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Pyretotherapy in neurosyphilis

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PYRETOTHERAPY IN NEUROSYPHILIS

BY

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* INTRODUCTION *

Syphilis, like the poor is always with us. "Age cannot wither it nor stale its infinite variety." It may scourge the entire body but it reaches its maximum in its attack on the central nervous system. It may be cured; of this, there is never any certainty. This uncertainty is so great that we may, with a large modicum of truth, proclaim that syphilis never dies, - it sleeps (47).

The constant progress in medical science has neglected, until the present generation, the neurosyphilitic patient. Ten years ago the parietic was doomed (5). The attitude of fatalism toward general paresis and certain resistant types of neurosyphilis finally resulted in investigations in an attempt to mimic nature's art of healing, creating a febrile reaction as a therapeutic agent, i.e. Pyretotherapy (50).

All are cognizant of the fact that a certain number of cases will develop serious central nervous system syphilis in spite of everything that can be done. But, on the other hand, there are many patients now entirely incapacitated and a burden to society, who might be leading relatively normal lives had they been properly and adequately treated during the early stages of their disease (62).

HISTORY

The appreciation of the value of pyretotherapy has its origin in the quite old observation that cases of mentally diseased patients improved following intercurrent disease accompanied by high fever. Hippocrates and Galen knew that diseases with fever may act favorably on "psychoses". (8) The Ancient Egyptians and Greeks and Romans utilized hot baths in the treatment of diseases. This is one of the oldest therapeutic procedures. They worked out elaborate devices for its administration. The therapeutic possibilities of many of the thermal springs of western Europe were discovered by the Romans. In this stage of the clinical application of the bath, attention was centered largely on its temperature and little on the fever produced in the patient. The situation not infrequently resulted in fatalities. (28)

In 1848 Koster studied the influence of malaria on mental disease, and at that time the erection of an insane asylum in a place that was constantly exposed to intermittent fever was considered. (8)

Nasse in the year of 1864 noted the favorable influence of malaria on mental disease and pointed out the especially striking results in dementia paralytica. (18)

Apparently it has either been forgotten or overlooked by the Medical world that Rosenblum, in Russia, in the years of 1864 and 1874, had made use of relapsing fever and malaria; he employed this means in the different psychoses, syphilitic and non-syphilitic. His publication appeared in the Odessa in 1876, and was not available to Nerancy (31) who states: "and therefore, I am unable to say whether he used malaria deliberately in paretics or whether he used it just along with his other cases." The fact is that he did not succeed in gaining followers; but

HISTORY

the influence of acute febrile diseases upon paretics was too obvious to be unobserved indefinitely.

The introduction, development, and systematic use of artificial fever therapy, which culminated in the malarial therapy in psychiatry and especially for paresis, is to be credited to Wagner Von Jauregg and his associates (50), who made their original proposals in 1887 (8). In the twenty years succeeding his original proposal he was deflected from the direct approach to the subject by intermediate experimentation with non-specific protein pyrexia. (I) Cauterization, tartarus stibiatus sloughs, which were kept open by basilic ointment for two or three months, cantherides blisters, and erysepelas streptococci were used, until in 1900 the experimental work with tuberculin was started. (50)

Wagner Von Jauregg in 1917 inoculated nine general paretics with tertian malaria. After ten years of observation he stated that three of these patients were still alive and active in their professions. Subsequent to this, these treatments were begun on a large scale in the Hamburg Clinics of Weygandt and Nonne. (I)

Kunde, Hall and Gerty (29) used combined typhoid vaccine in the treatment of general paresis in 1926.

The use of hot baths as a means of producing therapeutic fevers was again called to attention by Schamberg's experiments (53) in sterilizing chancres by immersing the animals in hot baths. (1928)

King et al (24) first applied diathermy to a case of paresis in October 1928. They repeated some work done on animals by Carl A. L. Bengner and Ronald Chrestir, who definitely proved that the general body temperature of animals could be raised by a high frequency current.

THEORIES OF ACTION

Theories of the mode of action of pyretotherapy are many and in controversy; these, for practical purposes, may be summed up under two general heads: first, those dealing with the thermal action on the spirochaete; and secondly, those dealing with the action of the defense mechanisms of the individual on the spirochaete and its toxins. (18)

The facts that tend to support the view that direct or indirect fever is responsible are as follows: 1. The spirochaete is susceptible to moderate elevations in temperature and the thermal death point of the organism in vitro is about forty-one degrees centigrade (or 105° F.) upon exposure of six hours duration. (21) 2. Weichbrodt and Jahnel (15) have shown that a rise in temperature up to 104° Fahrenheit and higher of an experimental animal in the thermostat was able to heal an artificially produced chancre and cause the disappearance of the spirochaetes. 3. This seems to coincide with Jahnel's (15) findings that spirochaetes were not found in brains of paretics that developed an antemortem pyrexia, or an intercurrent febrile affection two or three days before death. 4. The best results in general are obtained where the malarial fever is high and the patient has a good number of paroxysms (52). 5. Any inflammatory process producing a high fever lasting for hours has virtually as good an effect as malaria (52). 6. Fevers produced by hot air, hot baths, or diathermy yield good results either on syphilitic patients or on experimentally infected animals (52).

The literature provides fertile arguments which tend to discredit fever as a primary factor and these resolve themselves into the following: 1. Gerstman states (52); "One thing is sure, it is not the fever which is the important curative agency, it is only one of the factors in the vital

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reaction." 2. Rarely do we find temperatures as high as 105° Fahrenheit in malaria. 3. Good results have been obtained with temperatures not exceeding 104° Fahrenheit. 4. The so-called apyrexial malaria, in which the fever is held at 102° Fahrenheit, has been used with success. (21) 5. The fact that results with pyrexial agents such as tuberculin, sodium nucleinate, vaccines and serums have not been comparable to malaria also tends to indicate that the high fever is not the primary therapeutic agent (21).

The manner in which the reactive process influences the biologic changes in the life of the spirochaetes and their toxic products, on the one hand, and the response of the nervous tissue and the general organism of the syphilitic, on the other, is as yet purely hypothetical (35). Therefore, it is probably wise to discuss the various theories and not attempt to draw definite conclusions.

McIntosh (2) maintains that in therapeutic immunization two factors are at work, a specific and a non-specific. The former is a typical antibody response; while the latter appears to be mainly dependent upon a general stimulation of the tissues and leucocytes, in fact, to a process comparable to fever.

Gertsmann (15) maintains that the malaria therapy enhances a rise of the weakened protective and defensive mechanism by the reactivation of the specific cellular ability to inhibit the destructive action of the spirochaetes upon the nervous tissue, if not entirely to destroy the virus. He bases this conclusion upon the inability of all the investigators to find spirochaetes in brain tissues of successfully treated cases that died of an intercurrent affection.

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The theory of Plant and Steiner (15) is that the active immunity which is produced against the malaria infection is sufficient to produce also an inhibiting influence upon the growth and vitality of the spirochaetes.

Weygandt, Muehlens, and Kirschbaum (15) believe that the products resulting from the cleavage of albumins, as a result of the malaria infection, bring about a change in the organism, that is marked by a rise of its defensive mechanism, and by the production of antibodies against the malaria plasmodium. At the same time the protective antibodies against the syphilitic virus are mobilized.

Besides these hypotheses, based upon the theory of immunity, there are others; such as the activation of the cell protoplasm by non-specific protein and vaccines. Ellery remarks (12): "this shock protein therapy seems to me merely a mechanical method of calling forth a certain tissue response, as mechanical as driving a tack into the carpet and, just as a tack may be driven home with a hammer, the head of an ax etc, so may the tissue response be called forth", by the various non-specific proteins; with (15) the stimulation of the threshold barrier of permeability between the vascular system, the meninges, and the cerebro-spinal fluid.

According to the latter theory, advanced by Poetzel (15), this barrier is so altered that the passage of noxious substances from the blood stream to the brain is barred by the malaria. He bases his contention upon the Weil-Kofka hemolysin reaction, which is positive in the spinal fluid of 62.7% of untreated paretics, in about six percent of treated paretics, and in eight and eight-tenths percent of cases with complete remissions for two years after treatment. In 67.5% of treated, but, un-

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improved cases, the reaction remained positive. He explains the mechanism of the therapeutic effect of malaria to be due to the cessation or diminution of a catalyzing process by some as yet unknown complex albumins; which, because of the greater permeability of the meningeal and brain vessels, together with the hemolysins are thrown into the subarachnoid fluid and brain tissues. These catalyzing agents are considered by him to be productive of a progressively destructive brain process. The negative hemolysin reaction, therefore, indicates to him, a disappearance of these destructive agents.

Webb (52) is of the opinion that hemolyzed albuminous substances from the blood make their way through the meningeal and cerebral vessels and act as catalysts, these processes being favorably influenced by malaria.

Schultze's (15) investigation of the behavior of the Spatz iron reaction in the adventitial spaces of the brain capillaries may have some bearing on the question of permeability of the threshold barrier between the blood vessels and the cerebro-spinal fluid and the mode of the malaria therapy. He found that this reaction, which is strongly positive without exception in all cases of paresis, and invariably negative in non-syphilitic brain affections tested as controls, became weakly positive or entirely negative in the vast majority of treated paretics. Schultze interprets these findings as confirmatory of his hypothesis; of such alteration of the threshold barrier by the malaria that the brain tissue detritus is more easily absorbed and carried away in larger quantities by the capillaries. At the same time a greater amount of defensive substances are allowed to filter into the spirochaete infested nerve tissues.

Mehrtens et al (28) states that the permeability of the meninges

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was increased by fever produced by baths. Using Malamud's modification of Walter's technique they showed that the permeability quotient in all cases was lowered. In order to achieve this increased permeability it was necessary for the hyperpyrexia to be greater than 103° F., and to be continued for at least thirty minutes, and to be repeated at least five successive days.

