions and other interests seemed to have usurped the place they had previously held in his thoughts.

His physical condition had also improved. The pupils and fundus were unchanged and the tendon and superficial reflexes had not altered. Speech was clearer, his gait was smarter and Rombergism was not present. His general nutrition had improved and he had put on weight (14 lbs.).

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count.
10/9/29	+ +	$\frac{4}{5}\frac{4}{5}$ 330000000	+	weak +	30
29/5/30	+	4 4332000000	weak +	+ —	2.

CASE No. 4. A Male aged 33 years. Occupation - Motor-driver.

He was admitted to Gartloch on the 13th February 1929.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- A few months before his admission to Stobhill Hospital, be became bad-tempered, impulsive and was often violent, and, on account of this, and several errors of judgment, he lost his employment. He was very depressed and began to take mild seizures and then started to carry lighted papers about the house and to brandish razors. He was admitted to Stobhill Hospital on the 21st May 1928 where he was inoculated with benign tertiary malaria, but failed to develope any temperature.

He was admitted to Gartloch from Stobhill Hospital as an impulsive and homocidal patient.

He is one of a family of 19, of whom 14 died in infancy and 2 were still born.

He had been married for eleven years and has had three children; one child died in infancy, one is very deaf and the other child is apparently healthy.

There is no family history of insanity and he did not indulge in alcohol.

MENTAL CONDITION :- Facile, but able to give a good account of himself; he was not delusional and his memory was fairly good. He was quarrelsome and easily irritated, and was stubborn, unreasonable and aggressive if not allowed his own way. He was subject to impulses, when he would make unprovoked assaults on other patients and was untrustworthy, untruthful and stole from those/

those associating with him.

PHYSICAL CONDITION :- He was active and well-nourished. The heart and lungs were healthy and the urine showed no abnormal constituents.

The pupils were contracted and irregular in outline; they did not react to light and the response to accommodation was sluggish.

Examination of the fundus showed no abnormality.

The tendon reflexes were difficult to elicit and gave poor responses.

The superficial reflexes were active.

The response to the plantar reflex was a doubtful extensor.

There was a fine tremor of the tongue; speech was comparatively unaffected, but when asked to repeat an easy test sentence once or twice, the attempts became progressively poorer; syllables were missed out at first and latterly the sentence became a mere jumble of sounds.

Muscular co-ordination was good and there was no Rombergism.

There was noloss of muscular power and no disturbance of sensation.

TREATMENT :- He received a series of eight shocks commencing on the 18th June 1929. The final shock was administered on July 6th, 1929. The dosage of vaccine used increased from 300 - 900 million.

The highest temperatures recorded in each shock were as follows: 102.8°, 102.6°, 103.2°, 102.4°, 100.6°, 102.2°, 102.6°, 102°. F.

COURSE :- During the first month after treatment, there was little change in his condition. He was still quarrelsome and/

and frequently made unprovoked attacks on other patients. He regained some of the weight he had lost during the shocks.

At the end of August he had improved slightly; he was not so quarrelsome, nor so easily irritated and was more reasonable to deal with. He had gained 5 lbs. in weight and was better physically. His seizures - epileptiform in character -which had become more frequent about the beginning of the month were now occurring at longer intervals.

His mental condition showed no further improvement during the next nine months and at the end of May 1930, there was little, if any, gain to record. He was still quarrelsome and impulsive, at times unreasonable and at all times untrustworthy. His thieving tendencies were apparent whenever an opportunity to exercise them presented itself and, if taxed with the theft, he was plausible but untruthful in his explanation.

The seizures were occurring at longer intervals, but were still more frequent than before he received the course of shocks.

His physical condition showed little change.

The Argyll-Robertson pupil still persisted.

The fundus was unchanged.

Speech was clearer and his weight had increased slightly.

The tendon and superficial reflexes were unaltered.

The cerebro-spinal fluid showed the following changes :-

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell. Count
10/6/29	+ + + +	55555554330	+	+	56
13/3/30	+ +	55440000000	very weak +	very weak +	75.
6/6/30	Negative	55555543300	+	+	60

CASE No. 5. A Female aged 20 years. Unmarried. Occupation - None.

She was admitted to Gartloch on the 16th July 1929.

DIAGNOSIS :- General Paralysis of the Insane. (Juvenile ?.)

HISTORY :- When at school, the patient was the most intelligent member of the family and, on account of her mental abilities, was the only one who could be trusted to "go a message and bring back the correct change". Three weeks before admission, it was noticed that she was making mistakes and then she became nervous and excited, and believed that she was married and pregnant. There is no history of her having had fits. She is one of a family of nine, of whom four died in infancy. Her mother became very apathetic and sleepy before she died. Her father is an alcoholic and has had a "nervous breakdown"; her sister is very nervous and excitable and she has a cousin, who is an imbecile.

MENTAL CONDITION :- On admission, she was restless, excited and noisy, very confused and resistive, and at times impulsive. She was dirty in her habits and had to be fed. She used obscene and abusive language towards the staff, and spat and threw her food at them.

Prior to her treatment, she was in a confused and stuporose condition, which alternated with short periods when she was noisy, obscene and impulsive. She had no control of her bladder and bowels and had to be fed.

PHYSICAL CONDITION :- She was completely bed-ridden.

The heart and lungs were healthy and the urine contained no/

no abnormal constituents.

The pupils were unequal in size and did not react to light.

There was nothing abnormal in the fundus.

The reflexes of the upper extremity were exaggerated and sudden.

Those of the lower extremity were not elicited.

The superficial reflexes were present and were more brisk on the left side. The plantar reflex was flexor.

The tongue was tremulous and speech was slurring and indistinct.

Rombergism was extreme and the patient was unable to stand without support.

The gait was ataxic and very unsteady.

No examination of the sensory system was possible on account of the mental condition.

TREATMENT :- She received a series of eight shocks commencing on November 6th, 1929.

The dosage of vaccine used increased from 300 - 1500 million.

The highest temperatures recorded were :-

103.6°, 102.4°, 102°, 102.4°, 100.4°, 100.6°, 102.2°, 100°, 102°F.

COURSE :- After the first few shocks she became more observant and was obviously watching what was going on around her, but she did not attempt to speak and was quite unresponsive if addressed. Her habits had improved but were still faulty.

Two days after the last shock, however, she became noisy, excited and confused and this state continued for about a week, after which she was quieter. She uttered some obscenity occasionally, but still made no effort to answer any question or greeting. A severe acne on her face was exacerbated and became/

became pustular. One month after treatment, she was less confused and more in touch with her surroundings. She spoke occasionally and seemed to understand what was said to her, but a giggle was her usual response to a question. She was not noisy and she slept well at night. Her habits had improved and she made some attempt to attend to herself. She was capable of getting out of bed occasionally and no longer required to be fed.

