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THE CYTOLOGICAL STUDY OF THE CEREBRO-SPINAL FLUID BY ALZHEIMER'S METHOD, AND ITS DIAGNOSTIC VALUE IN PSYCHIATRY.[1]

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Methods.

The value of lumbar puncture as a diagnostic aid in psychiatry and neurology has been nullified to some extent by the defects of technique rather than by a lack of specific changes in the fluid due to pathological causes.

Prior to the year 1904, the centrifuge method of Widal and Ravaut was practically the only method for studying the cytology of the cerebro-spinal fluid. It answered a certain purpose very well, but the inaccuracies were soon apparent ; and while clinicians made use of the method for diagnosticating general paralysis, the pathologists generally severely criticised it, and doubted if it had any diagnostic value.

In the first place the cells were so very poorly stained that one

[1] Read at the semi-annual meeting of the New England Society of Psychiatry at the Colony of the Worcester Insane Asylum (Grafton, Mass.), Sept. 19, 1907.

could not distinguish the various types, and the only value was in finding an increase in the number of nuclei seen, without any regard to what cells were present to account for the increase. The cells were usually spoken of as lymphocytes, and the increase called a lymphocytosis. It is true that in certain cases of general paralysis there is a great increase in the number of cells, but the protean character of the disease, its extent and intensity, allows of many anatomical types. Hence we should look for some pronounced variation in the number and character of cells found in the cerebrospinal fluid. It is often difficult, by the above method, with a small count of cells, to decide whether to call the results positive or negative. Nissl (1) called attention to the fact that by this method a large count per field—8 or 10 cells—could occur in fluids without being of any pathological significance. The difficulty of comparing the results of various observers was also apparent, as one must necessarily perfect one's own technique and draw conclusions from experience—establishing one's own standards. Pomeroy (2) uses this method and reveals the inaccuracies of the same when he concludes that all the clinical facts must be considered before an opinion as to the cell count can be given. He also states that it is impossible to differentiate various cell types because of their poor staining qualities. It is very easy to see that in a clinically well-marked case of general paralysis lumbar puncture is superfluous as a means of diagnosis. But in very doubtful cases, where the physical signs are either absent or not sufficiently pronounced to warrant a diagnosis of general paralysis, lumbar puncture should be of the utmost value in aiding us to arrive at a positive diagnosis.

Fuchs and Rosenthal (3), in 1904, in order to overcome the inaccuracies of the centrifuge method, and establish some standard for comparison, utilised the ordinary hematological technique, the pipette and blood-counting chamber. The fluid was not centrifugalised, but drawn directly into the pipette, and a diluent used that would stain the cells. Knowing the degree of dilution, one could count the cells present in so many c.c. of fluid. Here at last a constant unit could be employed, and with a large number of cells per c.c., the method was fairly accurate. But with a small number of cells, the errors would vary from 30 to 90 per cent.

Jones (4) has shown how the inaccuracies could occur in counting a small number of cells. He proposes another method of utilising

the same principle, but we fail to see the advantages of his method over that of Fuchs and Rosenthal.

Cornell (5) utilises the last-mentioned method and obtains some good results. It must be admitted that the method is far in advance of the centrifuge method of old, as it allows to some extent a differential count (just how accurate will be discussed later). Cornell was able to differentiate the following cells :—

1. Small lymphocytes.
2. Large lymphocytes.
3. Polymorphonuclears.
4. Epithelioid.
5. Plasma cells.
6. Degenerated cells.

The lack of illustrations is a serious defect of this work, as one is in doubt as to the character of the cells from the description alone. This is especially true of the epithelioid cells. He was able to distinguish plasma cells, which were first described in the fluid by Fischer; the latter's results, however, were doubted by Nissl and others, because they were unable to distinguish these cells. One serious objection to the method is the fact that the cells are not fixed in the usual manner, and that in staining the fresh cells, they appear necessarily distorted and swollen. The inability to compare these cells with cells in the tissue, fixed and stained by the common methods, is a serious obstacle in accounting for their origin. We will also show later that Cornell failed to observe other cells that are of considerable importance in diagnosis. The lack of anatomical confirmation of his diagnosis is also to be regretted, as we cannot always be satisfied with the diagnosis of general paralysis made from the clinical picture alone.

Realising the importance of lumbar puncture, and the defects of the methods in use, Alzheimer (6), after much experimentation, finally evolved a method by which the cells are fixed with alcohol, after which they can be stained by the usual methods used in studying the histopathology of the cortex. This is accomplished by adding 96 per cent. alcohol to the cerebro-spinal fluid, which precipitates the proteid, and by centrifugalisation the cells are thrown down with the proteid in the form of a coagulum at the bottom of the tube. By his method a very clear differentiation of the various types of cells can be made, due to the excellent staining qualities of the cells thus treated.

In detail, the method of Alzheimer as used by us is as follows :—

1. Lumbar puncture in the usual manner.

2. 96 per cent. alcohol, in proportion to twice the amount of cerebro-spinal fluid, is added drop by drop and well mixed.
3. Centrifuge the mixture for one hour at high speed in a glass tube with conical end. (An ordinary electric urinary centrifuge apparatus can be employed, tube to be well stoppered to prevent evaporation.)
4. The supernatant fluid is poured off, leaving a small coagulum in the bottom of the tube.
5. Add absolute alcohol—alcohol and ether—ether, each separately for one hour, to dehydrate and harden coagulum.
6. The coagulum can now be gently loosened from the bottom of the tube by a long needle. The tube is then inverted, and the coagulum allowed to fall into the hand by a quick tap on the end of the tube. Care must be taken not to squeeze or handle the coagulum. The hand is placed over a small homeopathic vial, containing thin celloidin, and the coagulum allowed to drop into the celloidin, where it remains over night (12 hours usually).
7. Coagulum placed in thick celloidin, which is allowed to evaporate slowly.
8. Then mounted on blocks, and cut at 14 m.
9. Sections stained. (Celloidin should be removed from section by alcohol and ether before staining.)

The stains used by Alzheimer and by us were Unna's polychrome methylene blue and Pappenheim's pyronin-methyl green.[1] The

[1] *Pyronin Stain—*

Methyl green	0·30.
Pyronin,	0·25.
Alcohol, 96 %	2·50.
Glycerin	20.
5% aqueous sol. carbolic acid,	100.