Bratz and Schulze (3) as the result of anatomic studies, believe that the malarial parasites make the small vessels of the brain more permeable for protective substances.

Hoff and Silberstein (15) have, furthermore, shown that experimental inoculation of syphilitic testicular particles that were incubated in a mixture of spinal fluid and leucocytes of successfully treated paralytics, failed to produce syphilitic lesions in rabbits; while those incubated with a mixture of spinal fluid and leucocytes of untreated cases promptly produced the characteristic lesions. They also report that the spinal fluid and leucocytes mixture of the successfully treated cases immobilizes the spirochaetes within two hours and finally destroys them, while that of the untreated cases fails to affect them.

Donath and Heileg (15) worked on the hypotheses that the desired effects of malaria are due to mechanisms which increase the protective and immunizing mechanisms of the organism. They compared the behavior of the albumin cleavage in the blood of patients treated with non-specific proteins and vaccines on the one hand and with malaria on the other. As an indicator of this cleavage, the amount of amino acid developed in the blood plasma was ascertained. They found that with each fever reaction after non-specific protein and vaccine injection there was a considerable

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augmentation of the amino acid content in the blood, while in the case of the malaria fever reaction no augmentation was noticed. The reverse, however, was noted in the spinal fluid. Here a greater amount of amino acid was found during the malaria paroxysm than after the non-specific protein and vaccine fever reaction. These investigators ascribe these changes to a specific local reaction that is produced in the brain by the malaria.

These data were further tested in another manner by Pfeiffer, Standenatt, and Werber (5), and by Kafka (5), by estimating the sedimentation time, fibrin content, and sodium chloride of the blood plasma and the refraction, viscosity, and albumin content of the serum as well as the spinal fluid chemistry before, during, and after the fever. Their results seem to confirm the theory of Donath and Heileg that the malaria produces a specifically elective local reaction in the brain, which Wagner-Jauregg enunciated in 1925 (15).

Dermal Gummata have been reported appearing in paretics soon after good remissions, and, in so far as such Gummata are thought to be allergic reactions indicating parital immunity, it seems to be additional evidence that an immune reaction takes place during or directly subsequent to the malaria (21).

Mabride and Templeton (25) suggest that a combination of the quickening of metabolism with the removal of accumulated waste products, the action of the fever on the spirochaetes, the possibility of a biologic relationship between the plasmodium and the spirochaeta pallida, and the production of a specific antibody against the spirochaete were the means by which results were accomplished.

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Purves et al (49) expressed the opinion that malaria accomplishes the good results by means of the pyrexia, burning up the toxins affecting the cerebral cells in a sort of cleansing fire. The absence of any marked serologic changes shows that the syphilitic encephalitis is still uncured.

Freeman (15) found that there is an organization of the inflammatory exudate in the meninges and about the blood vessels. The exudate is then resorbed and the glial and vascular tissues regress to a considerable extent. Finally the cortex is reconstructed by resumed cellular polarity, restored lamination, and by a thickening of the cortex. No spirochaetes were found in his series of brains studied. Schamberg (52) has found them only exceptionally after malaria.

Breutsch and Bahr (4) basing a study of the mechanism of inoculation malaria on the histopathologic changes in paresis, regard the changes consisting of proliferating phenomena of the capillary endothelium as part of the reaction of the reticulo-endothelial system, being of the opinion, that, particularly at the time of the febrile attacks, plasma cells probably immigrate into the brain vessels, taking part in the phagocytosis of the liberated plasmodia.

BASIC PRINCIPLES IN THE TREATMENT OF NEUROSYPHILIS

The treatment must always be adapted to the individual patient. While a routine method of attack is often desirable in early syphilis, it is never to be applied when the nervous system is involved (58). Most important of all is the classification of the neurosyphilitic processes before treatment is begun (18). A collection of all information obtainable from both laboratory and clinical sources must be carefully scrutinized before one can decide on the individual plan of treatment (58).

Aged or markedly debilitated patients require special care and consideration. Never "hammer" them. Impending dissolution is greatly hastened by vigorous treatment and the over-ambitious therapist will receive full credit for the final demise (58).

All attempts should be directed towards a determination of the ability of the patient to develop an immunity to his own infection. The protective reactions of the body tissues are more marked in women than in men, especially when pregnancy supervenes (58).

Prognosis depends largely on the degree of fibrous tissue change with impairment of circulation and the amount of degeneration which has taken place; once these changes have occurred, we are dealing with late neurosyphilis, which at best is very resistant to even the most vigorous treatment (62).

The therapist at all times must refuse to be hurried. He must follow the general condition of the patient by weight, by the condition of his appetite, blood pressure, blood counts etc. If the treatment is poorly tolerated, frequent rest periods should be instituted (58), and in some cases therapy will have to be discontinued. The desire of the patient to get well is at no time an index for a vigorous therapeutic

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procedure, if the general condition of the patient does not warrant same.

INDICATIONS FOR PYRETOTHERAPY

In estimating the possible value of pyretotherapy for a patient with neurosyphilis the following general considerations should be carefully studied: First, the amount of good to be accomplished is inversely proportional to the amount of degeneration, both physical and mental. Secondly, the possibility of relapse should be borne in mind constantly. Thirdly, it must be remembered that almost one-half of the patients treated by this method will be able to resume some gainful occupation. Fourthly, the procedure has definitely decreased the death rate among patients having neurosyphilis, especially paresis (38).

The use of pyretotherapy is recommended when prolonged treatment with the routine antisyphilitic measures, which was started during the early manifestations of acute syphilis, has failed to control the unfavorable progress of the disease as manifested clinically and by spinal fluid (40). At the Colorado Psychopathic Hospital at Denver this form of therapy is used only on those cases not responding to chemotherapy; of these cases paresis is numerically and therapeutically the most important of the group (21).

Doctor Ebaugh (10) in classifying his cases for pyretotherapy, makes the following divisions; remarking on them as follows: first, cases of advanced parenchymatous neurosyphilis with definite evidence of mental deterioration and characteristic neurological findings; second, cases of parenchymatous neurosyphilis with a psychosis of pronounced functional coloring in which the neurological findings are of variable nature, in this group good remissions are particularly attainable; third, meningo-vasculo-parenchymatous neurosyphilis characterized clinically by transitory mental symptoms, delirious reactions and neurological

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irritative phenomena. All are types of paresis and are regarded as subjects for malarial therapy.

Tabes and cerebral syphilis, which clinically progressive in spite of active chemotherapy, are also treated with malaria and the results obtained are comparable to those obtained in paresis; those of cerebral syphilis which show clinical evidence of beginning parenchymatous involvement are especially suitable (21). However, Hoff and Kauders (9) reporting from Wagner Jauregg's clinic are optimistic in estimating the value of malaria in Tabes; they obtained 43% improvement with abeyance of single symptoms; in addition 32% of their cases were improved while 25% were unimproved. They state that the severe ataxic form of Tabes did not respond to treatment and that use of malaria is contraindicated in these cases. Dreyfus and Hanau (9) advise the use of malaria one year after other treatment has failed in cases of Tabes and agree with Nonne (9) that results obtained are not as good as those seen in the treatment of paresis. Rudolf (9) indicates malaria in the treatment of Tabes and states that it produces good results.

Kyrle (6) has shown that patients with latent neuro-lues, manifested by positive spinal fluid reactions without clinic evidence, will usually resist all sorts of intravenous routine treatments. These patients, under the influence of malarial inoculation, all clear up, although often it takes six to nine months before spinal fluid findings become normal. Schamberg (52) thinks such patients will probably do well under other "fever" treatments. Although he believes it is a little early to speak of the value of endothermy, he believes it is destined to play an important role in the treatment of neuro-lues. The various forms of

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pyretotherapy are compared in subsequent chapters.

CONTRAINDICATIONS TO PYRETOTHERAPY

The various agents of pyretotherapy present various contraindications to their use. In general, there must be within the patient sufficient latent power to regeneration if there is to be response to pyretotherapy: and, any accompanying systemic condition which tends to deprive the organism of these potentialities must constitute a contraindication until it can be removed or successfully moderated (21).

Malarial inoculation therapy will be used as a type because contraindications to its use are the greatest in number; the other agents will be compared with it. Old age with marked arteriosclerosis; (50 B) a run down physical condition, particularly with a circulatory or cardiac disability; (2) an advanced aneurysm; advanced liver and kidney disease (50 B), especially with the retention of nitrogenous end products in the blood (2); severe anaemia; diabetes; ascending urinary infection (50 B); neurosyphilis with concomittant or associated active pulmonary tuberculosis (2); pregnancy; chronic alcoholism; "rapidly progressing or galloping paresis"; and juvenile general paralysis, and primary optic atrophy are definite contraindications. Far advanced tabes with incontinence, ataxia etc. is a contraindication because these cases do not respond but are aggravated (21). Aortitis is not a contraindication if the subject is free from signs of heart failure (21).

The chief contraindications to typhoid vaccine therapy are few in number. They are: cardiovascular disease, active pulmonary disease, cachexia, and debilitation.

Diathermy and hot baths appear to be the safest of all fever treatments. Cases of myocarditis have been reported that were treated successfully. Indeed, I have been unable to find any data stating

CONTRAINDICATIONS TO PYRETOTHERAPY

definite contraindications.

The impractical aspects of the other agents of pyretotherapy are discussed in the following section.

COMPARISON OF THE VARIOUS AGENTS OF PYRETOTHERAPY

There is an inexorable logic in the light of which all agents of pyretotherapy for syphilis should be scrutinized. In general it is sound therapeutics to encourage and stimulate the development of methods with the lowest possible mortality. Next in principle stands the maxim that methods should be given preference which are as cheap as possible; as little disturbing to the patients effective economic and personal life as possible; and as readily accessible to the mass of patients through the services of their personal physician as possible (64).

