mentions reduplication following "disease or degeneration of cardiac muscle."

Mitral Regurgitation.—Of this there were 10 cases. In 8 of the 10 no reduplication was present. In 1 of the 2 positive cases there was reduplication of the first sound. This was in a case of pneumococcus bronchitis, with an old mitral lesion. As soon as the bronchitis cleared up, the reduplication cleared up, leaving the mitral regurgitation. Only one case, therefore, remains which showed a reduplication; in this case, of the second sound. Sansom[4] reports 2 cases with reduplication of the first sound. Ohastzow[3] states that in mitral regurgitation reduplication of the second sound is never met with.

Aortic and Mitral Regurgitation.—There were 2 cases; in one there was no reduplication; in the other there was reduplication of the first sound. In the latter case there was doubt as to the absence of myocardial degeneration.

Mitral Stenosis.—There were 3 cases, of which 2 were associated with regurgitation. In no case was there reduplication of the first sound. In two cases there was reduplication of the second sound. In the third case (associated with regurgitation) there was no reduplication. Broadbent,[9] Bramwell,[7] Cabot,[11] Allbut[12] and La Fevre[13] agree that mitral stenosis may cause reduplication of the second sound. Hayden reports 63 cases, with 26 instances of reduplication of the second sound. Sansom[4] reports 37 cases, 11 with reduplication of the second sound.

SUMMARY AND CONCLUSIONS.

Reduplication of the heart sounds is a not uncommon sign.

The cause may be either asynchronous contraction of the ventricles or the auricular sound.

Normal persons with thin chest walls usually show reduplication. Persons with thick chest walls should not.

In persons in whom no reduplication should be present it is a sign of positive value.

Reduplication of the first sound means that the heart is not working properly. This may be due to nervous interference, as in persons with bad habits, or it may mean that the heart is hampered by external agencies, by pressure, or by traction, or, finally, it may mean that the heart muscle is not efficient, either due to systemic disease or inherent conditions.

Reduplication of the second sound alone means an is usually only a more advanced degree of the same condition.

Reduplication of the second sound alone means an alteration in the relative blood pressure of the systemic and pulmonary circulations.[14]

58 Kirk Street.

11. Cabot: "Physical Diagnosis," p. 169.
12. Allbut: "System of Medicine," 1897, vol. v, p. 1018.
13. La Fevre: "Physical Diagnosis, p. 314.
14. For further literature reader may consult von Turgensen: "Erkrankungen des Kreislufsorgane." Johnston: Lancet, 1876. "Guy's Hospital Reports," vol. i and vi. Gibbs: Lancet, vol. i, 1901, p. 1601. Butler: "Diagnostics of Internal Medicine," p. 885.

Metatarsalgia.—W. E. Blodgett, in the *Physician and Surgeon*, states that the pain in the chronic type of metatarsalgia, as in the ordinary pronated foot, is due to general abnormal tension and pressure. In the acute type, however, the pain is due to such a displacement of the heads of the metatarsal bones that one of the branches of the external plantar nerve is squeezed between two of the metatarsal heads.

THE CULTIVATION OF SPIRILLUM OBERMEIERI.*

PRELIMINARY NOTE.

F. G. NOVY, M.D., AND R. E. KNAPP, B.S.
ANN ARBOR, MICH.

We have heretofore applied the term *Spirillum obermeieri* to the organism isolated by Dr. Charles Norris, from a case of relapsing fever which occurred in New York, in the belief that it was identical with that described by Obermeier in 1873. We will continue to use this term for the present, although, as will be shown, there is reason to believe that the eastern relapsing fever is not identical with the American disease. When further evidence is obtained regarding the non-identity of the organisms found in these regions it may be necessary to restrict the use of the term *Spirillum obermeieri* to the organism found in the eastern disease.

On the other hand, the African relapsing fever, known also as tick fever, has been shown conclusively to be due to a different organism, the *Spirillum duttoni.* As far as we know, the first observation on this organism was made by Dr. D. Nabarro, of the Sleeping Sickness Commission, who noted the presence of spirilla in the blood of a patient in Uganda as early as August, 1903, but this fact was not published until 1905. In November, 1904, the presence of spirilla in tick fever was announced by Ross and Milne and also by Dutton and Todd. This organism was brought to England by Todd, and to Germany by Koch, and has since been studied by several workers.