Two months after treatment, she was more alert and answered questions willingly. She was quite loquacious at times, but her conversation was foolish and she adopted an infantile style of speech. Her periodic outbursts had ceased and she was no longer impulsive. Her habits were clean, except for occasional lapses, and she was up all day and could walk without support, although her gait was still unsteady.

About the middle of the next month, she had a slight attack of catarrhal jaundice; this was transient however and cleared in about a week.

For the next four months, improvement continued and at the end of May 1930, she was well-behaved and agreeable, but childish and foolish in her outlook. She was cheerful and easily pleased and could answer simple questions correctly, although she was still mildly confused. Her habits were clean, she fed herself and could attend to most of her personal requirements. She helped occasionally with the ward work, wielding a duster with more enthusiasm than actual skill. She was not impulsive and required no sedative.

Her/

Her physical condition had also improved. She was up all day and usually had a walk in the grounds each afternoon. Rombergism was very slight, her gait was fairly steady and she did not require assistance in walking.

The tremor of the tongue was not so marked and her speech was clearer.

The superficial and deep reflexes had not changed, there was no alteration in the fundus and the Argyll-Robertson pupil persisted.

Her weight had increased.

The cerebro-spinal fluid showed the following changes :-

	Wassermann.	Colloidal Gold.	Pandy,	Ross Jones,	Cell Count.
30/10/29	+++++++	55555544000	+	+	61
6/6/30	++++++	55555543000	+	+	120.

CASE No. 6. A Female aged 22 years. Single. Occupation - Confectionery worker.

She was admitted to Gartloch on the 14th June 1927.

DIAGNOSIS :- Juvenile General Paralysis of the Insane.

HISTORY. :- She was apparently normal as a child and was quite an average pupil while at school. She became dull and depressed when she was 16 years of age and was "nervous" and easily upset. She continued in her employment for two years and then began to have attacks of "shaking and trembling". She was confused, childish and incoherent in her speech and, her condition becoming worse, she was admitted to Gartloch about one year later.

She is one of a family of 12 of whom 5 are dead. Her mother has had 6 miscarriages and one premature birth.

The other members of the family are reported to be'normal'.

MENTAL CONDITION :- When admitted to Gartloch, she was demented, helpless, dirty in her habits and had to be forcibly fed. Her speech was quite unintelligible and when spoken to, the only response she seemed capable of giving was a grin or a grimace and even such recognition was not certain. Her condition did not improve and before treatment, she was very noisy, completely out of touch with her surroundings and showed no signs of intelligence

PHYSICAL CONDITION:- She was completely bed-ridden.

The heart and lungs were healthy and the urine contained no abnormal constituents.

The pupils were dilated and equal and did not react to light.

Reaction to accommodation was uncertain.

Examination of the fundus showed no abnormality.
The tendon reflexes were exaggerated, more so on the left side.
The ankle jerks were not elicited.
The superficial reflexes were sluggish; swallowing was not impaired; the plantar reflex was extensor on the left and uncertain on the right.
The tongue could not be examined. Speech was unintelligible, being a mere incoherent chatter.
Muscular co-ordination was poor and Rombergism was very marked.
The gait was unsteady and shuffling in character. She was unable to stand without support and she walked with the knees bent and the shoulders drawn up.
Her mental state made an examination of the sensory system impossible.
TREATMENT :- She received a series of nine shocks commencing on November 6th, 1929. The final shock was administered on the 28th November.
The highest temperatures obtained were :-
104.8°, 105.2°, 104°, 103°, 103°, 103.4°, 102°, 103.4°, 103°.F.
The dosage of vaccine used increased from 300 - 1250 million.
COURSE :- At first she paid no attention when the injection was being made and even the pain of the needle did not seem to disturb her. But, after the third shock, she became very noisy and restless and this state increased with each subsequent shock. At the same time, she became more observant and latterly whimpered and struggled feebly as soon as she saw the needle. During the course of treatment her habits improved until they/

they were clean, but they became dirty again a few days after the last shock.

One month after treatment, she was much quieter and was taking some notice of what was going on in the ward. She made no attempt to speak and lay all day mumbling quietly to herself.

At the end of the next month, she was brighter, attempted to whistle at times and showed some rudiments of intelligence, as she now evidently associated certain persons with her bodily needs. Her habits had not improved, but she was quiet and was capable of getting out of bed occasionally.

For the next four months progress was slow and at the end of May, there was a slight improvement in her mental condition. She was quiet and had none of the noisy outbursts which had been frequent before treatment. Although she gave some response when called, she was hardly in touch with her surroundings, for she spoke very little and could not be made to answer any question however simple. Her habits were still faulty and she could not feed herself, but she did not refuse the food and on the whole was an easier case to nurse.

Physical improvement was more marked. She was up all day and her gait had improved until she could walk without assistance. Rombergism was only slight and muscular co-ordination was better. Her weight had increased.

The tendon and superficial reflexes and the pupil reactions were unchanged.

The cerebro-spinal fluid showed the following changes:-

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count.
10/6/29	+ + + + +	55555544330	+	+	63
6/6/30	+ + +	$\frac{55555}{44444}$322000	+	—	60

CASE No. 7. A Female aged 54 years. Married. Occupation - Housewife.

She was admitted to Gartloch on the 17th December 1928.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- One of a family of eight, of whom only three survive; she was married shortly after the War. Just before the onset of her illness, her husband and her brother died suddenly and these losses were supposed to have contributed to her mental breakdown. She became irritable and depressed and about a month later was admitted here. There was no history of insanity in the family, but she had been a "rolling stone" and was much addicted to alcohol. So far as was known, she had never been pregnant.

MENTAL CONDITION :- On admission she was dull and depressed and took little interest in her surroundings; excited and noisy at times, she was irritable and suspicious in regard to other patients. She was morbidly emotional and was a danger both to herself and to others, and was unable to answer even a simple question correctly.

Her mental condition slowly deteriorated and before the course of her treatment, she was wet and dirty in her habits and unable to feed herself. She was apathetic, showed no initiative and was emotional, noisy and violent at times. She was easily irritated, very confused and was delusional, but her ideas were not fixed and she seldom retained one for any length of time.

PHYSICAL CONDITION :- This had become poorer and she had lost/

lost weight steadily. Before treatment, she was bedridden and required constant attention.

Her heart was enlarged downwards to the left and the apex was outside the nipple line. The sounds were pure, but the second sound was accentuated in the aortic area; the transverse mediastinal dullness was increased.

The lungs were healthy and the urine contained no abnormal constituents.