The advantages of the various agents are briefly summarized.

Malaria: The concensus of opinion, based upon actual case data, is that malaria is the most effective method of treatment for patients suffering from neurosyphilis, especially dementia paralytica (43), and is the only method which offers reasonably uniform and lasting results. It is readily terminated by quinine. From the standpoint of the practitioner, it is a convenient way to shift the responsibility for the after effects, the stormy and prolonged convalescence, the partial or unsatisfactory result, and the death onto an institution whose broad back can well bear a mortality ranging, under the conditions of today, from five to thirty percent (64).

The most striking feature is the physical improvement characterized by an increase in weight and by a feeling of well being, which either precedes or accompanies the mental improvement in the parietic (21).

Relapsing fever: Placet (12) in 1926 reported his experiences, of six years duration, with the spirochaete of African relapsing fever, and judging from all data, considers that the results of malaria and relapsing fever treatment are about equally balanced. Relapsing fever is said to be less dangerous, as it does not weaken the patient, and the

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treatment is easier to carry out, especially as the infectious material is easily available by keeping the disease going in mice. The disease is easily controlled by salvarsan.

Sodoku, likewise, finds preference to malaria in that it does not weaken the patient as does the latter, and animals can be utilized in keeping the strain alive. It can be induced in patients more or less immune to malaria and may be used before or after malaria. It is promptly controlled by arsphenamine.

Diathermy: Therapeutic fever created by diathermy is considered superior to malaria in that the fever can be controlled (48). No serious sequellae such as jaundice or severe anaemia followed its use (13). Economically it has much in its favor as the patient can be ambulatory (13). It appears to be the safest of all fever treatments. By this method even patients suffering from myocarditis can be treated; indeed no contraindications are reported and the mortality is practically nil (34).

Non-specific proteins: This type of treatment is free from the objectionable feature of the deliberate inoculation of patients with a disease producing organism. Its development is an outgrowth of circumstances. The relatively high mortality due to malarial treatment, the immunity of some individuals to malaria, the difficulty of keeping an available strain of malaria, and the similarity known to exist between malarial paroxysms and the method of temperature rise following intravenous injections of protein stimulated its development. The chills can be produced at will. The height of the temperature can be approximately controlled by regulating the dose in each instance. The leucocytosis produced may be of advantage (18). Typhoid vaccine finds great favor.

COMPARISON OF THE VARIOUS AGENTS OF PYRETOTHERAPY

It possesses another favorable feature in that the patient may be treated at his or her home, since the injections are given every other day, and, if the patients' condition is satisfactory, he or she may even go about their business during the day they are not receiving treatment (16). Its chief merits probably lie in its relation as an adjunct to malaria, which will be discussed later; as it is more effective in reducing irreducible blood Wassermann reactions, especially if it is given intravenously (52).

Hot baths: Such risks as marasmic, arteriosclerotic and nephritic patients with hypertension may be treated quite satisfactorily by this method (28). The lightning pains, gastric crises, and charcot joints found in tabes yielded to hot baths more readily than to any other therapy previously used (28).

THE DISADVANTAGES ARE:

Malaria: Malaria is in no sense of the word a method for the general practitioner. It is a method that can be only satisfactorily applied by experts. It is not a method to be practiced here, there, and everywhere, that there may be a hospital bed on which to lay a patient. It belongs in centers which concentrate on the perfection of its technic with all the intensity and resources imaginable. It demands large experience and absolute patient control. It carries a relatively high mortality. The organism is not always available (64). The complications are numerous. In certain cases an immunity to the disease obstructs satisfactory treatment (29).

O'Leary in 1928 (38) estimated the death rate as 5%. Schamberg (52) estimates the average mortality in paretics at 8%. Neyman and Koenig (34) at 18%.

The chief argument against the treatment with malaria is that there is neurosyphilis in parts of the country where malaria is endemic. This is not a convincing argument for, in the first place, we (42) do not maintain that malaria produces immunity against neurosyphilis, nor that it is a specifically acting treatment. Moreover, indisputable evidence that paresis is as frequent in malarial countries as in malaria free countries is not available.

The argument that neuro-syphilis will have spontaneous remissions is often presented. The number of spontaneous remissions among one thousand untreated paretics in New York institutions was found to be about $3\frac{1}{2}\%$ (27). Tophoff (27) in an analysis of two hundred and eighty nine paretics, found four and eight tenths with complete spontaneous remissions. The figures illustrating the number of spontaneous remissions proved to be relatively small.

THE DISADVANTAGES ARE:

Relapsing Fever: Utilization of this method is not successful in the United States because there are no strains of sufficient virulence available to produce satisfactory results (18); the results are not particularly striking and it does not seem as if this would ever become a practical method (60). It also involves risk of life (29).

Diathermy: The chief danger is that of superficial or severe burns (28). It is still in the experimental stage and data is insufficient for definite conclusions.

Herd (19) investigated the application of diathermy to the head in a number of selected cases of neurosyphilis to determine if the heat element alone is of value, and found it to be of little or no benefit upon either serological or clinical findings.

Sodoku: In Sodoku, the post infectious neurosis at the seat of the inoculation is very extensive and the healing process is continued at least one-half to two months. General neuralgic and muscular pains precede the paroxysms of fever (50). The diagnosis of Sodoku by the demonstration of the causative organism directly or by animal inoculation may be difficult. Fortunately, there is a reliable serologic reaction; the technique is quite involved (18). Clinical and serologic improvement has resulted in some patients, which would indicate it has some therapeutic value. Much more work must be done before this method can be properly evaluated (18). The mortality is about ten percent. (34)

Non-Specific Protein: Reese (50) from studies with non-specific preparations such as peptone, milk, turpentine, and Aølan, concluded that non-specific stimulation alone is not effective in arresting the progress of paresis even if we assume that non-specific stimulation produces an

THE DISADVANTAGES ARE:

omnicellular activation. Of late, the Germans are using a preparation called Saproviton, (Boehme) which is a mixture of active saprophytes. While some authors have seen clinical improvement from its use in paretics, others have become discouraged. The Vienna School reports septic complications and it opposed the use of Saproviton (50). Sodium nucleinate (50) produces hyperpyrexia and leucocytosis, but results are uncertain and the number of remissions rather small. Chloride of ammonia as another type of therapy has been recommended (50). This, by producing a blood acidosis, resulted in improvement in paresis but only one encouraging report has been published. Secard of Paris (50) is apparently using antichancroid bacterium or Nicolle vaccine with success.

Combined Typhoid vaccine frequently fails to produce high fever consistently throughout a full course of treatment (29). Results do not approximate those of malaria.

Hot Water Baths: The amelioration of symptoms was not always permanent; the lightning pains and gastric crises above described tending to recur, particularly after intercurrent infections (28). Hollingsworth (20) studying the effects of hot baths in late syphilis, fails to confirm any clinical or laboratory benefit derived from heat.

PROCEDURES PREPARATORY TO PYRETOTHERAPY

Care prior to pyretotherapy has for its objective the placement of the patient in a favorable physical state. It is good policy to (21) give a course of chemotherapy, usually tryparsamide, prior to inoculation with malaria to cachectic and anemic patients. This, together with rest and a high caloric diet, serves to improve many otherwise unfavorable risks.

Attention should be directed toward the discovery of accompanying disease and it should be eliminated wherever possible. A complete physical examination with routine microscopic and chemical examinations of the blood and urine, and a radiographic examination of the heart, are essential. For instance, approximately 35% of Jefferson's and Johnson's (21) candidates for malaria showed evidence of cardiac or aortic disease. To be aware of the presence of such a condition is essential in deciding what form of pyretotherapy is to be used.

Existing infections such as those of the teeth and sinuses must be eliminated. Infected scratches and skin abrasions, common in psychotic patients, must be eliminated to prevent dangerous complications to which they may lead.

If agents causing secondary anaemia are used; the patient's blood should be typed. If malaria is considered, the patient's reaction to quinine should be tested. The latter may be accomplished by oral administration of five grains of quinine (21).

In the United States Veterans' Bureau (27) the patients are usually given a preliminary course of treatment with digitalis so as to prepare the heart for any circulatory emergency which may develop during the malarial paroxysms. Most of the patients have had course of treatment

PROCEDURES PREPARATORY TO PYRETOTHERAPY

with arsenicals, mercury, iodides, bismuth preparations, or tryparsamide, and it is believed that the good results obtained in the bureau are due to this combination of treatment.

Rickloff and Osborne (50 B) advise one full intensive course of treatment of arsphenamine and bismuth prior to malaria therapy.

In dealing with the diffuse cerebrospinal group, a three weeks preparatory treatment with mercury by innunction and potassium iodide by mouth or vein has been advised (58). At the end of this time six injections of bismuth or bismarsen are given, followed by salvarsan for six to eight injections with a return to a month of inunctions. The bismuth and salvarsan series are repeated and are followed by two courses of tryparsamide of fifteen injections each at weekly intervals. Bismuth is often given with the tryparsamide or between the courses of this useful drug. After an additional three months of inunctions the case should be re-studied, and the treatment plan modified in the light of the new findings. If the serology continues unchanged, fever therapy must be resorted to.

It is wise to begin treatment in tabes by the usual preliminary preparation with mercury and iodides. This avoids the troublesome complication of increased root pains so often encountered if this precaution is not observed (58).

A preliminary course of six injections of salvarsan (.4 gms) given as soon as the patient comes under observation is advisable prior to typhoid vaccine therapy (58). Injections are made on each fifth day. The iodides are also given in the usual dosage.

The concensus of opinion seems to be that preparatory treatment by drugs is desired prior to pyretotherapy.

MALARIA

Malaria, typhoid vaccine, diathermy, and hot baths are discussed in detail in the following sections. The other agents of pyretotherapy referred to in this paper will not be discussed in detail because of their relative impracticability.