Procedure—

1. Remove celloidin by abs. alc. and ether.
2. 80% alc.
3. Water.
4. Sections are carried on glass or platinum needle into dish of above sol. kept in a water bath at 40° C., 5-7 mins.
5. Quickly cool dish in running water.
6. Wash all superfluous stain in plain water.
7. Absolute alcohol to differentiate—until no more stain comes away from section.
8. Clear in Bergamot oil.
9. Mount in balsam.

latter was found to be the most satisfactory routine stain, as it gives excellent nuclear pictures, a slight tint to the protoplasm in most cells, and is considered specific for plasma cells, staining the protoplasm a deep red. Toluidin blue was also used with success when especially clear nuclear figures were desired; Scharlach R. was used to demonstrate the fat found in "Körnchen" cells. Instead of celloidin imbedding, paraffin may be used, with alcohol or Zenker fixation. This was tried by us, but the results did not seem to be as satisfactory as with the technique outlined above, the only advantage of the method being that sections could be cut a little thinner.

As to the method described by Alzheimer, we can say that it is the most satisfactory one yet devised. Because of the fixation, cells are stained in a manner easy of differentiation, and these cells can be compared with cells in the pia and cortex (stained in a similar manner), an interesting point when the origin of the cells has to be considered. The contrast between this method of treating the cerebro-spinal fluid and others in vogue before its publication can only be appreciated by one who has attempted to overcome the difficulties and inaccuracies of the latter, and to Alzheimer belongs the credit of devising a method that allows an accurate study of the cytology of the cerebro-spinal fluid in normal and morbid conditions.

The cells are caught in the coagulum and are found to be nearly evenly distributed throughout (see Fig. 6, Plate 16). It is possible that the very topmost layers of the coagulum may not contain as many cells as the bottom layer, but this is only true when a very small number of cells are present. But by cutting the coagulum in cross section, and staining at least six sections from various levels, and averaging the counts from these various sections, very little error as to character and number of cells is made. While the method is not a bedside one and requires some little time, yet the advantages are so great that one is amply repaid for the extra time spent upon the procedure. When the cells were present in sufficient numbers a differential count was made from 200 cells, using about six sections for the purpose. The unit for comparison of the counts in various fluids was the number found in 100 fields, as it was found that, in conditions other than general paralysis, the cells were so scarce it would be ridiculous to speak in fractions of a cell to one field, and the error would be greater. On the other hand, in general paralysis the number becomes large, up to 3400 cells in some cases

to 100 fields, but it is only necessary to count 200 cells, and keep track of the number of fields counted, and by simple multiplication to get the totals for 100 fields. Here the differential count is of the utmost importance.

Material and Scope of Investigation.

We have been fortunate enough to have at our disposal a large amount of material, both living and post mortem, and thus we have been able to study the cerebro-spinal fluid in both conditions; also to confirm our diagnosis and correlate our findings in the fluid by studying the cortex and pia in a number of cases. This correlation of the findings in the fluid with the cortical histopathology has been of great value, not only in confirming the clinical diagnosis, but also in establishing the identity of the various cell types.

Our cases total 82, and in some instances two punctures during life were made. In 3 cases of general paralysis, and 3 cases of organic dementia, both ante-mortem and post-mortem punctures were made, and in 2 cases of each of the above series autopsies were made. A detailed summary of all fluids will be found in Chart I. The number of fluids in various psychoses are as follows :—

19	cases	General Paralysis, A.M.
12	,,	General Paralysis, P.M. (Three punctured A.M., and autopsies in two of these, and also in five other cases.)
10	,,	Organic Dementia (arteriosclerotic, etc.), A.M.
8	,,	Organic Dementia. (Three punctured A.M. Autopsies in five cases, including two punctured A.M. and P.M.)
3	,,	Senile Dementia, A.M.
3	,,	Senile Dementia, P.M.
2	,,	Polyneuritic Delirium, A.M.
1	,,	Chronic Alcoholic Insanity, A.M.
1	,,	Chronic Alcoholic Insanity, P.M.
4	,,	Epilepsy, A.M.
4	,,	Manic-depressive Insanity, A.M.
1	,,	Manic-depressive Insanity, P.M.
1	,,	Involution Melancholia, A.M.
9	,,	Dementia Præcox, A.M.
1	,,	Dementia Præcox, P.M.
1	,,	Paralysis Agitans, P.M.
1	,,	Paranoia (?), P.M.

2 cases Idiocy (Spastic paraplegia) P.M. Died of cerebral softening.
1 ,, Morphinism, P.M.
1 ,, Toxic Delirium, P.M.
1 ,, Cerebral Lues, A.M.
1 ,, Neurasthenia, A.M.

Doubtful Cases.

2 ,, Organic Dementia (?) (1 A.M., 1 P.M. no autopsy).
2 ,, General Paralysis (?) (1 A.M., 1 P.M. no autopsy).

The primary object of the investigation was to compare the fluid of various psychoses, especially those psychoses that would be confused with general paralysis clinically, and we believe that by this method facts have been obtained that warrant the statement that changes occur in the cells of the cerebro-spinal fluid that are pathognomonic of general paralysis, so that from the fluid alone a positive diagnosis should usually be possible. (Of course this refers only to patients suffering from mental diseases.)

In order to substantiate our claims, we have utilised the anatomical material at our disposal, both to confirm the clinical diagnosis and establish the origin of the various cells. We have not taken up other conditions outside of the realm of psychiatry from lack of time and material, so that our conclusions refer entirely to this field.

In such conditions as organic dementia, dementia præcox, alcoholic insanity (acute and chronic), senile dementia and epilepsy, we have compared the findings with those of general paralysis and have come to definite conclusions. Many interesting points relating to the changes in post-mortem fluids have arisen, but we will only be able to mention them and their relation to acute toxic conditions, and we hope that, aside from obtaining facts for diagnostic purposes, this work will stimulate investigation in other fields of medicine, especially the post-mortem fluids in general diseases.

Cytology.

As we have stated above, no method previously in vogue has allowed such a perfect differentiation of the cells of the cerebro-spinal fluid. Consequently, we not only have been able to distinguish cells found by other observers, but have found cells

that we believe have not been described previously in the cerebro-spinal fluid.