The pupils were contracted and unequal in size; the right pupil was not circular and both were irregular in outline.

Reaction to light was sluggish and the excursion was poor.

The fundus showed no abnormality.

There was some tremor of the tongue and speech was slurring; syllables from words were omitted.

The tendon reflexes were exaggerated especially on the right side and the superficial reflexes were brisk.

The plantar reflexes were flexor.

There was no clonus.

Muscular co-ordination was poor and Rombergism was extreme. The gait was unsteady and shuffling in character.

Her mental condition precluded any examination of the sensory system.

TREATMENT:- She received a series of eight shocks commencing on 8th July 1929 and a second series of Eight shocks commencing on November 7th, 1929.

The dosage of vaccine used increased from 300 - 450 million in the first and from 300 - 1250 million in the second series. /

During the first course, she reacted to the injections severely but the responses in the second course were milder.

The highest temperatures obtained were :-

1st.Series:-104°,103.8°,105.2°,104°,104°,104°,103.8°,103.6°.F..

2nd.Series:-103.6°,104°,101.8°,103°,101°,102°,102.4°,102.8°,F.

COURSE :- During the shocks she became very excited, noisy and was resistive to all that was done for her. Her confusion became more profound and she was completely out of touch with her surroundings.

During the first month, she settled gradually, emerging from her confusion to some extent, but becoming much more emotional. She was quieter and her delusions now became more definite than they had ever previously been.

For the next month, progress was slow but steady. She ceased to express her delusions spontaneously, but if questioned, she would sometimes deny them and laugh at the suggestion and, at other times, agree although dubiously to what previously had been her sole and persistent topic of conversation. She had more control of her emotions and was more amiable and less easily irritated; she took more interest in her surroundings and showed some initiative.

No further improvement occurred during the next month and on the 7th November the second series of shocks was begun. During the treatment her confusion returned; she was violent and struggled fiercely against the ministrations of the nurses, spat at them and used abusive and obscene language towards them. She lost weight rapidly. She settled quickly after the final shock/

shock and soon became quieter and less confused. Her delusions were more prominent, but only for a few days before returning to the state previous to the second series of shocks. She continued to be emotional for a few weeks, but by the beginning of January 1930 she had become more stable and was well behaved. She did not express any delusions and was evasive if questioned; she was still foolish in her conversation, but she was very friendly and more reasonable to deal with.

For the next five months, progress was slower but steady and at the end of May 1930, her depression and apathy had given place to a cheerful and contented frame of mind and she showed more initiative, taking an active part in the life of the ward and attending the entertainments regularly. She was very observant and petty annoyances did not upset her to the same extent. She was more rational and easier to deal with and the complacancy, which had characterised her demeanour after the first course of shocks, was now less in evidence. She was not delusional, although her childish claims to affluence might have led one to believe she was; but, if questioned closely it could be seen that she herself knew her statements to have no foundation of fact and she could be made to admit that this was so.

Her physical condition had improved, slowly at first and then more rapidly after the second series of shocks.

At the end of December, five months after the first course of treatment, she was up all day, her gait was steadier and she was moving actively about the ward. Her habits were clean and she fed and attended to herself. At the end of May 1930, she was/

was heavier in weight and was up all day and out in the grounds with the walking parties. The pupils and fundus were unchanged but speech was clearer. The tendon reflexes were not so. exaggerated; Rombergism was only slight and the gait was smart and steady.

The cerebro-spinal fluid showed the following changes :-

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count.
10/6/29	++++++++++	55555555430	+	+	110
30/10/29	+ + + + +	55555543000	+	+	128
6/6/30	+ + + +	55555543300	+	+	57

CASE No. 8. A Male aged 17 years. Occupation - None.

He was admitted to Gartloch on the 18th February 1929.

DIAGNOSIS :- Cerebro-spinal Syphilis.

HISTORY :- The second child of a family of six, his was a natural and easy delivery; he was a healthy baby and had no illnesses of any moment during infancy. He began to walk about fourteen months and he talked soon afterwards. He commenced his schooling when five years old and seemed quite a normal child at that time. He attended the day school for three years, but was then sent to a school for defective children where he was a pupil for a further three years. He made no progress with his education and when he left school at twelve years of age, he could neither read nor write. His behaviour was bad and he was constantly in trouble. He frequented the streets, was wild, broke windows and his conduct became steadily worse until his parents had no control over him and he was admitted to Gartloch. He had no occupation as he was unemployable.

FAMILY HISTORY :- The eldest of the family is a girl aged 20 years, who is apparently normal.

The patient is the second child.

The next two, brothers, are at present in a school for defective children.

The two remaining children are dead, one dying at fourteen months of pneumonia and the last at two weeks of "wasting".

Both parents are alive and healthy; the mother gives no history/

history of abortion and all her children were full time.
History of previous mental disease in the family is denied.
MENTAL CONDITION :- On admission he was noisy and destructive, resistive to all treatment and had bad asocial and antisocial habits. Usually he could be found sitting on a chair, dull and apathetic and making no effort to employ his time. He took no interest in his surroundings and showed a total lack of initiative. He could not be induced to do any work and seldom could understand what was required of him; he made no attempt to answer questions put to him and was unable to perform even the simplest of calculations. In his infrequent outbursts of excitement, he was resistive, unruly and impulsive, and his language was abusive and obscene. These phases were usually of short duration and when he recovered he reverted into his usual state of apathy.
His mental condition showed little variation from the time of admission until the commencement of his treatment by Protein shock.
PHYSICAL CONDITION :- This was fairly good; he was well nourished the heart and lungs were healthy and the urine showed no abnormal constituents.
The pupils were widely dilated, but reacted to light and accommodation, although sluggishly and with poor excursion.
The left pupil was eccentric and the right was not circular.
The fundus showed no abnormality.
The tendon reflexes were present and more brisk on the right side than on the left.
The superficial reflexes were equal and active.

The plantar reflex was definitely flexor on the left side, but doubtful on the right.

Muscular co-ordination was good; there was no Rombergism and the gait was unaffected.

There was no tremor of the tongue, but he had a bad stutter.

There was no alteration of sensation.

TREATMENT :- He received a series of eight shocks commencing on the 18th July 1929. The final shock was given on the 2nd August 1929. He stood the shocks well, but with the first few injections, he had nausea and sickness after the rigor.

The highest temperatures recorded were :-

105^{0}, 105^{0}, 103^{0}, 104.6^{0}, 103.4^{0}, 103.6^{0}, 103.6^{0}, 103.6^{0}. F.

The dosage of vaccine used increased from 300 - 750 million.

COURSE :- There was no period of excitement in this case and improvement commenced very soon. A few days after the last shock, he began to take some interest in his surroundings, was more obedient and seemed to be coming out of his apathy. He improved steadily and began to show some initiative.

