

emotionally induced in the otherwise frankly epileptic, these statements gradually lost place in modern works until to-day it reappears in many clinical studies almost like a new fact, that many attacks in epileptics are emotionally induced. For some time the situation has been made the most of by many quacks in dealing with many excitable and neurotic epileptics. Any one having much to do with epileptics, especially one living in close contact with them in colonies and institutions, daily witnesses true epileptic attacks psychically induced. Many types of peculiar seizures are also seen which are not epileptic at all but possess many characteristics akin to genuine hysteric convulsions. No two neuroses, any more than two organic nervous disorders, are mutually exclusive. A luminous essay might easily be made from a study of the various psychoneuroses seen in epilepsy. Many phenomena now classed as epileptoid or epileptic manifestations such as the epileptic twilight state, day dreams, temporary absences following emotional affects, frights, panics, distractions, pure phantasies and a notable criminal disposition shown in cruelties and assaults, may all be shown in part if not wholly to be due to outbursts of incompletely repressed affects. There can be no doubt that many such symptoms compared with the same occurring in pure psychoneurotics are in no respect dissimilar in manifestations or cause. Not a few of the so-called reflex and traumatic epilepsies of the past have been but thinly disguised psychogenic convulsions. One must bear in mind that in such cases the ordinary so-called stigmas of hysteria are absent, but even tongue biting and incontinence of the bowels and urine may occur and yet the disorder be psychoneurosis. I have seen two cases of the latter sort proved out by observation and treatment. However, true that in the majority of epileptics tongue biting and passing of urine in the attack may be good evidence for an organic or genuine epilepsy, one needs to remember that such symptoms *can* occur and the case not be one of epilepsy.

In the light of the foregoing it is easier now to make disposal of many reports of atypical and bizarre epilepsies, especially such as have been reported by Brush, Newmark and Sanger Brown. It is obvious, therefore, in a given case of epilepsy which shows none of the make-up of the epileptic constitution and no physical or mental deterioration from the malady, that one should consider such a case with the greatest care in the light of our knowledge of affect epilepsy or a psychogenic convulsant in a neuropath. One also should remember that a few cases of dementia praecox have epileptoid attacks. I meet such patients almost weekly. If time permitted I could cite many illustrations of the fact. At present I have no less than four cases of mixed types of convulsive attacks to diagnose differentially. In a brief statement it may be said that psychoneurotic episodes are differentiated from the ordinary types of so-called genuine epilepsy in that the former are symptomatic expressions of incompletely repressed and painful affects, having greater constancy, are often prevented or repressed purely by suggestion, may be displaced or prevented by psychoanalysis and are usually unfavorably influenced by sedatives. The amnesic episodes are purely functional, and intelligence tests show no defects. The promptness and completeness by which the affect epilepsies may be cured make one wish that ordinary epileptic states were more frequently of this less grave nervous disorder. I attempt a partial analysis of every

case of genuine epilepsy in the hope of removing many of the psychic elements that may act as irritants to the true disorder. It often fortifies the ground gained in the improved and arrested cases of epilepsy. Careful psychoanalytic studies in true epilepsy are still to prove a mine of valuable and practical facts. It may yield data of practical points in treatment.

I wish to emphasize the great importance of establishing a central laboratory for research in convulsive disorders, the organization of which I made the basis of an address several years ago in the New Haven meeting of this association. Almost every other grave and wide-spread disorder which afflicts humanity by the thousands has had its special private or state endowment, and its laboratories busy in research. In the general study for the betterment of such human scourges as cancer, tuberculosis and insanity the cause of research into the nature and prevention of epilepsy seems to have lagged far behind. I am sure that no one thing would advance human welfare more than such a central laboratory for intensive research into the cause and prevention of epilepsy.

I trust the foregoing clinical exposition is of sufficient moment to warrant my further report on the several subjects at this time, and that it will be of sufficient interest to stimulate further clinical research into the still obscure clinical manifestations of this strange disease.