It is no doubt true that certain cells have been incorrectly classified before, because of poor staining qualities due to the methods used. We can be reasonably sure of the identity of lymphocytes, plasma cells, endothelial cells, phagocytes (endothelial class with lymphocytic inclusions), polymorphonuclear leucocytes, and "Körnchen" cells. Other cells are found in small numbers, and have been put in the unclassified list. They may be degenerated types of cells already mentioned. Some cells resemble fibroblasts and ependymal cells, but it is difficult to come to any definite conclusions as to their identity.

Nissl doubted if the cells of the cerebro-spinal fluid could come from the pia, because he found plasma cells in the pia in general paralysis, but was unable to demonstrate these cells in the fluid of patients with this disease, an error doubtless due to the technique employed. Alzheimer, in describing his method, mentions that plasma cells can be clearly seen by this method, and we can confirm his statements. It is also difficult at times to distinguish between large mononuclear leucocytes and endothelial cells in the fluid, but the presence of the former in a fluid with practically no polymorphonuclear cells would not be in harmony with our knowledge of the relation of mononuclears to the polymorphonuclears in the blood. And as contamination of the fluid with blood is in a large measure responsible for any excess of polymorphonuclears, the identity of such cells can be easily established. In most cases, then, where polymorphonuclear cells are absent, mononuclear cells, not lymphocytes, are better classed as endothelial.

1. Lymphocytes.

(*Fig.* 1, *Plate* 17.) (*A*, *Fig.* 1, *Plate* 15.)

We include both the large and small forms as differentiated by Cornell, also altered and transitional forms. The ordinary lymphocytes are found in all fluids, but aside from fluids of general paralysis they occur in very small numbers. The nucleus is small and round; sometimes oval, and slightly indented. The chromophilic granules are arranged in "clock-face" form around the periphery, and take a deep blue stain (pyronin stain). The protoplasm in unaltered forms is found as a thin line around the nucleus, and stains a faint

pink. It is usually wider on one side. The altered and transitional forms show a somewhat larger and deeper staining nucleus, and more protoplasm (Fig. 10, Plate 17). These altered forms are very common in general paralysis, and it is in harmony with the view regarding the origin of plasma cells to consider these altered forms as transitional states between lymphocytes and plasma cells. The lymphocytes come from the pia, and their excess in the fluids of general paralysis is easily explained by the fact that in this disease the pia is infiltrated by them in large numbers, especially in the adventitial sheaths of the blood vessels.

In general paralysis the differential count shows that they are the principal cells that are increased, varying from 33 to 94 per cent., and averaging 73 per cent. of the total count. The total count in general paralysis averages 450 to 100 fields, so that it is easy to see the actual and relative increase in the number of lymphocytes in this condition. In other conditions the total number present does not reach nearly the count in general paralysis. In cerebral arteriosclerosis (organic dementia) the average is only 23 to 100 fields, so that it is hardly possible that the two conditions would be confused from the lymphocyte count. The lymphocyte count is small in all other conditions examined, being highest in cerebral lues, *i.e.* 36 to 100 fields (see Chart II.). In dementia præcox, the average lymphocyte count is larger than in manic-depressive insanity, but the difference is slight, and at present must be left unexplained, as not enough cases have been examined to allow us to come to definite conclusions. In post-mortem fluids, generally, there is an actual increase in the number of lymphocytes, especially in general paralysis and cerebral arteriosclerosis, but in the former the percentage is lowered from 73 to 62.

2. Endothelial Cells.

(*Figs.* 4 *and* 5, *Plate* 17.) (*B, Fig.* 1, *Plate* 15.)

These cells are also a constant finding in all fluids examined (except one case of neurasthenia), but vary in number in the different diseases. They vary considerably in size and shape, often they are the largest cells found in the fluid. The nucleus is usually eccentrically placed, and is oval or " horse-shoe " in shape according to the various stages of its activity. The nucleus stains a faint blue

with pyronin stain and has very few chromatophilic granules. The protoplasm stains a homogeneous light pink and varies in amount. These cells, even when very small, are easily distinguished from lymphocytes, because of lack of chromatophilic granules and shape of nucleus : as they appear in so many forms they may be taken for new types of cells or resemble other familiar cells. Under certain pathological conditions they become phagocytic for lymphocytes and occasionally for their own type. They undoubtedly come from the lymph spaces in the pia, and are easily affected by pathological conditions. The average count of these cells in general paralysis is only 13 per cent. in the living fluid, but they increase to 24 per cent. in post-mortem fluids. They are only present 28 to 100 fields in organic dementia during life, but post-mortem fluids show an increase of these cells to 68 per cent. in this disease. As they show an increase post-mortem in other conditions where small numbers were found during life, it may be possible that the acute diseases which are the cause of death in these conditions may be responsible for this increase. Especially is this seen in organic dementia. In other cases where the post-mortem fluids have shown a relative and actual increase in these cells, the patients have died of some acute disease. This may be accounted for by the fact that at the time of death some changes occur which allow or cause desquamation of these cells so that they appear in large numbers in the fluid. There is apparently no relation between the length of time post-mortem fluid is taken and the number of the cells found, as in the case that showed the largest number the fluid was withdrawn one half-hour post-mortem. The reason for this increase will have to be left in doubt at present, as sufficient proof is not at hand for conclusive statements.

3. Phagocytes.

(*Figs.* 1, 2, 3, *Plate* 17.) (*Fig.* 2, *Plate* 15.)

Under certain pathological conditions endothelial cells become phagocytic. They have been described by Mallory in certain toxic conditions, such as typhoid fever. Here, of course, they are found in the tissues. They have also been described as occurring in the pia in epidemic cerebro-spinal meningitis (7), lately by Stuart M'Donald (8), and in tubercular meningitis they are numerous. But we have not as yet seen any description of these cells as occurring

in the cerebro-spinal fluid. M'Donald describes these cells and shows drawings of the same in the pia, but says nothing about their occurrence in the fluid. In cerebro-spinal meningitis these endothelial cells become phagocytic for polymorphonuclear leucocytes. Those found by us are phagocytic chiefly for lymphocytes. This difference in phagocytosis is readily harmonized when the acuteness and chronicity of the processes in which phagocytosis in each case occurs is considered. The nucleus is pushed towards the periphery, somewhat elongated and flattened, and the protoplasm is swelled to enormous proportions.