One month after treatment, he was brighter in every way. He had lost the vacant look, which previously had been his habitual expression and was less apathetic. He was more active and helped with the ward work of his own accord, although his sphere of utility was limited. He was less truculent and less quarrelsome.

Two months after treatment, he was showing some curiosity and began to ask questions, e.g., the difference between a mental hospital and an asylum. He was still destructive and, if displeased, would tear his clothes. He was now deemed capable/

capable of education and another patient, who had had some experience of teaching, was co-opted as his tutor.

Three months after treatment, his behaviour was better. He did not swear so often, seldom quarrelled and was amenable to discipline. He was useful in the ward and could be put to some simple task and trusted to carry it out correctly. His curiosity had become more active and it sometimes brought him into conflict with other patients. He showed more intelligence and the questions he asked portrayed the instinctive curiosity of a child, which, in his case, apparently was only now making itself manifest. He had made some slight progress with his education and was showing aptitude for the work.

Four months after treatment, he was alert and obedient, worked willingly about the ward and could be trusted to perform small tasks, now without supervision. He was not quarrelsome, but was rather mischievous, and this tendency towards practical joking sometimes brought him trouble. As he was no longer destructive, he was given a new suit; he appreciated this and took pride in keeping it neat and clean.

Six months after treatment, the improvement in his mental condition had been maintained. He showed the healthy boy's distaste for sedentary work, but had nevertheless advanced in his lessons. He could count up to 50 and had grasped the principles of division and subtraction, was acquainted with the letters of the alphabet and had made some progress with handwriting.

At the end of May, ten months after treatment, he was quiet, well-behaved and obedient. He had ceased to be destructive and was a/

a reliable and willing helper in the ward. He showed much interest in his surroundings and had made many friends among the patients. His curiosity was insatiable and the questions he asked sometimes showed a very fair degree of intelligence. He was neat, clean and tidy in his person and, unless employed, evidently found time hang heavily on his hands. He had made good progress with his education and, although slow to learn, had retained what he had once assimilated.

His bodily health had improved also; he had gained 9 lbs. in weight and his activity was such that he required some outlet for his energy.

The tendon and superficial reflexes showed no abnormality.

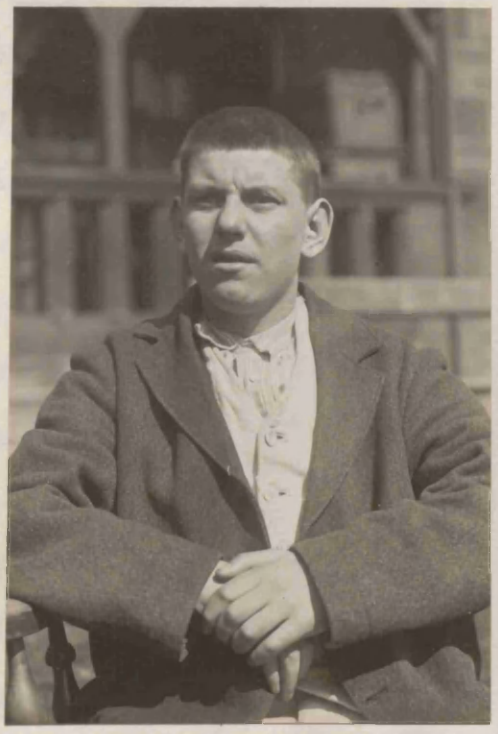
The pupils were still sluggish in reacting to light and accommodation, but were smarter than they had been before treatment.

The fundus was unchanged.

The cerebro-spinal fluid showed the following changes :-

	Wassermann.	Colloidal Gold.	Pandy.	Ross Jones.	Cell Count.
10/6/29	+ +	11122221110	+	+	180
13/3/30	negative	00000000000	—	—	184
29/5/30	negative	00000000000	—	—	5

These photographs indicate the improvement which took place in the appearance of case No.8 after treatment.
The first photograph was taken shortly after his admission to Gartloch, and the second about ten months after treatment by protein shock.



CASE No. 9. A Male aged 60 years. Occupation - Plate Marker.

He was admitted to Gartloch on the 28th March 1927.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- The early history is unknown. About seven months before his admission here his fellow workers noticed that his manner had changed. He walked about talking to himself and his actions were at times foolish. His condition got worse and he became excitable and emotional, and did not sleep well. He was subject to impulses and, on one occasion, he struck at his son with a knife. He had been in the habit of taking alcohol to excess. He was married and had had ten of a family; of these six members were alive and healthy. Of the four who were dead, one died seven days after birth, another four days after birth, and one was still born. His wife gave no history of abortion. There was no history of previous mental or nervous disease in the family.

MENTAL CONDITION :- On admission he was restless, excited and talkative, and was exalted and delusional in his ideas. He was emotional and quarrelsome and became violent and resistive at times, when he was difficult to control. His judgment was defective and he did not appreciate his position. This condition did not vary much until about a year after admission, when his sense of well-being gave place to a more depressed outlook. His health deteriorated from then, slowly at first and then more rapidly until ultimately, he was entirely confined to bed on account of both physical and mental conditions. Immediately/

Immediately prior to his course of injections, he was confused, emotional and delusional. He was destructive at times and was subject to frequent outbursts of excitement and required a constant sedative. He was completely disorientated and had no appreciation of his condition.

PHYSICAL CONDITION:- He was completely bedridden.

The heart and lungs were healthy and the urine showed no abnormal constituents.

The pupils were contracted and the right pupil was eccentric and irregular in outline. They did not react to light and reaction to accommodation was sluggish.

The fundus showed no abnormality.

There was a well marked tremor of the tongue and speech was slurring; syllables were omitted.

The ankle jerks were not elicited. The remaining tendon reflexes were present and more active on the left side than on the right, but all gave poor responses.

The superficial reflexes were active and there was no impairment of swallowing. The plantar reflex gave an extensor response on both sides.

There was no clonus.

Rombergism was well marked and muscular co-ordination was poor.

The gait was a combination of ataxia and shuffling; he was unable to walk without support.

There was no apparent loss of muscular power but nutrition had deteriorated since admission.

Attempted examination of the sensory system was found to be futile.

TREATMENT:- He received a series of eight shocks commencing/

commencing on the 18th July 1929. He reacted excessively to the first injection, but subsequent shocks were less severe. He received the final shock on 2nd August 1929. The dosage of vaccine used increased from 300 - 1250 million.

The highest temperatures recorded for each shock were as follows:- 106.2°, 104.2°, 101°, 101.2°, 103°, 101.6°, 99.2°, 100.2°. F.