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A CULTURE OF B. TUBERCULOSIS FROM THE BLOOD POST MORTEM OF A CASE OF MILIARY TUBERCULOSIS

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A careful review of the literature on tubercle bacillæmia has failed to show a single instance in which the tubercle bacillus has been grown from human blood. A few unsuccessful attempts to obtain such cultures are cited by Bergeron¹ in his review, which is dated 1904. Anderson² in 1909 made blood cultures from forty-eight cases of tuberculosis, all of which were negative. He was successful in obtaining three positive blood cultures from eight artificially infected rabbits, and this is the only recorded instance in which the tubercle bacillus has been cultivated from the blood of tuberculous subjects.

The reasons for such uniformly negative results are easily seen. Any one who has attempted to grow tubercle bacilli, even from material rich in organisms and uncontaminated, is familiar with the difficulty of getting the growth started. Complete aerobiosis, a carefully regulated temperature, carefully titrated mediums, and proper moisture are all necessary to induce Koch's bacillus to multiply on artificial soil. Cultures from the blood present several obstacles to the attainment of the above ideal conditions, chiefly the fact that the few organisms which might be present in the small amount of blood utilizable will in all probability be buried in a mass of red cells and fibrin if the blood is poured over solid mediums, and so be shut off from the access of oxygen in the air. Even should

1. Bergeron, André: Etude critique sur la présence du bacille de Koch dans le sang, Thèse 223, Paris, 1904.

2. Anderson, J. F.: The Presence of Tubercle Bacilli in the Circulating Blood in Clinical and Experimental Tuberculosis, Bull. 57, Hyg. Lab., U. S. P. H. S., 1909.

growth begin and a colony develop, it would be extremely difficult to find on the rough and heterogeneous surface of such a culture. Poured agar cultures and cultures in liquid mediums are open to a similar objection, namely, the conditions of partial anaerobiosis. The ideal method would seem to be to take the blood in sterile distilled water, centrifugalize at high speed and spread the sediment over the surface of suitable solid mediums. The writer has twice attempted this method without success, but still believes it to offer the best chances of success.

The other main reason for previous failure is the fact that tubercle bacilli cannot be demonstrated in the blood by any valid method in more than a small percentage of cases of tuberculosis. Fraenkel³ reviewed the whole subject very thoroughly in 1913, and after concluding that animal inoculation is the only safe test for the presence of tubercle bacilli in blood, compiled figures from the literature to show that about one hundred positive inoculations had resulted from five hundred experiments. He adds that many of these positive results are of questionable authenticity. In many instances the antiformin method had been used and the finding of acid-fast bacilli in tissues without gross tuberculous changes had been accepted as sufficient evidence of tuberculosis.⁴

It may therefore be of interest to compile the results of inoculating guinea-pigs with the blood of tuberculous patients and to note the number of cases in which the presence of the tubercle bacillus has been demonstrated by gross tuberculous changes in the test animals. Collecting the statistics embodied in papers⁵ published in the last three years (1911-1914), I have found that the blood from 1,060 cases of tuberculosis was so tested and that forty-five of the guinea-pigs used showed gross tuberculous changes. These figures indicate 4.2 per cent. positive results, but the actual figure is undoubtedly even lower, because in many of

the tests two guinea-pigs were used and in some instances, at least, both of them became infected.⁶

In view of this low figure it is clear that most attempts at cultivating *B. tuberculosis* from the blood are foreordained to failure. This is true particularly for cultures made *intra vitam*. With blood cultures made at necropsy, however, the outlook is more promising. Meisel⁷ reported eight positive inoculations from eleven cases, and Seidenberger and Seitz⁸ reported nine out of twenty-six, all the guinea-pigs showing gross changes. These figures, the only ones that I have been able to find bearing on this point, show 38 per cent. positive inoculations from blood taken at necropsy. It appears, therefore, that shortly before death tubercle bacilli appear in the blood stream either in greater numbers or with greater frequency than before this time.