The lymphocyte is centrally placed and surrounded by a light area or court. The outline of the protoplasm is only seen as a faint line outside of the lighter court. Often the lymphocytes are undergoing degeneration or digestion by the phagocyte, and consequently present various forms of karyorrhexis.

In some cases we have seen these phagocytes with endothelial inclusions, but it is difficult to distinguish between these types and degenerated lymphocytes (see Plate 17, Fig. 2).

Phagocytes were found in the fluid in very small numbers in four cases (living) in a series of nineteen general paralytic fluids, but were found in eight out of twelve cases of general paralysis, and in larger numbers, post-mortem. They are found in the pia in cases of general paralysis and organic dementia, but in small numbers. They evidently become phagocytic *in situ*. From the fact that they are so numerous post-mortem, one would infer that it was entirely a post-mortem phenomenon, but their occurrence during life is against this view. And as in the case of the endothelial cells, the length of time post-mortem seems to have no influence on their quantitative occurrence. The cause of death seems to have no relation to the number found.

4. Plasma Cells.

(*Figs.* 6, 7, 8, 9, *Plate* 17.) (*Fig.* 3, *Plate* 15.)

These cells have a nucleus similar to that of the lymphocytes, except that in most cases the clock-like arrangement of the chromatophilic granules is more pronounced; the remainder of the nucleus is stained a deeper blue. The nucleus is oval or round, and eccentrically placed. Frequently plasma cells are found with two or more nuclei, and are considered as degenerate types, the same as de-

scribed by Alzheimer in the cortex of general paralysis. Fig. 4, Plate 15, and Fig. 12, Plate 17, show a cell with a mitotic figure, whether a plasma cell or not cannot be determined. These mitotic figures are frequently seen in fluids of general paralysis. The protoplasm, by the pyronin, stains a deep red or pink (according to the extent of differentiation), and as the pyronin stain is supposed to be specific for the cells, it can be seen how important this stain is for the purpose of differentiation. Around the nucleus is usually seen a lighter area with the protoplasm on the periphery deeply stained. The protoplasm varies in form presumably according to the stage of cell-growth, and many young forms are hard to differentiate from lymphocytes. They differ but little from the cells found in the cortex and pia of brain and cord. So far in our series we have found them only in paralytic dementia, and have found them in all of these cases. Cornell found them in twenty-seven out of thirty-two cases, presumably in general paralysis, but does not mention their significance from a diagnostic standpoint. He also finds them in from 0·1 to 15 per cent., averaging 1·5 per cent. We were unable to find such a high percentage of plasma cells in general paralysis in our series; they vary from 1 per cent. to 6 per cent., and average 2 per cent., or, better described, one seldom sees over one or two plasma cells in a whole section. At present we believe that they are pathognomonic of general paralysis and are of equal value as a diagnostic factor with lymphocytosis. In one of our cases confirmed by autopsy (No. 26), there were only 110 cells seen in 100 fields, and 94 per cent. of these were lymphocytes and two plasma cells. When the fluid was obtained after death the plasma cells had increased to 8 per cent. The diagnosis of general paralysis was not only confirmed by a study of the cortex, but plasma cells were found in abundance in the pia of the cortex and cord. In all the cases of fluid taken P.M., there is a decided increase in plasma cells, varying in twelve cases from two to nine, averaging 5 per cent., a 3 per cent. increase over the cells during life. As to their occurrence in other syphilitic conditions, we have had but one case diagnosed as cerebral lues, and in this case they were absent. In two cases of organic dementia, post-mortem cells resembling plasma cells were found in the fluid, but only one seen in each case, and their identity was questionable. As they were not found in the pia of these cases, their presence in the fluid, if these are classed as plasma cells, cannot be explained.

5. "Körnchen" Cells.

(*Fig.* 13, *Plate* 17.) (*Fig.* 5, *Plate* 16.)

This is another type of phagocyte cell, filled with numerous fat droplets or fatty pigment. They were not found in the fluid of any living case. In one case of arteriosclerotic, brain disease (No. 65), with a focal softening in the first temporal convolution, the fluid taken post-mortem from the ventricles (lumbar puncture was unsatisfactory) showed a large number of these cells. As the brain had been handled, it may be possible that the softened area was damaged so that these cells escaped. The finding of such cells in the fluid is important from the fact that they can be identified and may help to locate the softening that has broken into the ventricle. One "Körnchen" cell was found in the case of an idiot (No. 83) (also ventricular fluid), who was subsequently found to have extensive cerebral softening. Hence we shall give them some attention. By pyronin, the nuclei of the cells show up darkly stained, about the size of a lymphocyte nucleus. It is eccentrically placed, and the protoplasm is bulged out, usually round or oval, the fat droplets taking a variety of shades of brown. With Scharlach R. they can easily be identified, as they stain a dark red, and although the material is hardly suitable for such a stain, still these granules can be definitely identified as fat. These cells were found in the pia in both cases of arteriosclerotic brain disease.

6. Polymorphonuclear Leucocytes.

(*Fig.* 15, *Plate* 17.)

From the observation of others, these cells have been given special importance when found in the fluid of general paralytics. Cornell lays special stress on increase of polymorphonuclear cells after epileptiform seizures in general paralysis. With the pyronin stain, the nuclei only are stained. No protoplasm is visible, and they are easily differentiated.

We found that they occurred in nearly all of our cases of general paralysis, varying from 1 to 39 per cent., even in clear fluids, and that they were present also in other conditions (also in clear fluids), but in very small numbers. Wherever we have found these cells in large numbers, however, it has been, with few exceptions, in fluids that were contaminated with blood at time of puncture.