MALARIA: The chronic malignant types of malarial strains should be avoided; the old rather than new strains should be used (22). The organism does not seem to lose its power no matter how many passages it takes. O'Leary's strain at the Mayo Clinic has passed (1927) through five hundred and twenty-five recorded hosts and is still going strong (1). The old strains free from gametes are not transmissible by the anopheles. The tertian and quartan types are preferable. The tertian type is more desirable than the quotidian type because it enables the patient to recuperate physically and mentally before the next paroxysm (55). Inoculations made intramuscularly more frequently result in a tertian pattern (9). Intravenous inoculation (21) tends to favor development of the quotidian pattern and consequently should not be used routinely.

Kolmar (27) advises eight to fifteen paroxysms, having made the observation that the more numerous the malarial paroxysms, the larger the percent of very good remissions. The best results were obtained in cases of thirteen to eighteen paroxysms.

Johnson and Jefferson (21) consider eight paroxysms sufficient as Wagner-Jauregg pointed out. A long severe course of malaria is apt to defeat the aims of the treatment by so debilitating the patient that his recuperative powers are irreparably damaged. They advise not to hesitate termination after three or four chills if the patient is in danger, probably re-inoculating a few months later. Combined typhoid vaccine may be used to

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round out a course if a second inoculation fails to cause sufficient reaction.

Transmission from donor to recipient is accomplished by subcutaneous or intra-muscular injection of two or three cubic centimeters of citrated malarial whole blood; citration being effected by drawing a half cubic centimeter of sodium citrate into the syringe before making the venapuncture.

Occasionally there is a slight febrile reaction from twelve to twenty-four hours after inoculation, followed by an incubation period from three to twenty-five days, as a rule in debilitated cases it is very short. The average patient is ambulatory during this stage and is allowed a general diet, high in calories. Provocative measures, such as intravenous injection of combined typhoid vaccine, may be employed to stimulate malarial paroxysms when their appearance is delayed.

With the appearance of paroxysms the patient is made bed-fast. The temperature and pulse are charted every hour so long as the temperature remains above one hundred and one degrees Fahrenheit, and every three hours during the intervals. Blood pressure is recorded daily during an afebrile period. Complete blood counts and urine examinations are made every other day. Blood chemistry determinations are made only on special indication since the routine examination of one hundred cases in the Psychopathic Hospital of Colorado (21) showed no variation in the blood chemistry due to malaria alone.

Alkaline drinks are forced; a light nutritious diet is given; the patient is kept under the covers and free from drafts. Patients are partially segregated for the purpose of improved nursing care. Contagion

MALARIA

is not considered a danger in inoculation malaria. Elimination is best accomplished by enemata.

Malaria is terminated with Quinine Bi-sulphate grains 10, three times daily until the blood has been plasmodia-free for fourteen days. For termination in emergency two cubic centimeters of one-percent solution of Quinine and urea hydrochloride is given intravenously.

After the termination of malaria the patient is given a high caloric, anemia diet. Administration of neo-arsphenamine or tryparsamide is begun because these workers feel it is valuable, both as a tonic and for its spirocheticidal effect. Physical rehabilitation is pushed as fast as possible. No patient is discharged to the out-patient department or referred back to the attending physician until he has regained a physical status comparable to that prior to his inoculation.

The indications for interruption are several:

1. A poor physical condition.
2. Intercurrent disease.
3. An increase in blood urea. A blood urea of over 20 milligrams per 100 cubic centimeters requires greater precautions. Usually the blood urea is equal to about one-half of the non-protein nitrogen, but in malarial infections such is not the case, as one may find a urea of 28 milligrams per 100 cubic centimeters with a non-protein nitrogen of only 39 milligrams (50). A urea increasing to 70 milligrams or over per 100 cubic centimeters of blood, with or without other signs of renal disease, is a positive indication for interruptions (8).
4. Systolic blood pressure below 95 millimeters during the interval between chills (8) or a pulse pressure below 20 millimeters of mercury (12).

MALARIA

5. Icteric index above fifty (8).
6. Red Blood Cell Count below two million (8).
7. A rapid progressive anaemia associated with a spontaneous cessation of chills (8).
8. Progressive diarrhoea accompanied by vomiting and dehydration (8).
9. Hemorrhagic encephalitis (8).
10. Hemorrhagic pachymeningitis (8).
11. Sepsis (8).
12. Rapid increase in the number of red cells invaded by malarial parasites (8), a parasite count of more than thirty-five in twenty-five consecutive fields (12).
13. Marasmus (8).
14. Congestion of lungs (12).
15. Congestive seizures (12).
16. Collapse (12).
17. Repeated hyperpyrexia i.e. over 106° F. (12), or a failure of the temperature to fall below normal in the interparoxysmal period.
18. Pulse rate over 150; respiratory rate over 60 per minute (12).
19. Albuminuria or haemoglobinuria other than transient (12).
20. Abnormal somnolence (12).

MALARIA

THE PROBLEMS AND THEIR TREATMENT ARE:

In debilitated patients the pyrexia not only appears soon after the inoculation, but frequently shows a tendency toward continuous high fever. As a rule it is best to terminate the treatment in these cases after two or three days of fever. Hyperpyrexia, i.e., fever of 106° F. or over, which persists over one hour must be actively combatted. Antipyretic drugs other than quinine are useless and dangerous. Warming the body surface by application of hot packs and warm bottles in patients who are chilling, stops the clonic muscular spasm of the chill, and the fever subsides. In the absence of chilling, hyperpyrexia is met by tepid sponging and colonic irrigations (21).

Circulatory collapse is treated as shock would be; the foot of the bed is raised, the body is warmed, and stimulation in the form of readily utilizable energy is supplied. Whiskey orally and dextrose intravenously are effective and glucose enemata are also employed. Malaria is promptly terminated. Digitalis is ineffectual (21).

Threatening heart failure requires termination. Cardiac tonics are dangerous, as during a rigorous disease with high fever, such as malaria, the toxic properties of these drugs are emphasized, while therapeutic advantages are negligible (21). Some (50) recommend giving cardiac stimulants such as caffeine, after the third to sixth chill even if the patient is in good physical condition.

The phenomena of blood pressure fluctuation is of special interest. It has frequently been stated that a systolic blood pressure below 90 millimeters of mercury is a dangerous sign. In fully 60% of Johnson's and Jefferson's cases (21), the systolic blood pressure fell

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below 90 millimeters of mercury during the course of the malaria, and in many instances during the paroxysmal period the systolic blood pressure has remained around 70 millimeters of mercury without danger to the patient.

Apparent mental complications are insignificant; except occasionally if true convulsions appear in which case the malaria must be terminated.

Epidural anaesthesia will frequently control shooting pains. Leuetic crises with girdle pain and severe vomiting require termination of malaria, when it brings them on (21).

Severe hemorrhages from the skin and mucous membranes require termination of the malaria. If it is necessary give transfusions; these are best given in a series of three or four with not over 100 cubic centimeters of blood in each (21).

Rupture of the spleen requires termination of malaria (21), and immediate surgical intervention (46).

Dependent edema responds usually to simple remedies such as hydrogogic cathartics, elevation of the foot of the bed, and measures directed to relieve anaemia, (21). Where herpes endangers the life of the patient, malaria should be terminated. Complete surveillance to prevent problems of secondary infection is in order (21).

Immunity to malaria may be noted in some patients usually against a certain strain of plasmodium. This disappears upon inoculation with blood containing a different strain of parasite (14); probably the "non-takes" by intravenous inoculation are due to cross agglutination (55).

For the preservation of malarial blood, one of the simplest procedures is that worked out by the Vienna and Hamburg Clinics (18), and is approximately as follows: - Several cubic centimeters of malaria

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infested blood are mixed with an equal amount of one-half of one percent sodium citrate in normal salt solution; and kept at or near body temperature. Blood treated in this way can be kept from twenty-four to forty-eight hours. By the use of a solution containing 5% sodium citrate and two-tenths cubic centimeters of 50% dextrose solution, into which twenty cubic centimeters of defibrinated (by agitation) malarial blood is injected, a strain of organisms has been transported from Rochester, Minnesota to Los Angeles, California, and successful inoculations made seventy-two hours after the blood was drawn. Vacuum bottles kept at body temperature were used for transportation (I).

York and Macfie (68) studied thirty-nine patients inoculated by the mosquito and found that the clinical results ran parallel with the inoculation of the asexual forms of the plasmodium, although the complications, relapses, and deaths were more numerous in the former.

One should not stop with one inoculation, but should continue to give the patients the benefit of the therapy as long as there is a reasonable chance for improvement (17B). Inoculations made on three different occasions showed improvement after the second, and further improvement after the third inoculation. These patients began to take more interest in things, were more tidy in their habits, and their general appearance was much better (17B).

DIATHERMY

GENERAL TECHNIQUE:

Successful treatment with diathermy depends on certain mechanical factors necessary to produce an elevation of temperature and to maintain it (33).

The work is based on the following premises: 1. The body may be considered an energy-producing and energy-dissipating mechanism, which is so kept in balance by the process of metabolism that its temperature normally remains constant. 2. If a means be provided whereby an outside source of energy can be dissipated into the body in the form of heat, and if at the same time precautions are taken to prevent the radiation of this energy, it is obvious that the general temperature of the body will rise because the energy gain will be greater than the energy loss. (24).

It is not absolutely necessary to have a special machine for this work, although such may be an advantage in shortening the time necessary to elevate the temperature. An ordinary high frequency machine is quite sufficient (57). Properly constructed electrodes must have an extensive edge because the current has a tendency to concentrate along the edges. Fenestration of electrodes is therefore necessary, and they should have undulating or festooned margins (33).