Between February and July, 1914, blood cultures were made at the Babies' Hospital from twenty-one cases of miliary tuberculosis. Ten cultures were made during life, fourteen after death, and in three cases cultures were made both before and after death. The quantity of blood taken varied from 1 to 5 c.c. Of these cultures only the one here reported was positive. In one other case a number of acid-fast bacilli were found in the culture at the end of two weeks, but the growth—if it was a growth—failed to develop further and later the contents of the tube failed to infect a guinea-pig. In another case the numerous acid-fast bacilli found in the smear were shown to have come from distilled water used in making the preparation for microscopic examination. These experiences emphasized to the writer the dangers of purely microscopic diagnosis in tuberculosis and the absolute necessity of corroboration by animal experiments.

The patient from whom the positive culture was obtained was a white boy 2½ years o'd, whose tuberculous infection dated back about two months and was the sequel of an attack of whooping-cough. The diagnosis of tuberculosis was made during life and corroborated at necropsy. Cheesy bronchial lymph-nodes, extensive caseous change, with a cavity in an area of old bronchopneumonia in the left upper lobe, tuberculous ulcers in the intestine and miliary tuberculosis of the lungs, spleen, liver and kidneys, were the principal pathologic findings.

Blood was taken for culture in the following manner: After opening the thorax, the pericardium was slit with scissors and the edges folded back. An area of about 2 x 2 cm. over the right ventricle was carefully seared with a red-hot knife. The knife was again heated and immediately plunged into the heart cavity. A sterile pipet was introduced into the opening and a little over 1 c.c. of fluid blood was withdrawn and transferred directly to a plain agar slant. The tube was laid so that the blood covered the surface and, when the necropsy was completed, sealed with paraffin and laid in a similar position in the incubator.

This culture, not originally taken for the purpose of demonstrating tubercle bacilli, remained apparently sterile, and it was decided to keep the tube as part of a series of blood cultures from tuberculous patients, which was begun at this time. The tubes of this series

3. Fraenkel, E.: Nachweis von Tuberkelbacillen im strömenden Blut. Schmidt's Jahrb. d. Med., 1913, cccxvii, 317.

4. In view of the work of so many investigators (Brem, Walter V.: Investigation of Blood for Tubercle Bacilli, THE JOURNAL A. M. A., Sept. 18, 1909, p. 909. Von Lehmann, A.: Eine Fehlerquelle bei der Antiforminmethode, Deutsch. med. Wchnschr., 1913, xxxix, 1556. Holmes, E. B.: A Study of the Alleged Presence of Tubercle Bacilli in the Circulating Blood; Am. Jour. Med. Sc., New Series, 1910, cxxxix, 99. Kahn, E.: Zum Nachweis der "Tuberkelbacillen" im strömenden Blut, München. med. Wchnschr., 1913, cx, 345. Dreesen, H.: Ueber das Vorkommen von Tuberkelbacillen im strömenden Blute, Med. Klin., 1913, ix, 580.) proving that acid-fast bacilli are frequently present in distilled water and therefore in reagents made up with distilled water, it would seem that the time has come to reject the antiformin method and all other methods in which the diagnosis of tuberculosis is made from simple microscopic demonstration of acid-fast bacilli and to discard the results of previous experiments based on such methods.