COURSE:- During the shocks and for some days after them, his mental symptoms were exacerbated. He was more noisy, emotional and restless, threw his pillows about and was extremely resistive. He was destructive and more impulsive than before and was completely disorientated. He required large doses of sedative each night.

One month after treatment, he had settled to some extent, becoming less noisy during the day and later less confused. He was not so restless, but still required a sedative, without which he slept poorly and shouted and sang for most of the night.

Two months after treatment, he had improved both mentally and physically. He was quiet, well-behaved and obedient and now required no sedative whatever. His confusion had largely cleared and he spent most of his time reading and helping occasionally with the ward work. He was facile and his exalted manner remained but he had a better grip on himself and on his emotions. He had put on weight and was steadier on his feet, and was up for the larger part of the day.

For the next four months he continued to improve and gradually lost his confusion. His simple and exalted manner remained, but his conversation became more rational and his behaviour continued/

continued good. He was allowed to attend the patients' dances, where he performed well.

Six months after treatment, he was quiet and his conduct was irreproachable. He was not impulsive nor destructive and he was a very useful helper in the ward. No trace of confusion remained and he could do simple calculations correctly. Orientation was good and his memory was fairly clear. He had retained his sense of well-being and was simple and rather facile, but he expressed no delusions. He slept well at night. His physical condition had kept pace with his mental improvement and the following is a summary of his bodily health six months after treatment.

He was up all day moving actively about the ward and he accompanied the nurses on messages throughout the institution.

The pupils had not changed and still showed the Argyll-Robertson phenomenon.

The fundus showed no change.

The tendon jerks and superficial reflexes were unchanged.

The tremor of the tongue was not so marked and speech was much clearer.

The gait was smarter, but still showed slight ataxia.

Rombergism was not present.

Muscular co-ordination was good and the weight had increased by 11 lbs.

His condition remained stationary until eight months after treatment when he again became confused and restless. The physical improvement was maintained, but it was considered/

considered advisable that he should receive a second course of treatment. A series of eight shocks was therefore administered commencing on March 31st, 1930; the final shock was given on the 16th April 1930.

The temperatures obtainedwere :-

102°, 103.4°, 102.6°, 102.2°, 101.8°, 104.8°, 103.8°, 102.8°.F.

After the second shock, he became noisy, restless and confused, and was completely disorientated. His cerebral condition had obviously become exacerbated. He settled slightly, but four days after he had received the final shock, he had a congestive seizure and died a few hours later.

Permission was refused to carry out a post mortem examination.

CASE No. 10. A Female aged 37 years. Married. Occupation - Housewife.

She was admitted to Gartloch on the 21st March 1929.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- The early history is unknown. During February 1929 she was in the Glasgow Royal Maternity Hospital, where she was delivered of a live child. At first she was apparently normal except for some "nervousness", but as this became more pronounced, she was removed to the Eastern District Hospital, from whence she was transferred here. She was admitted as being "simple, foolish and facile with no capacity for concentration, and with confusion and delusional ideas". Her husband, who had been a regular soldier contracted syphilis in 1919 and was treated with "606"; there were no late manifestations of the disease and he appeared to be cured. He married the patient in 1920. Previous to this, in 1916, she had had an illegitimate child, which is still alive. After marriage, she gave birth to six children, all of whom, with the exception of the last born (February 1929), died in infancy. In April 1928, she had had a miscarriage. She had no insane or alcoholic heredity.

MENTAL CONDITION :- She was simple and childish, and free and fatuous in her conversation. She told all her private affairs, including the details of her pregnancies, to anyone who cared to listen. She took little interest in her surroundings and was mildly confused and emotional.

PHYSICAL CONDITION:- She was well nourished and in fairly good/

good bodily health. Apart from the absence of the knee and ankle jerks and the presence of an Argyll-Robertson pupil, the nervous system showed little change.

The heart and lungs were healthy and the urine showed no abnormal constituents.

The cerebro-spinal fluid withdrawn on the 10th June 1929 was strongly positive to the Wassermann, Pandy and Ross Jones tests and the Colloidal Gold reaction gave a well marked Paretic curve.

TREATMENT :- She received a series of eight shocks commencing on July 8th, 1929. The final shock was received on July 24th. The dosage of vaccine used increased from 300 - 450 million. She developed very little tolerance and it was possible to repeat the same dose several times and elicit quite an adequate response. The highest temperatures recorded were as follows :- 102.8°,104°, 103°,103.4°, 103.2°, 102.8°, 102.2°, 103°, F.

COURSE:- She was less talkative during and immediately after the shocks and a fortnight later had improved mentally, inasmuch as she had a better control of her emotions and realised her position more keenly. She then became very depressed, wept when spoken to and stated that she "was the worst woman in the world and had disgraced us all". Her earlier indiscretions seemed to fill her mental horizon and cause her much unhappiness. In other matters also her sense of proportion was impaired. She was acutely conscious of imagined slights and sympathy was misconstrued into censure. This depressed and delusional phase continued for a few days, after which she became silent/

silent and reserved. Improvement then commenced and she slowly became more rational and less emotional, but any mention of her recent delusions was sufficient to provoke a storm of tears. Six weeks after the cessation of treatment, she was brighter, less easily upset and was taking a more active interest in the life of the ward. At the end of September however, she developed an intercurrent bronchopneumonia and died.

Her physical condition also had improved slowly and she had put on weight.

The post mortem examination showed the following condition.

There was a slight recent pleurisy over the bases of both lungs, the lower lobes of which were congested and oedematous and showed patches of bronchopneumonic consolidation.

The heart muscle was soft and showed slight fatty change.

The valves were healthy and competent and the walls of the arteries were healthy.

Both kidneys were enlarged, soft and thickened antero posteriorly. The capsules were adherent in places and on stripping, left a finely granular surface, with small haemorrhages and engorged veins. The appearance suggested a subacute parenchymatous nephritis.

The Dura. There was no appreciable thickening; there was some congestion of the inner surface.

The Pia-Arachnoid. There was slight thickening with patchy, milky opacities, most marked in the sulci. The membrane showed a moderate degree of congestion and was adherent in patches to the underlying cortex.

The Vessels and Sinuses showed no abnormality. The/

The Brain was firm in consistence; there was slight universal wasting and the hemispheres were equal in size and symmetrical.

Gyri & Sulci. There was slight general wasting with widening of the sulci.

Cortex. Some diminution in depth due to wasting.

White Matter. The vascular spaces were dilated.

Ventricles. There was no dilatation. There was slight granulation of the floor of the 4th ventricle.

CASE No. 11. A Male aged 38 years. Occupation - Clerk.

He was admitted to Gartloch on the 20th February 1928.

DIAGNOSIS :- General Paralysis of the Insane.