When extensive areas of the patient are treated with large amounts of current, ranging between four thousand to six thousand five hundred milliamperes, varying resistances are encountered depending largely on body thickness. In order to force four thousand milliamperes through the body with safety, the electrodes must be as large as possible. The regions above the iliac crests are the thinnest parts through which the current travels and here burns are likely to occur when currents above

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four thousand milliamperes are employed (33).

When a current above four thousand milliamperes is used, it is necessary to shunt a rheostat into the circuit, so arranged as to provide a passage of two-thirds of the current through the chest, one-third through the abdomen; however, several hundred treatments had been carried out successfully without a rheostat before its use was known and no outward (Continued on next page)

DIATHERMY

results were reported. With a special apparatus capable of delivering eight thousand milliamperes, it functions under load, with a voltage from thirty-five to one hundred and frequency between five hundred and one thousand five hundred kilocycles (33).

Insulation of the patient is accomplished by several blankets and a rubber sheet. These serve to prevent dissipation of heat from the patient who perspires most profusely (33).

The electrodes are made in three parts, one for the chest, one for the abdomen and a large one for the back, in thin people the abdominal electrode often being omitted. These are constructed of heavy blocked tin, and are cemented on sponge rubber pads, held in place by a scieltetics bandage jacket made of canton flannel (33).

The rate of rise of temperature depends on the mass of the patient, the amount of current employed and the efficiency of the insulation. In patients of low weight i.e., about one hundred and twenty pounds in weight and seventy inches tall, the rise of temperature is very rapid. In one or one and one-half hours a temperature of one hundred five degrees Fahrenheit is commonly reached. After this the patient's temperature rises one to two degrees high; with heavier patients the rise of temperature is slower and the current is usually kept on for about three hours. When hyperpyrexia occurs the covers are removed and if necessary cold sponge baths are given; the temperature being reduced with no untoward effects save vomiting in a patient whose rectal temperature rose to one hundred eight degrees Fahrenheit. (33)

Neyman and Osborne (33) tried to keep the temperature above one hundred three and five tenths degrees Fahrenheit for at least five hours;

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in some retaining same for nine hours.

The current should be started gradually at about three thousand milliamperes and not increased until the patient begins to perspire freely. It must be remembered that the final temperature overshoots the temperature reached when the current is turned off. Rectal temperature readings should be taken every fifteen minutes after the temperature reaches one hundred and four degrees Fahrenheit (33).

As would be expected, the discomfort from this high body temperature is very great; practically all patients except the depressed or demented types require some opiate after they have been in the treatment an hour or so. Hyoscin, morphine and cactin (the ordinary H.M.C. tablet) seems to be the most satisfactory combination. In addition to relieving the discomfort this remedy partially stops the sweating (23).

The chief problem concerns the blood pressure. At first it shows a systolic rise and later a diastolic drop; thus a pronounced increase in pulse pressure is frequently observed. Pressures of one hundred sixty systolic and zero diastolic are not uncommon, and are not usually due to an aortic dilatation, but rather to an increase in the heart rate and a dilatation of the peripheral vessels. After a series of treatments the blood pressure, both systolic and diastolic, is uniformly decreased and remains permanently at the lower level. No heart murmurs appear for the first time during the treatment (33).

Burns are a great risk, usually annoying, but rarely fatal, and occur usually because of faulty technique. A trained person should be in constant attendance, so that the current can be turned off if the patient complains of excessive heat on any particular part of the body. Localized

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burns are most apt to occur over bony points. They need not interfere with subsequent treatment as they may be annointed with salve and covered with a strip of rubber, such as a part of a rubber glove (33).

A rise in the body temperature after the current is shut off may occur; and the fever may reach an alarming height, due to an **unbalance** in the thermo-regulative center. This may occur in a few minutes after the treatment is discontinued, or several hours later. This should be combatted by removing the blankets, by tepid sponging, cold liquids by mouth, enemata etc.

The indications for interruption of treatment are: (57)

1. A urea increased to seventy milligrams or over per hundred cubic centimeters of blood with or without signs of renal disease.
2. Systolic pressure below ninety-five millimeters during the course of the treatment.
3. Beginning bronchitis.
4. Persistent muttering delerium.
5. Signs of Pulmonary edema.
6. Weakened cardiac sound
7. Marked exhaustion following treatment.
8. Thermoregulative center unbalanced as discussed above.

HOT BATHS

Mehrtens and Pouppirt (28) utilized a temperature of 110° F.: the patient was emmersed until the temperature of the patient reached a point within a degree and a half of the fever desired. Then the temperature of the bath water was gradually reduced until it corresponded with the temperature of the patient; each bath lasted one hour. The fever can be maintained for an additional hour by wrapping the patient in blankets and placing a few hot water bottles in bed. Liquids may be administered by mouth but they must be hot. As soon as it was found that no serious effects were to result from the hot baths, a number of private patients of the Soper-Mills Clinic (6) were allowed to take baths at home under the supervision of a relative; none of them suffered any untoward result. They gave one to two daily baths; one course consisting of fourteen baths; followed by a period of rest.

The psychologic reactions varied with the temperature. At temperatures of 98° to 102° F., the patients were calm and cooperative; on elevation of the temperature to 103° F., the patient frequently became restless and anxious and made efforts to elevate his limbs out of the water; as the temperature was raised to 105° they would become quieter and rather apathetic. Temperatures above 105° F. often resulted in mild confusion, extending in unusual cases for an hour after the patients return to bed.

Cady and Ewerhardt (67) placed their patients in a full length tub and the initial temperature varied from 38° C. to forty one and six tenths degrees C. (100.4° to 107° F.) according to the patients preference. Hot water was run in so the bath temperature gradually rose to 42° - 45° C. (104° - 111° F.). The patient's temperature rose to from 39° to 41° C. (102.3° - 106° F.) in twenty to forty minutes and continued for twenty to

HOT BATHS

forty minutes longer, when the patient was allowed to cool off either in the tub or in a cool shower bath.

The chief problems are: The patients become greatly fatigued. They often lose from three to five pounds weight per bath; however, this loss is made up readily by adequate diet before the next morning. The pulse becomes increased. The blood pressure in the majority of cases is reduced; the average reduction in this series (28) was fifty millimeters of mercury in the systolic reading and twenty millimeters in the diastolic reading. On the following day the blood pressure usually rose to its former level.

The basal metabolic rate was difficult to obtain, but in those cases where it was obtained and increase of eighty to one hundred percent was noted.

TYPHOID VACCINE

O'Leary (39) treated forty-eight cases using the following technique. He gave from one to four courses, each of which consisted of twenty intravenous injections. Injections were given every other day, and the courses were repeated at intervals of five to seven months. It was the practice to give twenty-five million bacilli at the first injection, and to increase the subsequent injections gradually, in order to produce the maximum reaction within the bounds of safety.

Wilson (18) injected intravenously the old strain of United States Army typhoid vaccine every other day until the patient had had ten days of fever. The vaccine is given in divided doses. One half the desired dose is given, and two hours later the remainder is given, thus a higher fever is produced. In two to three hours after the second injection the peak of the temperature elevation curve is reached and in seven to nine hours the temperature drops back to normal. On alternate days the patient feels no ill effects. On the first day one tenth cubic centimeters or one hundred million organisms, are given; with each successive treatment thereafter the dose is increased until on the tenth day, when each of the two injections contains one cubic centimeter or one billion killed bacteria. A liquid diet is given on fever days, and rarely does the patient lose weight. Common discomforts such as fever, chills, headache, epigastric pain, nausea, vomiting etc., are treated routinely.

It is important to maintain the temperature for at least four to eight hours or longer, and this can be accomplished during the chill period and period of early rise in temperature by wrapping the patient in warm blankets with hot water bottles placed about the body. The more robust the individual the better and higher the temperature reaction will be. (16)

TYPHOID VACCINE

The consistent use of one brand of vaccine does away with uncertainty of dosage (29).

A chill which lasts over twenty-five minutes requires a careful watching of the patient as he may have cardiac failure (29).

The complete course is usually eighteen paroxysms; followed by a recuperative rest period for several weeks. Often eating of high caloric extra meals is advised to regain weight and strength.

COMPLICATIONS OF PYRETOTHERAPY IN NEUROSYPHILIS

Complications are discussed under five main headings; first, those associated with administration of the therapeutic agent; second, those due to the therapeutic agent during the febrile period, these in turn being subdivided into mental and physical; third, those complications of syphilis stirred up during the febrile period; and fourth, those complications of the therapeutic agent and syphilis noted after the discontinuance of the therapeutic agent; and fifth, a miscellaneous group not well understood.

The complications associated with the administration of the therapeutic agent are met chiefly in Sodoku, and diathermy, the former manifesting a post-infectious necrosis at the seat of the inoculation, the necrosis being very extensive and slow healing, often lasting for a period of two months(50). Diathermy may give rise to severe burns, over areas exposed, which heal slowly.

The complications of mental character due to the therapeutic agent during the febrile period, are encountered chiefly in malaria. Delerium, ranging from a very mild muttering during the height of the temperature to an excited phase requiring physical restraint, is often present; occasionally a few hallucinations and delusions of a transitory character also make their appearance. These disappear with the cessation of the fever (36).

The complications of physical character due to the therapeutic agent during the febrile period, are the most numerous.

The weight loss in malaria varies from three to fifteen pounds,

COMPLICATIONS OF PYRETOTHERAPY IN NEUROSYPHILIS

the average being about eight pounds. This is soon compensated with a return to the weight previous to malarial inoculation, after interruption of same, with a continuance to gain in all successful cases (36).

In the nonspecific forms of protein therapy there is generally some weight loss but appreciably less in degree than is encountered in malaria (16).