In our preliminary note[1] we pointed out the probability that tick and relapsing fevers were two distinct diseases, due to different species of spirilla, and in the main paper[2] it was definitely shown that these two organisms were distinct species, and at that time we named the spirochete of tick fever *Spirillum duttoni.* Our conclusion regarding the specific difference of the two organisms was based on a comparison of (1) the animal reactions of the New York spirillum, as ascertained by Norris and his co-workers and by ourselves, with those described by Dutton and Todd and later by Breinl and Kinghorn; (2) the morphologic characteristics presented by our organism with those of the tick fever spirillum in specimens sent by Dr. Todd, and (3) the arrangement of flagella as demonstrated in this laboratory for the New York spirillum and by Zettnow for that of tick fever. Our belief that a full confirmation of this view would be afforded when cross experiments were made with sera of animals immunized to these two spirilla has been realized by the subsequent work of Breinl[3] and by still more recent tests made with our serum by Dr. Schilling at the Institute for Infectious Diseases in Berlin.

It will be seen from the above facts that a recent note made by Breinl and Kinghorn[4] and implying that our conclusion was reached merely from " a study of the two slides sent from these laboratories and of the few experiments given by Dutton and Todd" is not a fair state-

* From the Hygienic Laboratory, University of Michigan. This investigation has been aided by a grant from the Rockefeller Institute for Medical Research.

1. THE JOURNAL, Jan. 13, 1906.
2. Studies on *Spirillum Obermeieri* and Related Organisms, Jour. of Infect. Dis., May, 1906, vol. iii, pp. 291-393.
3. The Specific Nature of the Spirocheta of the African Tick Fever, The Lancet, June, 16, 1906.
4. A. Breinl and A. Kinghorn: An Experimental Study of the Parasite of the African Tick Fever (*Spirochæta duttoni*), Memoir XXI, The Liverpool School of Tropical Medicine, September, 1906.

ment of fact. In his paper of June 16, Breinl suggested the specific name *"duttoni,"* the same as used previously by ourselves. We have employed the generic name *Spirillum* in preference to *Spirochæta* for the reason that the type species of the latter genus, *Sp. plicatilis,* was said by Schaudinn to possess an undulating membrane, but no flagella. Furthermore, the term *Spirillum* expresses our view regarding the bacterial nature of these organisms.

In our article of last May, a brief discussion is given to the relation of the New York spirochete to that of the relapsing fever met with in Bombay, and the statement is made that the evidence on hand points to the existence of three relapsing fevers in man. It is unnecessary to recapitulate the reasons which led us to take this view, but it will be of interest to present in this connection some observations which have been made by Captain I. P. Mackie, I.M.S., and communicated by letter to one of us (Novy). It is generally understood, as a result of the studies of the earlier workers, that the spirillum of relapsing fever does not infect animals other than the monkey. Captain Mackie has produced the disease in rabbits, white English rats, black Bombay rats and in mice, but failed to infect pigeons and goats. In these animals the spirilla appear in less than 24 hours and sometimes disappear in less than 48 hours, but often increase to 56 or more hours. They never become numerous and do not reappear; that is, there is no relapse. These results are in accord with those of Gabritschewsky. The very scanty number of spirilla in his rats is in striking contrast with the result obtained with our *Sp. obermeieri* and with *Sp. duttoni.* Moreover, tests made by Captain Mackie with some hyperimmune serum which we sent him showed that it possessed no agglutinating, germicidal or lysogenic action even in dilutions of 1 to 10. Control tests with some of this serum were made in Ann Arbor, at about the same time as the Bombay tests, and these showed that the serum possessed undiminished activity toward our spirillum. The latter was promptly agglutinated by the serum in dilutions of 1 to 10 and even 1 to 200. Unless it is assumed that our serum had lost its properties while in transit, especially in going through the Red Sea, it would appear that the Bombay relapsing fever is etiologically different from that of New York. The question of the identity of these organisms will be investigated further and we hope to be able to make direct comparisons of the living organisms.

CULTIVATION EXPERIMENTS.