In two cases of general paralysis (Nos. 22 and 71), irrespective of

seizures, the count was 30 per cent. and 39 per cent. respectively, but it was distinctly noted at the time that the fluid was " bloody." In one case (No. 35), however, without seizures and apparently a clear fluid, they were present to the number of 39 per cent. The average in general paralysis, in the living cases, was 9 per cent., and in post-mortem cases only 1 per cent. This is difficult to explain, but apparently they are more constant in general paralysis than in other conditions. We feel satisfied that the presence of polymorphonuclears in any large numbers can usually be accounted for by blood contamination, and can therefore attach no definite significance to their presence. In arteriosclerotic dementia they were present in nine fluids, varying from one to five to a count. One case of " cloudy " fluid showed 4 cells. The average for ten cases was 2·5. In one case, marked " bloody," they were present to the number of 64 per cent., and the count was 120 cells. In post-mortem fluids of arteriosclerotic they were absent in three fluids that were clear, and 16 per cent. were present in one count where the fluid was " bloody." They were absent in three cases of senile dementia, all " clear." In alcoholic (acute) condition they were absent in one case, " clear," present in two cases,—8 and 12 respectively,—the former " turbid " and the latter " clear." Their presence in such small numbers can have no special significance. It is possible with a poorly stained specimen to confuse these cells with endothelial cells, and that probably accounts for the fact that Cornell gave them such an importance in paralytic dementia. The question of mononuclears has been previously discussed, and we would emphasize the fact that where so few polymorphonuclears are found, still fewer mononuclears are to be found, and one must be suspicious of counting them as such; Cornell speaks constantly of mononuclear increase and is not clear in regard to the same.

7. Undifferentiated Cells.

In this class we have placed cells that we found, that did not conform to the types above described. In some instances they may be altered forms of the cells described, or degenerate forms, and in some cases we have found cells that resembled the fibroblasts (Plate 17, Fig. 14) found in the pia. These cells in the fluid are distinguished by their large oval or spindle-shaped nuclei with sparse and faintly-staining chromatic granules, but relatively slight amount of faintly pink-stained protoplasm, often only seen at the

poles of the cell. They were present in small numbers in almost all of our cases of general paraylsis and organic dementia post-mortem, and in some cases of general paralysis ante-mortem. Their significance at present is not clear; they seem to be of no great importance in diagnosis. They seem to take part in the general cell increase in the fluid post-mortem. Cells possibly ependymal in origin are also here included.

Differential Counts in Various Psychoses.

(*Charts I. and II.*)

Differential counts were made in all cases where the total cell count was over 50 to 100 fields. We will consider here the fluids of living cases only, as the value of the count for diagnostic purposes is the most important feature of the work. As would be expected from what we have said, the count is most important in general paralysis. Here we get positive findings; in all other conditions examined by us the cell findings can be considered negative. The great difference between the counts in general paralysis and other psychoses can be seen at a glance on Chart II. The total count in general paralysis varies from 110 to 1500 (the average being 450). The following proportions are taken from the average of nineteen cases:—

Lymphocytes, 73 per cent.
Endothelial cells, 13 per cent.
Plasma cells, 2 per cent.
Phagocytes (in four cases), 1 per cent.
Polymorphonuclears, 9 per cent.
Unclassified, 2 per cent.

So we see that the total number of cells is due in a large measure to a true lymphocytosis.

From our work so far, we can say that a lymphocytosis always occurs in general paralysis, and as a diagnostic factor is of the utmost importance. When the total count is over 100 per 100 fields, and contamination by blood eliminated, it is almost safe to say that the puncture is diagnostic of general paralysis. The presence of plasma cells even in so small amount as 1 per cent. is the strongest evidence of general paralysis, and confirms the evidence of the lymphocytosis, so that the lymphocytosis and presence of plasma cells together establish the diagnosis. In other conditions we found often a high

cell count, but the differential count showed that the large count was due to some other cause than a lymphocytosis.

In case No. 43 the count was 120, but only 31 per cent. lymphocytes, 5 per cent. endothelial, and 64 per cent. polymorphonuclears. Here a suspicious plasma cell was found, but the fluid was extremely bloody, so that we considered the puncture negative. The clinical diagnosis was organic dementia (hemiplegic). In another case (No. 34), with a clinical diagnosis of general paralysis (?), the total count was only 80, and differential count as follows: lymphocytes, 37 per cent.; endothelial cells, 30 per cent.; polymorphonuclear, 30 per cent. In this case the fluid was bloody. As these two cases have not come to autopsy, we cannot justify our diagnosis made upon the evidence of the findings in cerebro-spinal fluid, but from the findings in our other cases of general paralysis, four of which were confirmed at autopsy, we feel reasonably sure of calling the above two cases negative.

It is surprising to see the difference between the total cell count in other conditions and that in general paralysis. In no other series of cases did the count approach that in general paralysis, except where the fluid was bloody and the large cell count could be explained by an increase in polymorphonuclears. By consulting Chart II. the counts in the various conditions can be easily compared with those in general paralysis. In dementia præcox there is apparently an increase of lymphocytes, not to the same extent as in general paralysis, and we are unable to explain this fact. Especially is this true of the catatonic forms and in cases of many years duration. Thus in one case (No. 66), of fourteen years duration—a profoundly demented person—the total count was 150 cells for 100 fields: 74 per cent. lymphocytes, 22 per cent. endothelial, and 4 per cent. unclassified. In another case (No. 29), of six years duration—in a catatonic stupor—the cell count was 290: 84 per cent. lymphocytes, 12 per cent. endothelial, and 4 per cent. polymorphonuclears (clear fluid). The absence of plasma cells differentiates these fluids from that of general paralysis. In early cases of dementia præcox, however, where the lumbar puncture would be of importance as an aid to diagnosis, there seems to be no increase in lymphocytes.

Correlation with Autopsy Findings.

Chart III. shows in a general way the proportion of cells found in the pia compared with the same elements as found in the cerebro-

CHART I.