Secondary anaemia is encountered in all cases of malarial inoculation, the average reduction in the red cell count being about 25%. Occasionally a 50% reduction was seen without serious results. The haemoglobin reduction in all cases corresponds to the degree of destruction of the red blood cells. A leukopenia was to be expected and was found in most cases; a leucocytosis in the eyes of these authors is always an indication for a further search for complications (8) due to secondary invaders. The combined typhoid vaccine caused secondary anaemia in almost all cases, this being very much less than that found in malaria; recovery from same occurring more quickly, the average time being one week after inoculation (16). An increase in red blood cells up to one million per cubic centimeter, an increase in haemoglobin, and an increase of three thousand to four thousand white blood cells per cubic centimeter were noted in cases where hyperpyrexia was produced by diathermy. This phenomenon is probably due to a concentration of the blood as a result of the loss of fluid through perspiration (13). Progressive weakness and fatigue were quite marked especially in malaria (36); these manifestations being less pronounced in the combined typhoid vaccine cases. Hot bath pyretotherapy was followed by great fatigue, in some severe enough that the patients

COMPLICATIONS OF PYRETOTHERAPY IN NEUROSYPHILIS

were unable to walk to their rooms (13).

Jaundice usually varies with the degree of red blood cell destruction and liberation of blood pigments.

Mild toxic dermatitis of the erythematous type has been chiefly encountered in cases treated with combined typhoid vaccine (39). Herpes Simplex, was encountered chiefly in malarial inoculation cases. It ordinarily is not important, but if, as is rarely the case, the ophthalmic division of the trigeminal nerve is infected, the eye of the patient becomes endangered (21). Ebaugh and Jefferson (11) have reported in detail a case of dendritic keratitis due to ophthalmic herpes, which resulted in the clouding of the cornea and impairment of vision.

Various degrees of toxemia; sweats; headaches; fever chills; bladder disturbances, especially inability to urinate; acidosis; and dependent edema, are encountered. 87% had nausea and vomiting right after a chill induced by typhoid vaccine (29).

Neuralgic and muscle pains often precede the paroxysms of fever in Sodoku (50).

Driver et al (8) reports a case of general paresis with hemiplegia; a fresh hemiplegia having developed during a malarial paroxysm.

A frequent occurrence is the condition of circulatory collapse. This being most probably due to the severe fatigue and the disturbance of vasomotor tone, similar to that occurring in shock. In fact, the clinical picture of this condition is similar to that occurring in shock. The patient is weak and pale, the skin is cold and clammy, the arterial and venous pressure falls rapidly, the pulse becomes soft and rapid, and finally syncope supervenes (21). In these cases peripheral venous stasis

COMPLICATIONS OF PYRETOTHERAPY IN NEUROSYPHILIS

and pulmonary congestion is strikingly absent, and the blood apparently becomes static in the splanchnic vessels. This condition is more common in those individuals showing aortitis and other cardiac lesions.

The complications of syphilis stirred up during the febrile period consist in a lighting of gastric crises and an increase in severity of the lightning pains (36), by malaria during chills, but subsiding during the intervals. On several occasions the gastric crises and lightning pains appeared for the first time, but lasted only as long as the fever (8). Possibilities of aggravation of vascular syphilis, such as an aortitis or a myocarditis, should always be borne in mind (21). Occasionally we have the appearance of a previously recognized hepatitis which, as reported in one case by O'Leary, persisted until intramuscular injections of mercury and intravenous injections of sodium iodide were substituted for the ineffective quinine (36).

The spleen in malaria is known to be more vulnerable than normally, probably due to the increase in fibrous tissue in the capsules and septums with resultant loss of elasticity that occurs in syphilis, and hence more susceptible to spontaneous rupture. At least ten authentic cases are reported to have followed malaria inoculation. Increased susceptibility, as mentioned above, is probably due to the loss of elasticity that must accompany a fibrotic process such as has been seen in the spleen in these cases. This applies to capsule as well as pulp. The enlargement is due to edema; engorgement with blood; wandering mononuclear cells and endothelial cells filled with parasites and debris of destroyed red blood cells. This apparently cannot occur within an inelastic capsule and septa

COMPLICATIONS OF PYRETOTHERAPY IN NEUROSYPHILIS

up to a certain degree in these patients, without rupture. The cases reported occurred in patients of ages 30 to 60, and the male sex predominating, by a high figure over the female sex. This complication manifests itself by a sudden collapse followed by an attack of severe weakness, which either ensued on a chill or followed exertion, such as a jump or resisting restraint. Abdominal pain was a predominant symptom in two of these cases. In several Kehr's sign was observed, i.e. pain very violent in character in the left shoulder. The patient occasionally vomits, has a tender abdomen, and shows the cardinal signs of hemorrhage.

(46)

The complications of the therapeutic agent and syphilis noted after the discontinuance of the therapeutic agent are: An acceleration of the degenerative processes; and, rarely, a chronic malarial infection.

The miscellaneous group of complications includes the dangers of virulent infections of the skin and the underlying tissues, and is always imminent in the violently disturbed patient. These usually start from self-inflicted wounds, such as scratches, abrasions, and contusions. Constant surveillance is essential and such seemingly unimportant matters must receive careful dressing and care in order to avoid catastrophe in the form of cellulitis (21). Hemorrhages from the skin and mucous membranes have been reported to occur; the cause is not known (21).

METHOD OF FORECASTING COMPLICATIONS

The patient should be under continuous supervision of a resident physician who is familiar with the complications of these procedures and who is on the alert for stigmata of same.

Temperature and pulse readings should be charted every hour or oftener so long as the temperature remains above 101° Fahrenheit and at least every three hours during the intervals.

Blood pressure readings should be recorded daily during the afebrile periods; and as frequently as deemed necessary by the attendant during the febrile periods.

Blood counts and urine analyses should be made frequently, at least every other day.

Blood chemistry determinations are made only on special indication (21); in patients showing evidence of toxicity. Repeated urea estimations (36) at daily intervals are of value. An increase in blood urea may be due to an increase in urea formation resulting from accentuated tissue catabolism, and hence must be correlated with other data before renal involvement is diagnosed.

Correlation of Clinical and Laboratory data is essential and it must be remembered that each case is different and must be handled accordingly.

PROCEDURES AFTER PYRETOTHERAPY

There is no unanimity of opinion as to the value of giving both the febrile therapy, and tryparsamide and its adjuvants, in any single case. Some believe that the results are better when malaria is used alone in the treatment of Paresis.

Solomon (61) is of the opinion that the combination is likely to be more satisfactory. His general method is to follow cases treated by malaria with long courses of tryparsamide. Johnson and Jefferson (21) feel it is valuable, both as a tonic and for its spirocheticidal effect.

Wilson (67) follows typhoid vaccine therapy by tryparsamide.

In reference to hot bath therapy Cody and Ewerhardt (6) state "in Wassermann-fast patients it tends to cause reduction in their serological reactions when used in conjunction with drug therapy". Mehrtens and Pouppirt (28) state that hot baths may be applied along with antisyphilitic therapy; it is even probably that the hyperpyrexia tends to intensify the therapeutic effect of the antisyphilitic medication.

O'Leary (36) in his experience with postmalarial antisyphilitic treatment noted a rapid decline in the patient's general health when the arsenical preparations were given shortly after malaria. This decline stopped when the intravenous medication was stopped. He advises a period of six months or more to intervene after pyretotherapy; thus doing away with deleterious effects of after treatment procedures.

It would seem that antisyphilitic medication may be used with safety six months after the malaria, but whether it is essential or not is, as yet, undecided.

RESULTS

The consensus of opinion is that a period of years must elapse before deductions are made from a new method of treatment; also, that in a disease which produces extensive destruction in the nervous tissue, which we know has little, if any regenerative power, it is folly to speak of cure even in the most liberal sense of the word. However, we must admit that in the treatment of general paralysis much has been accomplished if the system of treatment is capable of arresting the progress of the disease or putting the patient in remission (30). The conception of remission in general paralysis is not based on serologic reversals but is estimated on the patients economic status as a result of the treatment. If the laborer becomes a wage earner again; or if a lawyer after treatment resumes his practice of law, he is considered to be in complete remission. A bank cashier, who, after treatment, is able to carry out the duties of a competent bookkeeper etc., would be an example of only partial remission.

O'Leary (44 B) on observing 984 cases of neurosyphilis treated with malaria in the last nine years, gives data which cannot be surpassed for general information as to results with this form of therapy. His appraisal of dementia paralytica cases was based on the clinical status of the patient at least one year after the course had been given. If patients were treated in an asylum a remission was interpreted as evidence of sufficient improvement to warrant a paroling of the patient. Of the 186 cases treated, 35% showed complete remission and 35% showed sufficient benefit to be permitted to go on to their homes. Serologic results were discouraging, as they give no data for same. Of 200 cases of early dementia paralytica, 46% showed complete remission; fair results being obtained in 35%; serologically excellent results (i.e. negative) being obtained in 42%

RESULTS

of the cases and fair results in 45%.

The results in asymptomatic dementia paralytica have been highly satisfactory; included in this group were cases in which the serologic reactions were of the so-called chronic relapsing type; that is serologic reactions considered characteristic of dementia paralytica, became negative while the patient was under treatment, only to become positive again when the treatment was discontinued. Three fourths of the patients manifested decided clinical improvement and the serologic tests of the spinal fluid of half of them became completely reversed to negative. This type of case calls especially to attention the value of malarial inoculation therapy.

Of the 65 cases of the tabetic form of dementia paralytica, results were less striking. In 55% of the cases the progress of the disease was arrested to the extent that the patient could be classified as having a complete remission, whereas in an additional 39% the patients were capable of working at an occupation of one sort or the other. In only 24% were all tests of spinal fluid completely changed to negative.

Driver et al (8) publishing a summary of cases of general paralysis treated with malaria, recorded in the literature to April 1, 1926, show 27 $\frac{1}{2}$ % greatly improved with full remission; 26 $\frac{1}{2}$ % moderately improved with incomplete remissions and 46% unimproved where the condition became worse or death supervened. Total number of cases was 2,336.