5. Rumpf: München. med. Wchnschr., 1912, No. 36. Bernard, Debré and Baron: Recherches sur la bacillémie chez les tuberculeux, Bull. Soc. d'étude scientif. sur la tubercul., 1912, ii, 154. Querner, E.: Ueber Vorkommen von Tuberkelbacillen im strömenden Blut, München. med. Wchnschr., 1913, cx, 401. Bacmeister: Virulente Tuberkelbacillen im Blut nach der diagnostischen Tuberculininjektion, München. med. Wchnschr., 1913, No. 9, p. 343. De Verbizier, A.: Nouvelles recherches sur la présence du bacille de Koch dans le sang circulant des tuberculeux, Rév. de méd., 1913, xxxiii, 161. Fraenkel, E.: Tuberkelbacillen im strömenden Blut, Deutsch. med. Wchnschr., 1913, xxxix, 737. Rist, Armand-Détille and Lévy-Bruhl: Sur la prétendue bacillémie des tuberculeux, Bull. Soc. d'études scientif. sur la tubercul., 1913, iii, 19. Rothacker and Charon: Das Vorkommen von Tuberkelbacillen im strömenden Blut, Centralbl. f. Bakteriöl., 1913, cxix, 478. Elsaesser, J.: Tuberkelbacillen im Blutstrom bei Lungentuberkulose, Beitr. z. klin. Tuberk., 1913, xxvi, 367. Kachel: Ueber Tuberkelbacillen im strömenden Blut, Beitr. z. klin. d. Tuberk., 1913, xxviii, 275. Moewes and Brautigam: Tuberkelbacillen im Blute, Deutsch. med. Wchnschr., 1913, xxxix, 2031. Klopstock and Seligmann: Zur Frage des Vorkommens von Tuberkelbacillen im strömenden Blut, Ztschr. f. Hyg. u. Infektionskrankh., 1913, cxvii, 77. Haas, W.: Ueber den Nachweis von Tuberkelbacillen im strömenden Blut bei chirurgischen Tuberkulosen, Beitr. z. klin. Chir., 1914, xc, 78. Storath, E.: Ueber Bedeutung und Auftreten virulenter Tuberkelbacillen im Blut nach der diagnostischen Tuberculininjektion, Ztschr. f. Tuberk., 1914, xxii, 1. Mayer, A.: Ueber das Vorkommen von Tuberkelbacillen im strömenden Blut und in der menschlichen Milch, Ztschr. f. Tuberk., 1913, xxi, 447. Seidenberger and Seitz: Ueber das Vorkommen von Tuberkelbacillen im Herzblute bei chronischer und latenter Tuberkulose, Virchows Arch. f. path. Anat., 1914, ccxv, 89. Liebermeister: Deutsch. med. Wchnschr., March 13, 1913 (Discussion).

6. It has been objected that guinea-pig inoculation is not a perfect test for the presence of tubercle bacilli in tissues because one bacillus will not certainly cause infection. This is true. Nevertheless, since purely microscopic methods are not above suspicion, animal inoculation is at present the only satisfactory test. It is also very delicate since Selter (Vortrag auf d. Niederrhein, Ges. f. Nat. u. Heilk., Bonn, July, 1912, Discussion), as is well known, showed that ten bacilli almost certainly infect a guinea-pig.

7. Meisel, W.: Vorkommen von Tuberkelbacillen im Blute bei der allgemeinen Miliartuberkulose, Wien. med. Wchnschr., 1884, Nos. 39 and 40.

8. Seidenberger and Seitz: See Footnote 5.

were examined microscopically once or twice a week. In the process of examination the contents of the tube were scraped with the platinum loop and partly redistributed over the surface. This not only gave access of air to the bacilli present but probably formed a layer of serum on the agar surface in which the bacilli could multiply. It is certain that plain agar is not a suitable medium for initial cultures of the tubercle bacillus and the successful growth in this case must be attributed to some such fortuitous circumstance.

After two weeks' incubation two or three acid-fast rods were seen in smears from the culture but as these were not perfectly typical no transplants were made. When the culture was one month old a clump of acid-fast bacilli, consisting of about twenty organisms, was found. These looked much more like genuine tubercle bacilli but were so closely clumped that identification was not then clear. Transplants were now made to glycerin-veal-agar, blood-agar, coagulated egg and to tubes of the egg-broth medium recently devised by Besredka and Jupille. The last proved to be the most suitable medium and showed at the end of two weeks small crumb-like masses of acid-fast bacilli which were identical morphologically with genuine tubercle bacilli. Transplants were again made and the growth carried, in the same medium, to the fifth generation. Two cubic centimeters of a month-old culture in egg-broth belonging to the third generation were injected subcutaneously into the abdomen of each of two guinea-pigs. Four weeks later one of these died and showed a cheesy nodule at the site of inoculation, miliary tubercles of the inguinal lymph-nodes, tuberculous peritonitis, the great omentum rolled up and caseous and miliary tuberculosis of the liver, spleen and lungs. (Probably in this case the needle had pierced the peritoneum.) The second guinea-pig died five weeks after inoculation and showed enlarged, cheesy inguinal lymph-nodes, partly caseous retroperitoneal nodes and miliary tuberculosis of the spleen, liver, right kidney and lungs.