He had been apparently healthy until a few weeks before admission, when he had had a convulsion with vomiting, followed by confusion. Prior to treatment, he was confused, foolish in his actions and had exalted ideas. He showed the physical signs of general paralysis; his heart and lungs were healthy. The cerebro-spinal fluid was strongly positive to the Wassermann, Pandy and Ross Jones tests and the Colloidal Gold reaction gave a well marked Paretic curve. The duration of the disease was about eighteen months.

A course of treatment was commenced on June 19th, 1920, but after the second shock on June 20th, he developed lobar pneumonia and died two days later.

After the first shock, he was excited and restless and was continually coming out of bed, despite the efforts of the nursing staff to restrain him.

In the post mortem examination, both lungs were found to be congested and consolidated at the bases.

The heart was of average size with healthy musculature and undamaged valves.

The liver was enlarged and showed evidence of fatty infiltration.

The spleen was enlarged, dark and pulpy.

The meninges were thickened, moist and adherent to the cortex.

The brain was soft, with wide sulci and a cortex thinner than/

than normal.

The ventricles were dilated with fluid. No granulations were seen on the floor of the 4th ventricle.

CASE No. 12. A Male aged 26 years. Occupation - Warehousemen.
He was admitted to Gartloch on the 20th August 1929.

DIAGNOSIS :- General Paralysis of the Insane.

HISTORY :- He was always a "backward boy". He left school at 14 years of age and obtained employment as a warehouseman, which position he held until compelled to resign on account of his illness. In 1925 his friends noticed that he could not hold his tea-cup safely and often let it fall. On consulting a doctor, he was sent to the V. D. dispensary of the Western Infirmary, Glasgow where he was treated for twenty months without improvement. He managed to continue in his employment for about a year, but then crusts formed on his feet, his toe nails dropped off and he was unable to walk. He was admitted to the Western Infirmary and remained there for four months. When discharged he went on holiday, but he became delusional, imagining that he was a great musician, and his behaviour was very extravagent. He was then admitted to Stobhill Hospital, where he received a course of benign tertiary malaria. After this treatment, he was blind for about a fortnight. His condition improved slightly, but after having two teeth extracted eight months later, he began to take convulsions. These were succeeded by a state of great excitement in which he attempted suicide. He was re-admitted to Stobhill Hospital where he gradually became more demented and completely bedridden.

MENTAL CONDITION :- On admission, he was stupid, confused and completely disorientated. His memory was poor and he was/

was incapable of performing the simplest of calculations. He had some loss of emotional control; he expressed no delusions, but lay stolidly in bed all day doing nothing to employ his time.

PHYSICAL CONDITION :- He was completely bed-ridden. The heart was moderately enlarged but the sounds were pure. The lungs were healthy and the urine showed no abnormal constituents. The pupils were contracted, equal and regular. They did not respond to light.

Examination of the fundus showed a bilateral optic atrophy with distorted discs.

The tendon jerks were exaggerated on the right side, but gave a diminished response on the left.

The superficial reflexes were brisk and swallowing was not impaired. Babinski's sign was present on both sides.

There was a marked tremor of the lips and tongue and speech was practically incoherent.

Rombergism was present to a marked degree.

Co-ordination of the arms was poor and there was definite athetosis

The gait of the right leg was spastic and that of the left, ataxic. He was unable to walk without support.

There was some disturbance of sensation; the tactile sense and the perception of superficial pain being impaired on the right leg. Appreciation of weight was practically lost.

The hand grips were weak, but there was still good muscular power in the legs.

The cerebro-spinal fluid was positive to the Wassermann, Pandy and Ross Jones reactions and the Colloidal Gold test gave a/

a Paretic curve.

TREATMENT :- He received a series of eight shocks commencing on the 29th October 1929. The final shock was given on November 7th, 1929. He reacted well and there were no ill-effects. The dosage of vaccine used increased from 300 - 1500 million. The highest temperatures recorded were :-
105°, 105.4°, 102.6°, 103 °, 103.6°, 103.4°, 103.4°, 103°. F.

COURSE :- Improvement set in during the course of the shocks and, one week after his final temperature, he was less confused, took some interest in his surroundings and had some appreciation of his condition. His speech was clearer and handwriting had improved. He could rise unaided from his bed and walk without support, although his gait was still unsteady. Progress was made for another week, when he had an attack of projectile vomiting and lapsed back into his previous confused state. All physical gain was lost during the next few days and his mental condition became steadily worse. A clonic spasm, continuous during sleep, started in the right hand and forearm and this was followed about a week later by a congestive seizure and an attack of vomiting. The twitching of the right hand became worse and he had a transient paresis of the right side of the face. There was some improvement during the next three weeks. The twitchings ceased, speech was more distinct and there was less confusion. This respite was of short duration, for on the 23rd December, the twitching returned, this time involving the right leg also. He sank into a state of stupor with incontinence of bowels and bladder and grave impairment of deglutition. It was now noticed that he appeared to be blind.

For the next month there was little change in his condition and on the 20th February he had a severe congestive seizure. This was followed by another about an hour later and for the next three days, these seizures occurred in rapid succession. On the 22nd February, his temperature rose gradually to 105.6°F. and trophic vesicles appeared on his back and his legs. These were followed by an urticarial rash covering the whole body. He vomitted small quantities of brownish fluid.

From this time the course of the disease was rapidly downwards. He became very emaciated and trophic sores appeared over the sacrum and bony prominencies. Consciousness was not regained; congestive seizures were frequent; convulsive twitchings, now involving both sides of the body and the face, were continuous and odontoprisis was distressing and persistent.

The patient died on the 23rd March 1930.

The post mortem findings were as follows :-

The right pleura was adherent and the right lung was congested and consolidated at the base. There were small patches of the tissue gangrenous.

The left lung and pleura were congested.

The heart was moderate in size and the valves, musculature and arteries showed no signs of disease.

The liver was enlarged, congested, "nutmeg".

The spleen was larger than normal, and soft and pulpy.

The meninges were bulging, tremendously thickened and the dura was adherent to the skull cap.

There was staining of the dura and a thin false membrane, partly/

partly organised, was present and most marked on the left side. The pia-arachnoid was adherent to the cortex and tore the brain substance on stripping, leaving a mouse-eaten appearance. The membrane was especially thick and opaque over the left Sylvian fissure.