The *Spirillum obermeieri* has been maintained in this laboratory since November, 1905, by consecutive passage through rats. Although during this time many hundreds of attempts to secure cultures on artificial media have been made, they have given uniformly negative results. In the defibrinated blood of infected rats the spirilla retain their vitality for a variable length of time, depending on the stage of the disease during which the blood is drawn. If drawn during the decline stage, that is to say, at a time when the organisms have reached their maximum and are beginning to decrease in numbers, the spirilla will often die out in less than 24 hours. This is due, as we have shown, to the presence of specific germicidal bodies. On the other hand, in "onset blood" drawn during the early stage of the disease, the spirilla may live for several weeks. Thus we have seen living spirilla in such blood kept for 30 to 37 days and have been able to infect rats with blood kept for 40 days. Moreover, we have been able to make use of this fact in shipping the virus to distant points, to Dr. Todd at Liverpool and to Professor C. Fraenkel at Halle.

In our first series of attempts at cultivating the spirilla on blood agar we were, as a rule, unable to keep the organisms alive for more than two or three days. Since then, however, we have been somewhat more successful and have kept them on blood agar for 22 to 28 days, and in some experiments now in progress they are still alive and numerous on the thirtieth day. As yet, however, no evidence has been obtained of actual multiplication *in vitro.* The organisms which are found to persist we prefer to regard as mere survivals until actual subcultures have been obtained.

The successful results obtained by Levaditi in the cultivation of *Sp. gallinarum, Sp. duttoni* and *Sp. refringens* in collodium sacs led us to apply this method to our spirillum. With this object in view, the collodium sacs were filled with rat or rabbit blood, or corresponding sera, heated and unheated, and after inoculation with spirilla blood these sacs were placed in the peritoneal cavity of rabbits. After three to seven days the sacs were removed and contents were examined with negative results. Apparently the rabbit is unsuited for sac cultures.

We were finally led to make the trials under conditions approaching the natural state as much as possible. For this purpose the collodium sacs were filled with uncoagulated rat blood and after inoculation were placed at once in the peritoneal cavity of a white rat. Three days later, on removal, the sacs were found to contain active spirilla and in increased numbers. From the sacs, transplants were made to new ones and the result was equally satisfactory. The spirilla were found to be in an extremely active condition and were undoubtedly multiplying.

From this time on the transplantations were made regularly, every three or four days, from sac to sac. After a few passages the uncoagulated blood was replaced by defibrinated rat blood or by rat serum. Defibrinated rabbit blood has also been employed to some extent, but whether it will continue to be a favorable medium we are unable to state. Two sacs were inoculated each time and placed in the peritoneal cavity of a rat. Each sac had a capacity of from 2.5 to 3.0 c.c. and was sealed so as to leave within as little air as possible. It is a noteworthy fact that on removal from the rat the sacs are invariably greatly distended as a result of osmotic changes. Furthermore, the air which was originally present is in large part and at times wholly absorbed.

Since October 13 the spirilla have been carried through twenty consecutive passages in sixty-eight days, and presumably they can be kept multiplying under these conditions indefinitely. The spirilla in the sac culture are never as numerous as in the blood of rats. They rarely exceed more than 5 to 10 per field of the 1/12th inch objective, as contrasted with several hundred per field met with in the blood of rats during the maximum period of infection. The inoculation of the sac contents (blood or serum) into rats, it is interesting to note, is followed by a mild infection in which the spirilla are not much more numerous than in the sacs. Moreover, in such infection they persist for a day or two longer than is the case with the active virus.

When the sac is allowed to remain in the rat for seven days the spirilla decrease greatly in numbers and may even disappear. In the opened culture sacs after removal from the rat, and kept at room temperature, the spirilla die out in a day or two.

Throughout this series the spirilla have preserved their form unchanged. They appear either as single cells (8 microns) or of double length (16 microns), but at times even longer spirals are found. The latter are the result of end-to-end union by means of flagella, as we have heretofore shown. As in the case of blood preparations, no evidence is observed of division other than transverse. One observation in this connection is deserving of special emphasis owing to its bearing on the question as to whether spirochetes multiply by transverse or longitudinal division. In these cultures it is not unusual to find short spirals of two or three turns, and from 4 to 6 microns in length. These may occur singly or in pairs (8 to 12 microns long), showing the pale division zone. The width of the short form is the same as that of the longer cells. The occurrence of these short spirals is readily explainable as the result of transverse division. It may further be stated that the cultural spirals usually stain solid by the Romanowsky method, but at times they may show granulations which to some extent may be due to granules deposited from the medium.

SAC CULTURES IN RAT SERUM.