No.	Name.	Sex.	Diagnosis.	Type.	Age.	Duration.	Fluid. A.M. or P.M.	Hrs. P.M.	Autopsy ?	Cause of Death.	Character of Fluid.	Cells in 100 Fields.	Lympho-cytes.		Endo-thellial Cells.		Plasma Cells.		Phago-cytic Endo-thellial Cells.		Poly-morpho-nuclear Leu-cocytes.		Other Cells. + Un-classified.	
													%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
8[1]	M. O'B.	F.	General paralysis	Demented	30	3 yrs.	A.M.	...	Yes	...	Clear	702	79	...	8	...	6	...	...	...	4	...	3	...
9	M. F.	F.	Do. do.	Do.	46	3 ,,	,,	...	...	...	,,	680	87	...	9	...	3	...	...	...	1	...	...	...
10[2]	G. G.	F.	Do. do.	Do.	50	2 ,,	,,	...	...	...	,,	1500	90	...	5	...	3	...	...	...	2	...	...	...
14	F. H.	F.	Do. do.	Do.	28	1 ,,	,,	...	...	...	,,	200	73	...	14	...	4	...	...	...	7	...	2	...
18	M. W.	F.	Do. do.	Do.	51	½ ,,	,,	...	...	...	Sl. bloody	128	79	...	11	...	4	...	...	...	1	...	5	...
22	C. S.	F.	Do. do.	Expansive tabetic	31	6 ,,	,,	...	...	...	Turbid	600	47	...	20	...	1	...	...	...	30	...	2	...
23[2]	G. G.	F.	Do. do.	Demented	50	2 ,,	,,	...	...	...	Clear	620	80	...	15	...	1	...	1	...	3	...	...	...
25	J. P.	F.	Do. do.	Expansive Convulsions	40	2 ,,	,,	...	...	...	,,	385	64	...	30	...	2	...	2	...	...	...	2	...
26[3]	C. C.	F.	Do. do.	Demented	38	1½ ,,	,,	...	Yes	...	,,	110	94	...	4	...	2	...	...	...	...	...	...	...
36	C. B.	F.	Do. do.	Expansive	35	1½ ,,	,,	...	...	...	,,	200	79	...	12	...	3	...	...	...	6	...	...	...
35	L. H.	F.	Do. do.	Demented	31	1 ,,	,,	...	...	...	,,	275	33	...	21	...	3	...	...	...	39	...	4	...
53	F. E.	M.	Do. do.	Expansive	38	2½ ,,	,,	...	...	...	,,	900	80	...	4	...	1	...	1	...	10	...	4	...
56	A. O'C.	M.	Do. do.	Do.	46	5 ,,	,,	...	...	...	,,	500	71	...	11	...	3	...	...	...	15	...	...	...
60	H. W.	M.	Do. do.	Demented	36	4 ,,	,,	...	...	...	Bloody	260	72	...	24	...	2	...	...	...	2	...	...	...
61[4]	A. S.	M.	Do. do.	Expansive Tabetic	59	1¼ ,,	,,	...	...	...	Clear	260	83	...	12	...	3	...	...	...	2	...	...	...
63	J. C.	M.	Do. do.	Do. do.	38	2 ,,	,,	...	...	...	,,	340	90	...	6	...	1	...	1	...	2	...	...	...
71	C. E.	M.	Do. do.	Demented Hemiplegic	48	6 ,,	,,	...	...	...	Bloody	127	50	...	10	...	1	...	...	...	39	...	...	...
99	T. A.	M.	Do. do.	Expansive	51	1½ ,,	,,	...	...	...	Sl. bloody	520	86	...	8	...	1	...	...	...	5	...	...	...
106	E. W.	F.	Do. do.	Do.	51	2 ,,	,,	...	...	...	Clear	280	64	...	33	...	1?	...	...	...	3	...	...	...
1	W. G.	M.	General paralysis	Depressed	38	2 yrs.	P.M	6	Yes	Exhaustion	Turbid	2130	66	...	19	...	8	...	6	...	1	...	...	...
2	A. P.	M.	Do. do.	Demented	52	1½ ,,	,,	20	Yes	Broncho-pneumonia	,,	1000	59	...	32	...	4	...	4	...	1	...	...	...
6	W.	M.	Do. do.	Do.	44	9 ,,	,,	20	No	Septicæmia	,,	753	59	...	17	...	9	...	...	...	1	...	14	...
28	M. M.	F.	Do. do.	Do.	67	2 ,,	,,	1	Yes	Myocarditis	Sl. turbid	2320	46	...	40	...	3	...	10	...	1	...	...	...
41[3]	C. C.	F.	Do. do.	Do.	38	1½ ,,	,,	8	Yes	Broncho-pneumonia	Bloody	3400	78	...	3	...	7	...	...	...	1	...	11	...
50	M. H.	F.	Do. do.	Depressed	42	7 ,,	,,	6½	No	Do. do.	Blood-tinged	1596	52	...	30	...	5	...	5	...	...	...	8	...
51[1]	M. O'B.	F.	Do. do.	Demented	30	3 ,,	,,	12	Yes	Do. do.	Clear	1660	43	...	44	...	9	...	1	...	...	...	3	...
181[4]	A. S.	M.	Do. do.	Expansive Tabetic	59	1¼ ,,	,,	8	No	Exhaustion	,,	858	81	...	16	...	2	...	...	...	...	...	1	...
96	H. B.	M.	Do. do.	Depressed	49	2⅓ ,,	,,	18	Yes	Broncho-pneumonia	Sl. bloody	800	62	...	22	...	3	...	1	...	2	...	10	...
97	E. T.	M.	Do. do.	Expansive	67	1½ ,,	,,	½	No	Do. do.	Clear	2800	82	...	13	...	3	...	2	...	...	...	...	...
101	J. G.	M.	Do. do.	Demented	66	5 ,,	,,	15	No	Cerebral-hæmorrhage	Blood-tinged	500	77	...	13	...	5	...	...	...	2	...	3	...
7	J. E.	M.	Do. do.	Depressed	44	½ ,,	,,	33	Yes	Exhaustion	Sl. turbid	2100	65	...	24	...	10	...	1	...	...	...	...	...
13[5]	S. L. D.	F.	Organic dementia	Art.-sclerotic hemiplegic	72	1 yrs.	A.M.	...	...	...	Sl. turbid	8	...	+	...	+	...	...	...	...	...	...	...	...
17[6]	A. P.	F.	Do. do.	Demented-aphasic	46	2½ ,,	,,	...	Yes	...	Clear	8	...	+	...	+	...	...	...	...	...	...	...	...
24	M. F.	F.	Do. do.	Demented-aphasic-hemiplegic	62	6 ,,	,,	...	...	...	Sl. cloudy	80	48	...	46	...	...	...	...	...	2	...	4	...
31	M. C.	F.	Do. do.	Traumatic lesion of skull	57	4 ,,	,,	...	...	...	Clear	16	...	+	...	+	...	...	...	...	...	...	...	...
38	C. B.	F.	Do. do.	Simple dementia	56	1 ,,	,,	...	...	...	,,	11	...	+	...	+	...	...	...	...	...	...	...	...
39	C. O'H.	F.	Do. do.	Demented-aphasic	71	3 ,,	,,	...	...	...	,,	7	...	+	...	+	...	...	...	...	...	+	...	...
49[7]	S. D.	F.	Do. do.	Do. do.	79	3 ,,	,,	...	Yes	...	,,	12	...	+	...	+	...	...	...	...	...	+	...	...
54	G. D.	M.	Do. do.	Delusional type	54	¾ ,,	,,	...	...	...	,,	42	...	+	...	+	...	...	...	...	...	+	...	...
76	E. P.	F.	Do. do.	Aphasic	69	8 ,,	,,	...	...	...	,,	20	...	+	...	+	...	...	...	...	...	+	...	+
32	J. M.	F.	Do. do.	Simple dementia	60	2 ,,	,,	...	...	...	,,	18	...	+	...	+	...	...	...	...	...	...	...	...
64	M. B.	F.	Organic dementia	Hemiplegia	54	2½ yrs.	P.M.	1½	No	Entero-colitis. Shock	Sl. turbid	2157	8	...	89	...	?	...	2	...	...	...	1	...
65[7]	S. D.	F.	Do. do.	Demented-aphasic	79	3 ,,	,,	20	Yes	Cerebral softening	Bloody	1320	34	...	43	...	...	...	...	...	6	...	17 (10 in low chain)	...
78[5]	S. L. D.	F.	Do. do.	Hemiplegia	72	1 ,,	,,	1¼	No	Do. do.	Clear	873	21	...	70	...	...	...	...	...	...	...	9	...
80	M. H.	F.	Do. do.	Arterio-sclerotic dementia	82	3 ,,	,,	8	Yes	Broncho-pneumonia	,,	1250	39	...	50	...	1?	...	...	...	1	...	9	...
94[6]	A. P.	F.	Do. do.	Demented-aphasic	46	2½ ,,	,,	3	Yes	Pulmonary tuberculosis	Bloody	330	14	...	67	...	...	...	...	...	...	...	19	...
98	H. M.	F.	Do. do.	Arteriosclerotic dementia	67	2 ,,	,,	1½	No	Broncho-pneumonia	Sl. bloody	800	15	...	82	...	...	...	2	...	1	...	...	...
103	W. H.	M.	Do. do.	Depressed hypochondriac	59	½ ,,	,,	3	Yes	Suicide (cut-throat)	Sl. turbid	1200	7	...	84	...	...	...	1	?	1	...	7	...
110	J. M.	M.	Do. do.	Arteriosclerotic	67	2 ,,	,,	7	Yes	Chronic myocarditis	Sl. turbid	320	59	...	32	...	...	...	...	...	...	...	9	...