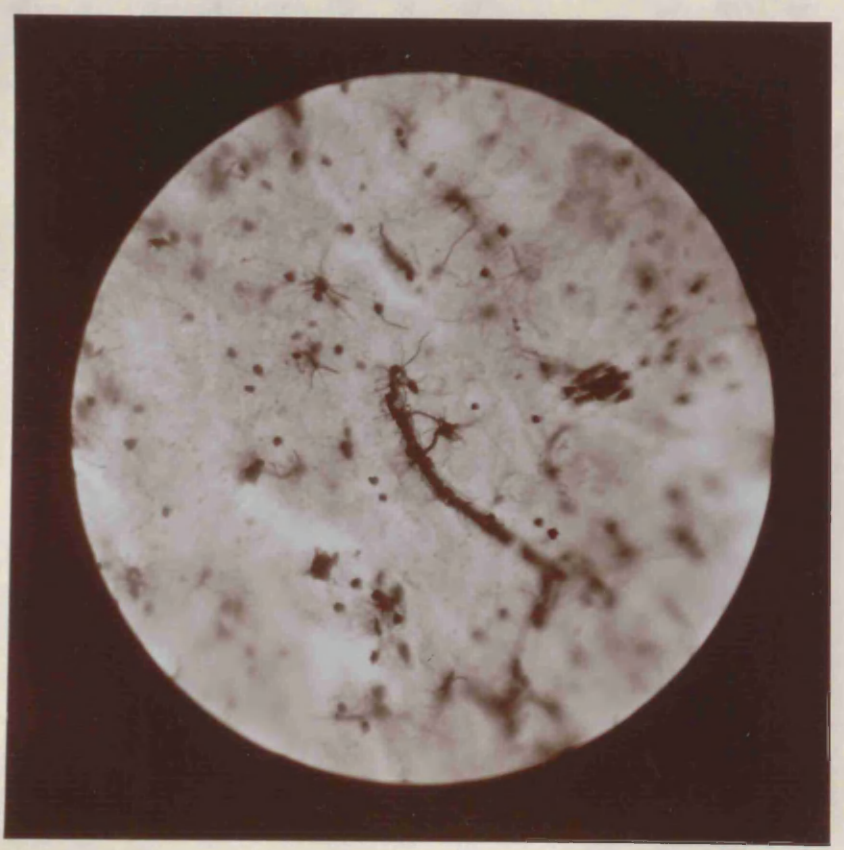
The brain substance was oedematous and wasted, the atrophy being most marked in the frontal and temporal lobes.

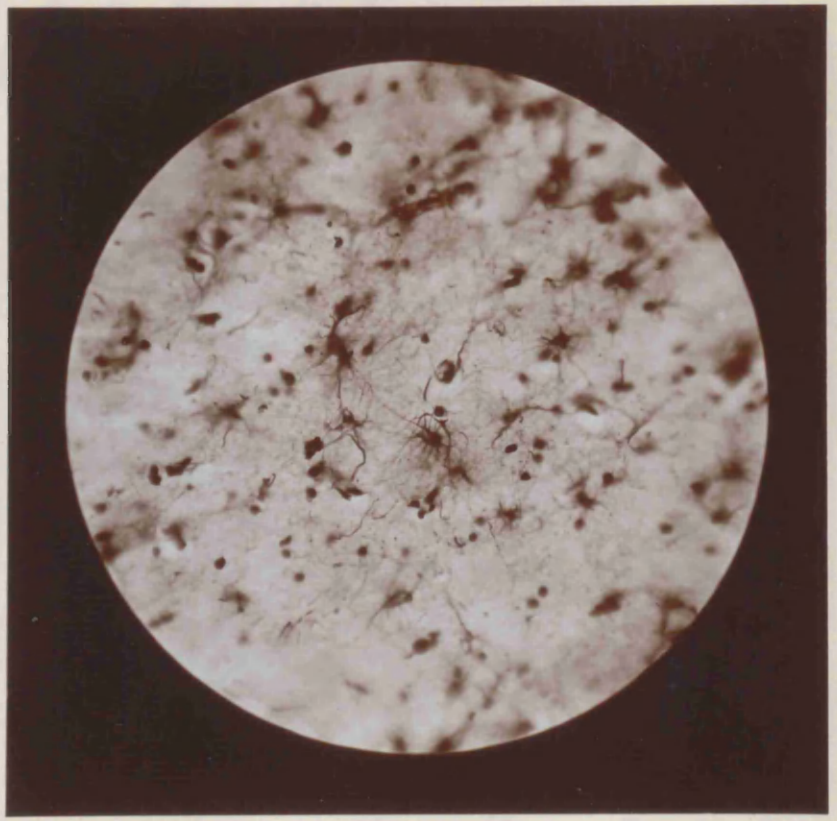
The sulci were widened and the cortex was thinner than usual.

The vascular spaces in the white matter were dilated.

The ventricles were distended with fluid. The floor of the 4th ventricle had the typical ground glass appearance found in general paralysis.

MICROPHOTOGRAPHS of sections taken from the left motor area of the cortex of case No.12. The sections were cut in the freezing microtome and stained by Ford Robertson's method. They show the extreme gliosis present and the abnormal thickness of the sub-pial felting.





A survey of treatment and results.

It must be recognised, that in treating cases of neurosyphilis, improvement can only take place as far as the organic changes in the brain will allow, and the value may be questioned, of this form of therapy, which can, at the best, merely arrest the course of the disease, and in many cases prolong the life of the patient in a state of dementia. The fault lies partly in the system which will not allow a patient treatment in an institution, until he has reached a stage when he is certifiable as a person of unsound mind, and when irremediable damage has already been done to the nervous system and other organs.

One advantage of treatment with T.A.B. Vaccine, is that it can be applied anywhere and is eminently suited for use in general practice where the patient is seen in the earliest stage of the disease. The technique is simple, the pyrexia self-controlled - each bout of fever must be separately induced, and the temperature in individual shocks is easily controlled when necessary. There is no incubation period and therefore no delay. The response is certain and occurs within two hours of the injection being made.

The material is easily procurable, standardised, inexpensive, and requires no special means of transport or storage as does malaria. A living organism is not introduced/

introduced and so there is no possibility of relapse or of infecting others. No precautions are necessary therefore to prevent the spread of an infection. There is no transference of blood from one patient to another. The dosage of the vaccine can be estimated accurately and forms a rough means of regulating the induced pyrexia. This is not possible where a living organism is used, the multiplicity and toxicity of which are outside the control of the physician. In some cases a tolerance for the vaccine is quickly developed. This is a decided disadvantage, as it makes a satisfactory response difficult to elicit. Although acute dilatation of the heart is said to be common in treatment with T.A.B. vaccine, no case occurred in this series. Anaemia is not a feature, and there is no evidence to suppose that the liver is damaged in the same way as in malaria. Only one case in the series showed any trace of jaundice. This was slight and transitory, and as it occurred three months after the cessation of treatment, it is doubtful if it can be ascribed to the results of the pyrexia. Complications of the treatment are few, and apart from the aggravation of the cerebral condition, and the increased liability of the patient to develop respiratory diseases, are of little consequence. Albuminuria appeared commonly during the shocks but invariably cleared soon after they had ceased.