Smears made by rubbing portions of the spleens of these animals on new, clean slides showed innumerable acid-fast bacilli resembling in all respects genuine tubercle bacilli.

I regard it as a matter of good fortune that this culture, made on an unsuitable medium, should have been successful. The other attempts, as has been stated, all gave negative results. About fifty tubes and flasks in all were inoculated and several methods employed. Among these may be mentioned placing blood in shallow, broad-based flasks containing, variously, glycerin-beef-broth, glycerin-veal-broth without peptone or salt, and Besredka's egg-broth; and in slants or flasks of glycerin-beef-agar, glycerin-bob-veal-agar, coagulated egg and glycerin-blood-veal-agar. In two cases the hemolyzed and centrifugalized blood was spread on glycerin-veal-agar in large, wide-mouthed bottles. In all cases the containers were carefully sealed with paraffin, rubber caps or lead foil. Of the cultural methods named none seems satisfactory except the last. I hope that this method may be tried more fully and believe that it may yield a number of positive results, especially with cultures from the heart's blood at necropsy.

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RABIES

ITS DIAGNOSIS IN ANIMALS AND PREVENTION IN MAN

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On account of the increasing prevalence of the disease,¹ and in view of the ease with which the general practitioner may administer the prophylactic measures at the home of the patient, even if he is situated at a place some distance from the laboratory which supplies the material for treatment, a brief consideration of some phases of rabies in their bearing on diagnosis and prophylaxis may not be out of order.

Diseases which are contracted by man solely from one of the lower animals afford better opportunities for effectual prevention than other infectious diseases; and when the animal concerned is a large domestic quadruped, the problem becomes easier in proportion to the simplicity with which the animal may be controlled. Rabies has been eradicated in the island of Great Britain, both in human beings and in animals, the measures adopted being merely the muzzling of all dogs and prohibition on the importation of canines except after a quarantine sufficiently long to prevent the admission of a rabid animal to the island. Unfortunately in the United States, owing to state laws, general muzzling of all dogs is impossible, and rabid dogs may pass from one state to another, spreading the disease so that eradication by this means seems impossible for the present at least. Since this is the case, it becomes the duty of each individual physician to familiarize himself with the nature of the disease and its prevention so that each may contribute his share toward diminishing the mortality rate among human beings.

Since rabies is transmitted to man almost entirely by dogs, knowledge of the characteristics and of the diagnosis of the disease in that animal is of more importance than the diagnosis in man himself. Clinically the diagnosis is seldom difficult when the disease is advanced. As Huttyra and Marek² state:

The symptoms of irritation, the aggressive conduct and subsequent paralysis, particularly the appearance of bulbar paralysis, forms a very characteristic picture of the disease, and the diagnosis is made easier by the existing suspicion of infection. Statements that no bite has been received must be taken with reservation, as slight wounds are inflicted not infrequently without the knowledge of the owner. In making the diagnosis the former behavior and temperament of the animal must be taken into consideration.

Laboratory methods when properly performed are sufficient to make a diagnosis, but the work is greatly facilitated and correspondingly expedited if clinical evidence is at hand in addition, and therefore animals which are not manifestly rabid should not be killed as soon as they have bitten but should be confined for observation by a competent veterinarian. If the animal shows no symptoms in fourteen days³ there is no danger of the person bitten contracting rabies from

1. Hart, George H.: *Circ.* 129, U. S. Dept. Agric., Bureau of Animal Industry, 1908. Mohler, John R.: *Farmer's Bull.* 449, U. S. Dept. Agric., Bureau of Animal Industry, 1911. Kerr, J. W., and Stimson, A. M.: *The Prevalence of Rabies in the United States*, *THE JOURNAL A. M. A.*, Sept. 25, 1909, p. 989.
2. Huttyra and Marek: *Pathology and Therapy of Diseases of Domestic Animals*, translated by Mohler and Eichhorn, i, 483.
3. Hart, George H.: *Circ.* 129, U. S. Dept. Agric., Bureau of Animal Industry, 1908, p. 15.