CHART II.

Summary of Cell Counts. Ante-mortem Fluids.

No. of Fluids.	Diagnosis.	Cells in 100 Fields.	Cells in 100 Fields. Average.	Lympho-cytes. Per cent.	Endo-thelial Cells. Per cent.	Plasma Cells. Per cent.	Phagocytes. Per cent.	Polymorpho-nuclear leucocytes. Per cent.	Other Cells. + Unclassified. Per cent.
19	General paralysis. . .	110–1500	450	73	13	2	1% of 4 cases	9	3% of 7 cases
10	Organic dementia . .	8–80	22	+	+	...	...	+	...
3	Senile dementia . . .	7–31	17	+	+	...	...	...	...
2	Polyneuritic delirium .	20–24	22	+	+	...	...	+	...
1	Chr. alcoholic insanity .	...	24	+	+	...	...	+	+
4	Epilepsy	12–52	45	+	+	...	...	+	+
4	Manic-depressive. . .	11–49	22	+	+	...	...	...	...
1	Involution melancholia	...	336	9	2	...	...	86	3
9	Dementia præcox . .	14–290	67	57	40	...	...	3	...
1	Cerebral lues	...	49	74	26	...	...	...	...
1	Neurasthenia	...	6	+	...	...	...	+	...
1	Organic dementia? . .	...	120	31	5	1?	...	64 (bloody)	...
1	General paresis? . . .	...	80	37	30	...	...	30 (bloody)	...

+ indicates that cells were present in these conditions, but in such a small number that percentages were valueless.

Summary of Cell Counts. Post-mortem Fluids.

No. of Fluids.	Diagnosis.	Cells in 100 Fields.	Cells in 100 Fields. Average.	Lympho-cytes. Per cent.	Endo-thelial Cells. Per cent.	Plasma Cells. Per cent.	Phagocytes. Per cent.	Polymorph-leucocytes. Per cent.	Other Cells. + Unclassified. Per cent.	Körnchen Cells. Per cent.
12	General paralysis . .	500–3400	1660	62	24	5	3 (9 cases)	1 (7 cases)	5 (6 cases)	
8	Organic dementia . .	320–2157	1000	19	68	(2 cells? in 2 cases)	5 cells in 3 cases	1 (4 cases)	6 (7 cases)	(10% in 1 case
3	Senile dementia . . .	340–800	420	26	63	(2 cells? in 2 cases)	...	...	10	
1	Manic-depressive . .	...	960	23	75	...	1	...	1	
1	Chr. alcoholic insanity .	...	86	60	32	...	...	3	5	
1	Dementia præcox . .	...	8	+	+	...	...	...	...	
1	Paranoia	...	156	54	41	...	...	...	5	
1	Paralysis agitans. . .	...	800	10	49	...	...	32	9	
2	Idiotic paraplegia . .	64–520	292	6	90	...	...	4	...	1 in 1 case
1	Morphinism	...	100	44	46	...	...	10	...	
1	Toxic delirium . . .	...	54	29	39	...	...	...	32	
1	Organic dementia? . .	...	45	+	+	...	...	+	+	
1	General paresis? . . .	...	556	66	30	...	4	...	...	

N.B.—Note the uniform increase in the total number of cells in the post-mortem fluids in the majority of psychoses.

CHART III.

Correlation of Cells in Fluids and Pia.