Sickness and headache occurred occasionally during the rigor. The optic nerve was not affected except in one case, where a well marked optic atrophy was accentuated and the patient became blind. He had previously had an attack of blindness after inoculation with malaria, and it should be noted that he had undergone a prolonged course of arsenical treatment before being subjected to his course of shocks.

Hyperpyrexia did not occur and focal reactions were not troublesome. In one case, an acne of the face was exacerbated. Cardiac complications caused no anxiety.

The results of treatment were satisfactory. In most cases a remission, varying in degree, of the mental and physical signs was caused. In advanced cases improvement occurred more in the bodily health, although the mental condition shared in the general gain. The greater part of the progress was made during the first four months after treatment.

Of twelve cases treated, four died, two of an exacerbation of the meningo-encephalitis, and two of pneumonia. One of the former pair had an eight months remission before death which was precipitated by a second course of shocks. Of the latter two, one died/

died two months after treatment, and the other contracted pneumonia in the midst of the treatment. Mental improvement was great in four cases, moderate in one case and slight in three cases. One case did not improve mentally. Physical improvement was great in five cases, moderate in two cases and slight in two cases.

These numbers include the patient who died after an eight months remission. Of seven patients who were completely bedridden, six after the treatment were enabled to be up all day, and the seventh case improved sufficiently to be up for part of the day. Of four patients who were dirty in their habits, three became clean. The fourth was a case of Juvenile General paralysis.

Of five patients who were unable to feed themselves, four improved sufficiently to do so, and in addition, to attend to most of their own requirements.

Of six patients who were on a constant sedative, five improved sufficiently to warrant it being entirely withdrawn.

These changes indicate a saving in the drug and laundry bills, as well as an appreciable lightening of the duties of the nursing staff. Eight patients increased considerably in weight. In one the increase was transient and only slight.

Motor restlessness was usually controlled quickly, but in some cases it was aggravated for a week or two by the treatment. Noisy and excited cases settled down rapidly, and the behavious of impulsive patients gradually became better.

Delusional ideas in some cases were abolished, and in others receded into the background.

Confusion was usually slow in clearing.

The physical signs of disease improved quickly.

Rombergism was generally the first abnormal sign to be influenced and a steadying of the gait was seen early.

The improvement in muscular co-ordination influenced speech, and articulation became clearer.

Tendon reflexes, in advanced cases, where the jerks were lost, usually remained unaltered, but in more recent cases where the jerks were still spastic, these sometimes approached nearer to normal.

The superficial reflexes did not alter.

The Argyll-Robertson pupil, when definitely present, usually persisted, but in one case it was abolished, the pupils reacting smartly to light and accommodation, where before the response to light had been entirely lost. In examining general paralytics, however, it was found that in the same case, the response to light varied from time to time. In the only patient who had

had/

had seizures before treatment, these were increased in frequency after the shocks.

In both cases which relapsed, the deterioration was mostly confined to the mental condition. Bodily health was fairly well maintained.

Clinical findings generally could be correlated with the laboratory results, but the degree of improvement in the patients condition was not always reflected equally in his serological changes.

The Wasserman reaction was diminished in intensity in all cases, and in two instances became negative.

The colloidal gold curve in all cases tended to approach nearer to normal. One case became negative.

The globulin content showed a tendency to diminish and the cell count to be reduced. In one case the count was increased although the patient had benefited clinically and the serological results were improved.

Although in untreated cases of general paralysis, the laboratory results tend to vary, a reduction in the intensity of the Wassermann and Colloidal gold tests in 100% of a series of treated cases, is too significant to ascribe to anything but the effects of that treatment. The following table shows the results of the tests carried out before and after treatment.

PATIENT	WASSERMANN	COLLOIDAL GOLD	PANDY	ROSS JONES	CELL COUNTS
1	+++++++++ ++++++	55555555540 55555554300	+ +	+ +	45 43
2	+++++++++ +++++	5555555$^{4}_{5}$40 55555543200	+ + +	+ + +	53 48
3	+ + +	$^{44}_{55}$330000000 44332000000	+ weak +	weak + $\pm$	30 2
4	++++ -	55555554330 55555543300	+ +	+ +	56 60
5	+++++++ ++++++	55555544300 55555543000	+ +	+ +	61 120
6	+++++ +++	55555544330 55555322000 44444	+ +	+ -	63 60
7	++++++++++ ++++	55555555430 55555543300	+ +	+ +	110 57
8	++ -	11122221110 00000000000	+ -	+ -	180 5

CONCLUSIONS.

1. "Protein Shock" therapy, induced by the intravenous injection of T.A.B. vaccine, although possibly not so striking in its results as therapeutic malaria, is a useful and easily administered form of treatment for neurosyphilis, and is probably the most effective alternative to the more rigorous microbic method.

2. It possesses certain advantages over the other, not the least of which is that it can be suited to individual requirements, and lends itself to spacing of the intervals between shocks and groups of shocks. Exhaustion of the tissues can thus be avoided and more satisfactory responses elicited than where the bouts of fever occur in a continuous series.

3. It is tolerated well by debilitated and advanced cases and is more applicable to their needs than is an actual fever, from which they cannot be conveniently rested.

4. Although it is liable to hasten the course of the disease to a fatal termination by exacerbation of the pre-existing meningo-encephalitis, or by promoting the onset of some intercurrent disease such as pneumonia, these objections seem to be common to all forms of pyrexial treatment.

5. It confers an immunity on the patient to the typhoid group of infections. Although this is incidental, it is a valuable asset to those confined in an institution.

6. It causes a remission in the mental and physical signs, the degree of improvement depending largely on the stage of the/

the disease.

7. In most instances it retards or arrests the course of the disease and prolongs the life of the patient. Although early cases must necessarily have the most hopeful prognosis, some degree of improvement may be expected even in patients advanced in the disease.

8. It causes a generalised bodily improvement with mitigation or disappearance of the physical signs of disease, and an increase in weight.

9. Mental improvement is less marked than physical, and varies from a complete remission of the symptoms to improvement in the behaviour, habits and initiative of the patient.

10. The classical grandoise and exalted type of case, the one in whom a spontaneous remission most commonly occurs, gives the most spectacular and rapid result, but the depressed and apathetic type, although slower in responding, gains steadily. Improvement is least marked in the demented patient.

11. The results in cerebro-spinal syphilis are also satisfactory.

12. The serological results vary after treatment, but tend to follow the course of the clinical picture. The degree of change in both, however, does not always correspond.

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