Johnson and Jefferson (21) reporting on 130 cases of paretics treated with inoculation malaria report complete arrest clinically in 32% of the cases, incomplete arrest or improvement in 22%, unimproved 24% and deceased 22%. In general there was a tendency toward complete

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serological recovery in those who obtained good remissions. Among those not becoming completely negative serologically, various modifications occur. Certain cases of parenchymatous neurosyphilis, with a psychosis of pronounced functional coloring, often fail to show any remission of their psychosis even though physical improvement is present. In studying this group, they have reached the conclusion that the answer to the failure lies, not in the realm of histopathology, but in that of psychopathology. The psychosis in these patients shows, even at the onset, evidence of regression and dissociation, which signify their pernicious character. The discovery of personality defects in the parietic group is no uncommon thing and, that in some instances these should result in grave dissociation of the personality, is but an indication of the importance of psychopathology in the practice of neuro-psychiatry.

O'Leary and Welsh (44 B) in considering results in cases of tabes dorsalis treated by malarial inoculation divide them into four groups: Those frankly tabetic patients, with positive reactions of the spinal fluid; tabetic patients with gastric crises and negative serologic tests; tabetic patients with negative reactions of the spinal fluid and persistent, intractable lightning pains; and patients with primary optic atrophy as a complication of tabes dorsalis.

Their results in frankly tabetic patients with positive reactions of the spinal fluid, do not substantiate the impression that the results in the treatment of tabes dorsalis by malaria were less favorable than in the treatment of dementia paralytica. In 116 tabetic patients, 42 were decidedly improved, and 41% were benefited by malarial treatment. In 43% of all cases in this group, the reversal to negative of all serologic tests

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of the spinal fluid was complete. Twenty-five tabetic patients with gastric crises and negative serologic results showed that in 31% these crises almost completely disappeared after malarial treatment, whereas in 56% the interval between attacks was greatly increased and the severity of the spells lessened. The use of tryparsamide and a bismuth preparation following malarial treatment has been of material value to these patients. 12 Tabetic patients with persistent "lightning" pains showed 11% were entirely relieved, and 22% were benefited by malarial therapy. Forty-eight cases with primary atrophy as a complication of Tabes Dorsalis showed only a temporary arrest in the progressive loss of vision. In 22% of the cases the process was slowed.

Bering concluded (9) from a study of 65 cases observed and followed up for two and one-half years, that malaria treatment resulted in improvement in from 75 to 80% of cases of Tabes.

O'Leary and Welsh (44 B) report the most satisfactory results in the group of cases included under the heading of asymptomatic neurosyphilis; i.e. cases in which the reaction of the spinal fluid was positive but in which the symptoms and signs were insufficient to permit a diagnosis of neurosyphilis. In 42% of these 74 cases the spinal fluid became negative after malarial therapy, while in an additional 37% the serologic evidence was reduced to a negative globulin test and cell count, and the Wassermann test remained positive. All these patients had received intensive antisyphilitic treatment without favorable influence on the serologic tests previous to malarial inoculation.

O'Leary and Welsh (44 B) found the results with treatment with malaria of 17 patients with congenital neurosyphilis discouraging.

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Congenital cases of dementia paralytica, the tabetic form of dementia paralytica, tabes dorsalis, gastric crisis and optic atrophy were included in this group, and although certain patients derived systemic benefit, the results were far less beneficial than those noted in corresponding types of acquired neurosyphilis; only 8% getting fair results.

Their results were discouraging, although no significant ill effects were noted in meningovascular neurosyphilis. Severe neurorecurrences, manifested by syphilitic meningitis with high pleocytosis, and clinical evidence of severe chronic meningitis, developed in three cases of acute syphilis following the inadequate use of neoarsphenamine, during the acute stages of their disease.

Solomon and his co-workers (59) called attention to the fact that clinical and serologic improvement has resulted in some patients treated by Sodoku, which would indicate that it has some therapeutic value.

Urechia and Mihalesci (65) published results of injections of brewer's yeast in the treatment of 104 paretics. They claim that of these, 35 were subsequently more or less able to return to work, 35 were improved, and 34 were unimproved.

Tuberculin is obsolete now in the treatment of neurosyphilis. The first report in 1901 (50) included 69 paretics with many more favorable remissions than occurred in 69 controls treated with mercury and iodides. A. Pilez of Vienna reported twenty six and eight tenths percent complete remissions in paretics, while Weygandt of Hamburg had success in thirty-three and one third percent of his cases.

Placet in 1926 (12) reported his experience over six years

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with the spirochaete of African relapsing fever and considered the results of malaria and relapsing fever about equally balanced.

Henderson (18) says relapsing fever produces no favorable results in the United States because there are not strains of sufficient virulence available. Solomon (6) does not believe it will ever become a practical method.

O'Leary (37) in 1929 reported that the results in injection of typhoid vaccine in place of inoculation malaria are very encouraging, stating the percentage of remissions and serologic reversals as slightly less than when malaria is used.

O'Leary in 1930 (39) treated 48 cases with one to four courses of typhoid vaccine and concluded that in the paretic group no economic remissions were produced comparable to those observed following treatment by malaria; and serologic changes had not been significant. Likewise, in the non-paretic group the results were not encouraging. He advises the use of typhoid vaccine merely as an adjuvant to malaria where malaria has aborted.

Epstein and Paul (13) in 1933, in reporting their results on the treatment of neurosyphilis by diathermic hyperpyrexia, obtained the most striking results in a group of 13 tabetics. Six showed marked improvement and 4 manifested some improvement especially in the relief of crises and lightning pains. Their opinion is that diathermy should be used as an adjunct in the treatment of neurosyphilis. Severe types of paresis could not be controlled.

In their first publication on the use of diathermy Neyman and Osborne (33) reported on the treatment of 25 cases of paresis, of which

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three were depressed, seven grandiose, eleven slowly dementing and five totally demented at the beginning of treatment. They report complete remission in sixteen percent, although serologic changes did not correspond to the amount of clinical improvement. They found a decrease in cells in all except two cases, and the colloidal gold decreased in intensity in ten and became practically negative in five.

J. E. Potter (48) states that diathermy is considered superior to malaria in that the fever can be controlled, and says that no serious sequellae have followed its use in selected cases.

Mehrtens and Pouppirt (28) reporting their results on cases where hot baths were used, report that in twenty cases of Tabes, every patient showed improvement in some way. The lightning pains, gastric crises and charcot joints yielded to hot baths more readily than any other therapy previously used. Amelioration of symptoms was not always permanent, although the relapses were further apart, less severe and more amenable to another series of baths.

LABORATORY

The consensus of opinion regarding studies of the spinal fluid and blood, is that they do not afford a true index of the value of pyretotherapy (40). In general there is a tendency toward complete serological recovery in those who obtain good remissions of the disease. The cases without complete serological recovery present various modifications. There is no strict parallelism existing between the clinical improvement and the improvement in the serology, cell count etc. However, during the later stages a greater parallelism is approached (37).

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Results are often markedly confused by the fact that pyretotherapy is followed by chemotherapy (21). Likewise, no parallelism was found between the serological improvement and the maximum of temperature, while in malaria parallelism is evident between the number of chills and the percentage of improved cases (14).

Birley (2) in discussing problems in the treatment of neurosyphilis, maintains that the Wassermann reaction is not specific biologically, and its value as a guide to and as an indication for treatment cannot, therefore, be regarded as absolute.

Ferraro and Fong (14) observed that the spinal fluid Wassermann was third in order of improvement following "inoculation malaria". The rate of improvement within the first six months was twenty percent, increasing to ninety percent in thirty-six months. Sixty-eight percent of the cases of thirty-six months standing showed a complete negative reaction. He reported thirty-nine cases.

The blood and spinal fluid Wassermans in cases treated by diathermy, shows some change for the better, the complete reversals being relatively few: However, sufficient numbers of cases had not been reported to justify many remarks.

After typhoid vaccine therapy modification was encountered in the blood and spinal fluid Wassermans. The blood Wassermann was reduced from a four plus to a negative reaction; while the spinal fluid Wassermann was changed from one hundred percent positive reaction in all dilutions to negative reactions in at least fifty percent of the cases (16).

Hot baths in Wassermann-fast patients tend to cause reductions in their serological reactions when used in conjunction with drug therapy.

LABORATORY

Hot baths alone cause very little change (6).

In all cases of malaria therapy a secondary anaemia develops. Driver and all (8) report an average red cell count decrease of 25%, and they have occasionally seen a 50% reduction without serious results. The haemoglobin is reduced in all cases corresponding to the degree of destruction of the red blood cells. Leukopenia is expected and was found in most cases. A leucocytosis warranted a search for complications. The secondary anaemia after typhoid vaccine is not quite as severe.

In typhoid and paratyphoid vaccine therapy a leukopenia generally occurs during the height of the chills and a leukocytosis of twelve thousand or more at the peak of the temperature (16).

The blood picture in diathermy undergoes a change due, in large part, to concentration phenomena, as pointed out above. The red blood cells, white corpuscles, and haemoglobin increase. There is a relative increase of polymorphonuclear leucocytes and eosinophiles, with a corresponding decrease of the small and large mononuclear leucocytes (52). Hot baths cause a transient leucocytosis during the bath, followed by a brief reduction in the white cells (6).

Ferraro and Fong (14) observed that the spinal fluid cell count was the first of the laboratory findings to improve following inoculation malaria. The pleocytosis may be reduced within a few days following the institution of treatment. About 50% of the cases showed a complete reversion to the normal number of cells in twenty-four months. The globulin content, although improving, shows less pronounced changes than the cell count.