In view of the fact that Prowazek and others are inclined to consider spirochetes as protozoa and as cell parasites, it was desirable to ascertain whether or not the spirilla could be maintained in active multiplication in a clear serum. Accordingly, the spirilla were inoculated into rat serum, completely freed from corpuscles by centrifugation. Up to the present time we have effected seven consecutive passages in such serum in the space of twenty-four days. At each passage a control sac containing defibrinated rat blood was placed in the rat. The serum cultures, although totally devoid of corpuscles, were in every respect as rich in spirilla as the blood cultures. The conclusion to be deduced from these experiments is that multiplication of spirilla may take place without any intracellular stage. The occasional presence of spirilla in a cell is to be regarded as an accident rather than as an expression of an unrecognized cycle.

THE TUBERCULOSIS DISPENSARY: ITS METHODS, VALUE, AND LIMITATIONS.*

EDWARD O. OTIS, M.D.

Visiting Physician at the Massachusetts State Sanatorium at Rutland; Senior Physician of the Tuberculosis Department of the Boston Dispensary.

BOSTON.

Out-patient clinics for chest diseases have existed for a long time in connection with the great London chest hospitals. In Edinburgh, the Royal Victoria Dispensary for Tuberculosis was established in 1887, and is conducted according to the modern conception of such an institution.[1] The Emile Roux Antituberculosis Dispensary, however, founded at Lille, France, in 1900, by Dr. Calmette, seems to have been especially instrumental in the establishment in rapid succession of many similar institutions in France, Germany, Belgium, Portugal and other countries in Europe, as well as in the United States. The psychologic moment had apparently arrived for this distinct and notable advance in the tuberculosis warfare.

In 1899, the managers of the Boston Dispensary, at my suggestion, established a tuberculosis clinic in connection with that institution, which, so far as I am aware, was one of the first, if not the first, of the kind in this country; soon afterward others were founded in New York City and elsewhere. Whatever observations are offered in this paper are largely the result of experience in the tuberculosis department of the Boston Dispensary.

Not only has the tuberculosis dispensary proved to be a very valuable and distinct addition to the armament of the antituberculosis forces, but it has also introduced a new conception of out-patient service to the poor, which is being recognized in clinics other than those solely devoted to this one disease. This new idea is that the patient is not only and simply to be regarded and treated as a case with a number, illustrating a disease, but as a social unit, a human being, whose habits of life and whose environment are discordant with the conditions of healthy existence; consequently, paramount attention is devoted to the reorganization of such vicious habits, and the transformation, so far as possible, of the environment into a wholesome one, for such, in fact, is an essential part of the treatment of pulmonary tuberculosis. In order to accomplish this, the patient is studied socially, both at the clinic and by the "visitor" or nurse at his home. His habits, mode of life at home and at work, his surroundings, physical and moral assets, and limitations, his pecuniary condition, are all the subject of careful inquiry and consideration. Based on the results of such social investigation, together with the medical findings, the treatment is instituted, which in itself is more social than medical.

There is yet another reason why the social side of the tuberculosis dispensary should be particularly accentuated; for the object of such a dispensary, unlike that in other clinics, is not only to help and cure those suffering from tuberculosis, but to prevent others from becoming infected by them—*prevention* is quite as important as the care and treatment of the disease; indeed, more so, from the point of view of the community.

In order, then, that any effectual and continuous application of the hygienic-dietetic treatment—the established treatment of the day—can be carried out, we must possess not only an exact and complete knowledge of the patient's social condition as indicated above, but we must as well obtain and retain control over him when the treatment is pursued at home, and this obviously can only be done with the willing coöperation of the patient, for his attendance on the dispensary is voluntary. Furthermore, the patient must be thoroughly educated in the tuberculosis hygiene both by the physician and visitor or nurse, so that his immediate family, his workshop neighbors, or the community may not become infected through his carelessness or ignorance.

In the tuberculosis dispensary as at present constituted in France, England and this country, the examination and treatment of the tuberculous individual forms an integral part of the plan, as well as the social side as above referred to. In Germany at the so-called *Fürsorgestellen*, "advice and precaution" stations, education and advice are the principal object of attainment, and the direct treatment is referred to the local or family physician—thus resembling closely the work of the tuberculosis associations.

In the recently initiated tuberculosis "classes" first

* Read in the Section on Pharmacology of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

1. R. W. Phillips, Edinburgh Med. Jour., January, 1906, p. 9.