The colloidal gold after inoculation malaria was the most

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resistant to treatment. Only twelve of thirty-nine showed improvement within twelve months (14). Thereafter the improvement increases gradually although the reversal to an absolute normal curve is rare. After diathermy it tends to decrease in intensity and the paretic curve often becomes atypically tabetic; Neyman and Osborne report the former in ten cases, the latter in five, out of twenty-five cases (33).

Goldsmith's (16) findings in typhoid vaccine therapy coincide with those of Kunde and his co-workers. They found that a most striking reduction occurs in the colloidal mastic or gold curve. In 80% of all the cases treated, there were varying degrees of modification from a high paretic curve to a negative one. Occasionally the colloidal gold curve is reduced by hot baths (6).

Diathermy causes an increase in the non-protein nitrogen of the blood. The carbon dioxide capacity of the blood plasma decreases while the chlorides in the blood and the calcium in the serum show only a slight variation (52). An increase in urea nitrogen to seventy milligrams or over per one hundred cubic centimeters, with or without other signs of renal disease is given as a sign for interruption of malaria (1) and discontinuance of diathermy treatments. These phenomena are discussed above.

A fall in blood cholesterol averaging about 10%, and a rise in blood sugar averaging about 10%, are often caused by very hot baths. No material influence upon the urea nitrogen, blood uric acid or proteolytic or lipolytic enzymes has been observed (54).

CASE I: (44) PARESIS TREATED BY MALARIA

Patient was a middle-aged successful lawyer. During the winter of 1925 his business associates noted unusual extravagance, and a decrease in the acuity of his judgment and decision. The changes progressed rapidly, he became irritable, agitated, destructive, and threatening, and was placed in an asylum. Four months later he was admitted to the Mayo Clinic; at this time the Wassermann reactions on the blood and spinal fluid were strongly positive, the Nonne reaction was positive, lymphocytes numbered 91, polymorphonuclear leucocytes 20, and the colloidal benzoin reaction was 002 320 333 333 000. He was inoculated with *Plasmodium vivax*. The course was stormy because of extreme dementia, but he nevertheless completed a series of twelve pyrexial paroxysms. Convalescence extended over a period of two months; he has had no antisyphilitic treatment since the treatment by malaria two and a half years ago. He still is in a complete remission and has regained and maintained a successful law practice. Two years later inoculation malaria, the spinal fluid and blood were completely negative in all factors and objective signs of paresis were not present.

This is an example of an ideal type of paresis to treat by malaria. Although the patient was acutely demented, very little cerebral degeneration had occurred. This case also presents a striking example of the value of the treatment, unaided by any other type of antisyphilitic medication, in producing complete remission; and complete serological reversal.

CASE II: (9) TABES TREATED WITH MALARIA

Patient J. B., male, age 40, had been unable to work since 1923, complaining of pains and increasing ataxia; previously discharged from two hospitals "cured of syphilis". The condition at examination presented typical tabes; the blood Wassermann was 1 - 2; spinal fluid Wassermann 0 - 0; protein 28; sugar 51; gold curve 111233220. He received thirteen malarial paroxysms. Twenty-eight months later he was receiving neoarsphenamine in the outpatient department; was selling newspapers, supporting self; having slight pain which patient estimates to be decreased 70%; ataxia apparently increasing; spinal fluid Wassermann 0 - 0; sugar 82; protein 75; gold curve 000,000,000.

This case illustrates the fact that if advanced degeneration has taken place in the central nervous system, efforts with pyretotherapy are quite futile. This case did get a good serological result.

CASE III: (17) NEUROSYPHILIS TREATED BY TYPHOID VACCINE

Male, aged 26 years, acquired syphilis in 1918, and received an indeterminate amount of treatment at the time. In November 1926, the Wassermann reaction of the blood and of the spinal fluid was strongly positive; the Nonne reaction was positive; there were twenty-two lymphocytes for each cubic millimeter in the spinal fluid, and a Zone II or tabetic type of colloidal benzoin curve. The neurologic examination was negative for signs of parenchymatous neurosyphilis, although the patient's family had noted a change in personality, forgetfulness, and loss of ambition. A diagnosis of neurosyphilis was made, possibly of

CASE III (Continued)

the paresis sine paresi type. Between November 1926, and June 1927, the patient received two courses of combined intravenous and intraspinal injections, in conjunction with forty-six intramuscular injections of succinimide of mercury and large doses of iodides. At the end of this time the spinal fluid was strongly positive, and treatment by malaria was recommended. He gave a history of having had malaria in 1920. He was inoculated with two different strains of the Plasmodium vivax a week apart, but they failed to "take". The injection of foreign protein and of whole blood did not precipitate the chills and fever. Following a course of quinine, typhoid vaccine was given intravenously. Fifteen injections were given at intervals of two days. The initial injection contained 25,000,000 bacilli, and the dose of each subsequent injection was increased until 400,000,000 bacilli were given at each of the last three treatments. On the day of the last injection the patient noticed icterus. Within three days he was markedly jaundiced, and the test of hepatic function showed the extreme degree of dye retention, serum bilirubin of 22.4 milligrams, and a direct Van den Bergh reaction. The blood smears were still negative for Plasmodium vivax. Duodenal lavage was carried out, mild cathartics were given, and a diagnosis of mild toxic hepatitis was made. In less than three weeks the jaundice had disappeared. Two months later the tests of hepatic function were negative and the patient had gained eight pounds. It was suggested that he should not receive treatment for the next nine months. On his return at the end of this time he had gained twenty pounds; he had lost many of his "neurotic complaints", and had carried on his work during the previous nine months. There was no change of significance in either the blood

CASE III (Continued)

or spinal fluid. Practically the same status was noted when he returned a year later.

CASE IV: (16) NEUROSYPHILIS WITH A CARDIAC COMPLICATION TREATED BY COMBINED TYPHOID VACCINE

R. D. C. - age 30 years, colored man, brought in by police and relatives showing much confusion with only partial orientation. Physical examination reveals dilated pupils, react sluggishly to light and accommodation; fine tremor of tongue, deep reflexes hyperactive, superficial present and active. Heart marked increase in cardiac dullness to left, loud rumbling systolic murmur heard in pulmonic area, transmitted along left border of the sternum. Pulse too accentuated and roughened, thrill felt in pulmonic area, apex beat prominent and diffuse. Pulse "84" per minute, Blood Pressure 132/86. Serology: Blood Wassermann 100% in plain blood and Cholesterinized C.S.F. 75% in 1 c.c., 50% in $\frac{1}{2}$ c.c., 0 % in $\frac{1}{4}$ c.c. Colloidal mastic shows a negative curve. Mental findings: Hallucinations auditory and visual; disorientation, memory defects, poor insight and judgment. Diagnosis: Psychosis with cerebrospinal lues. Patient was given a series of nearsphenamine and bismuth intramuscularly with spinal drainage. After that he received 16 injections of combined typhoid vaccine and when that was completed he again received a series of 6 injections of nearsphenamine and bismuth with spinal drainage. He began to improve following treatment and by the time typhoid was completed he was normally reactive, mentally, in all directions with good memory and fair amount of insight and judgment. His temperature range during treatment was as high as 106° the average being 104°. There was little

CASE IV (Continued)

untoward reaction despite the fact that patient had a marked cardiac condition. He is working and apparently has made complete remission in his condition. Serology previous to his parole shows blood Wassermann negative in plain blood; 75% in cholesterinized blood; C.S.F. negative. Colloidal mastic 3-4-4-3-2-1-1-0-0.

This case is interesting for several reasons. First, the man had a definite cardiac condition, yet despite the high temperature range, he showed no untoward physical difficulty. Second, while mastic curve previous to treatment was negative, it jumped to a rather high luetic zone curve after treatment despite the fact that the C. S. F. became negative with some reduction in the blood Wassermann, which again illustrates irregularity which may occur in the serology as against clinical improvement manifested.

CASE V: (54) CASE TREATED BY HOT BATHS

T. L., colored man, married, age 49. Chief complaint was pain in the back, leg and the occipital region. Venereal exposure "many years ago". On physical examination he had a Blood Pressure of 178/114. Neurologic examination shows an Argyll-Robertson pupil. No cranial nerve palsies. Arm reflexes normal. No incoordination or sensory disturbances. Abdominal and cremasteric reflexes present. K.J. present. A.J. left present and right absent. Laboratory: Wassermann: Kolmer ~~4~~3-0-0-0; Kahn 0-0-0. Spinal fluid, cells 23.6, sugar positive, globulin slightly increased. Colloidal gold 3333221000. Wassermann negative. Diagnosis: Cerebrospinal lues and hypertension.

CASE V: (Continued)

He received 7 forty-five minute baths, one day apart, the body temperature being elevated to 104°-105° F., and gradually diminished reaching normal about one hour after the bath. His pains disappeared after the fifth bath. The day after the baths were discontinued the Wassermann was: Kolmer ~~3~~2-0-0-0, Kahn 0-0-0; Cerebralspinal fluid cells 17; protein very slightly increased; sugar positive. Wassermann was positive 1; Colloidal gold was 2222100000; Blood Pressure 158/80. Since his baths he received a total of 0.3 gm. of bismuth. After that the Wassermann was Kolmer 0-0-0-0; Kahn 0-0-0.

CASE VI: (33) CASE TREATED BY DIATHERMY

F. M., depressed type of dementia paralytica, having a cell count of 58, Pandy reaction ~~4~~, Wassermann ~~4~~, Colloidal gold 5554432100, before treatment. He received 10 treatments. The temperature was kept above 103.5° F. for twelve hours. After treatment his cell count dropped down to 3, the Pandy reaction became ~~3~~, Wassermann ~~4~~, Colloidal gold 5555543100. Clinically he was in remission and returned to his former occupation. The total days spent in the hospital were 124.

This case illustrates the value of diathermy in producing clinical remission in cases where little degeneration has occurred. Serological reversals are not as encouraging as observed in malaria.

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