Pathological Findings.	(1) Fluid Examined. (2) Pia Examined.	Plasma Cells.	Endothelial Cells.	Phagocytes.	Fibroblasts.	Lympho-cytes.	Poly-morpho-nuclear Cells.	Mast Cells.	Un-classi-fied.
General paresis.	Fluid, No. 1	8%	19%	6%	...	66%	1%	...	...
	Autopsy, No. 1188. Cerebellum	Many	Few	One	Few	Many	...	...	...
	Lt. precentral	Many (frequently with double nuclei)	Numerous	Two	Many	Many	...	...	...
	Dorsal cord	Many	,,	...	Many	Many	...	...	...
	Choroidal ependyma	...	...	None	...	...	...	...	...
General paresis.	Fluid, No. 2	8%	19%	6%	...	59%	1%	...	...
	Autopsy, No. 1189. Rt. sup. frontal	Many (some multi-nuclear)	Many	None	Some	...	...	...	...
	Rt. precentral	Many	Numerous (small variety)	,,	,,	Many	...	...	...
	Dorsal cord	,,	,,	,,	,,	,,	...	...	...
	Lumbar cord	,,	,,	,,	,,	,,	...	...	...
General paresis.	Fluid, No. 7	10%	24%	1%	...	65%	...	...	...
	Autopsy, No. 1190. Cortex	Many	Numerous	None	...	Many	...	...	...
General paresis.	Fluid, No. 51	9%	44%	1%	...	43%	...	...	3%
	,, No. 8	6%	8%	...	...	79%	4%	...	3%
	Autopsy, No. 1194. Lt. sup. front.	Many	Many	One	Numerous	Many	...	...	...
	Rt. sup. frontal	,,	,,	0	,,	,,	...	...	...
	Cerebellum	,,	,,	0	,,	,,	...	...	...
	Floor of IV. ventricle	...	...	0	...	...	...	...	...
	Dorsal cord	Many	Very few	0	,,	,,	...	...	...
General paresis.	Fluid, No. 28	3%	40%	10%	...	46%	1%	...	...
	Autopsy, No. 1192. Cortex	Many	Many	0	...	Many	...	...	...
	Cervical cord	Numerous	Few	0	...	...	...	...	...
General paresis.	Fluid, No. 41	7%	3%	...	...	78%	1%	...	11%
	,, No. 26	2%	4%	...	...	94%	...	...	...
	Autopsy, No. 1193. Cerebellum	Many	Numerous	One	...	Many	...	...	...
	Lt. frontal	,,	,,	0	...	,,	...	Two	...
	Rt. precentral	,,	,,	0	...	,,	...	...	...
	Cord	,,	,,	0	Numerous	,,	...	...	...

Cerebral arterio-sclerosis Chronic lepto-meningitis	Fluid, No. 80 . . . . . Autopsy, No. 1197. Cortex .	1°/₀ (?) 0	50°/₀ Many	... Several	... Present	39°/₀ Few	1°/₀ ...	... ...	9°/₀ ...	
General paresis .	Fluid, No. 25 . . . . . Autopsy, No. 1206. Rt. frontal	2°/₀ Many (some with double nuclei)	30°/₀ Many (frequently pigment laden)	2°/₀ 0	... ...	64°/₀ Many	... ...	... ...	2°/₀ ...	
Cortical atrophy ?	Fluid, No. 17 . . . . . ,, No. 94 . . . . . Autopsy, No. 1202. Rt. frontal	 0	+ 67°/₀ ...	 0	... ...	+ 14°/₀ Few	... ...	... ...	... 19°/₀ ...	
Thrombosis, ascending parietal artery with softening	Fluid, No. 93 . . . . . Autopsy, No. 1201. Rt. pre-central	... One (?)	75°/₀ Many	1°/₀ ...	... ...	23°/₀ 0	... ...	... ...	1°/₀ ...	
Cortical softenings	Fluid, No. 182 . . . Autopsy, No. 1199 . . .	... ...	84°/₀ ...	... ...	... ...	9°/₀ ...	7°/₀ ...	... ...	... ...	Part of pia examined normal. Areas of softening not examined.
General paresis .	Fluid, No. 96 . . . . . Autopsy, No. 1203. Rt. frontal Rt. precentral . . . Cord	3°/₀ Many ,, Present	22°/₀	1°/₀ 0 0 0	... ...	62°/₀ Few ,, ,,	2°/₀	... ...	10°/₀	
Normal brain and cord	Fluid, No. 103 . . . Autopsy, No. 1204. Cord . Lt. precentral . . . Rt. frontal	... ...	84°/ ... Increased ,,	1°/₀ (?) ... 0 ...	... ...	7°/₀ ... Sl. increase ,,	1°/₀	... ...	7°/₀	Normal pia.
Normal brain and cord	Fluid, No. 91 . . . . . Autopsy, No. 1200. Rt. frontal	... 0	46°/₀ Few	... 0	... Increased	44°/₀ Rare	10°/₀ ...	... ...	... ...	
Cerebral arterio-sclerosis	Fluid, No. 82 . . . . . Autopsy, No. 1198. Lt. pre-central	... 0	49°/₀ Few	... 0	... Increased	10°/₀ Few	32°/₀ ...	... ...	9°/₀ ...	

Strictly speaking the pathological lesions found in cases marked "general paresis" were those of chronic exudative meningo-encephalitis, but when taken together with the clinical picture the former diagnosis seems justified.

spinal fluid. By glancing over this table it is evident that the pia mater is the origin of most of the cells found in the fluid, and that the numbers are in a general way correlated.

Here, again, the plasma cell is worthy of the greatest consideration. Numerous plasma cells were found in the pia of every section examined in cases of general paralysis, whether cortex or cord, and, as a rule, sections of the pia as far apart as possible were taken for this purpose. In our series only in otherwise clearly defined cases of general paralysis were plasma cells definitely found, and in all of these cases, whether living or dead, the cerebro-spinal fluid contained plasma cells.

A very few phagocytic endothelial cells were found in the pia of those cases of general paralysis of the eight autopsies, whereas they appeared in the fluid of seven cases. Doubtless further search would have shown a greater number in the pia. As phagocytes also occurred in the post-mortem tissues, we cannot attach as great significance to them as to the plasma cells.

Polymorphonuclear leucocytes were not demonstrated in the pia of our cases, though it is well known that they do occur in rapidly progressing cases.

Pial lymphocytosis in these cases is quite characteristic of general paralysis, and corresponds very closely with the degree of lymphocytosis in the fluid. Endothelial cell proliferation seems to be a common occurrence in a variety of conditions.

So we find that in the pia of the cases which came to autopsy are found approximately the same kind and number of cells which appear in the corresponding fluids, and notably that in general paralysis the pia, showing an excess of lymphocytes, is without doubt the seat of origin of the same cells in the cerebro-spinal fluid.

In conclusion we desire to extend our sincere thanks to Dr Chas. W. Page, Superintendent of the Danvers Insane Hospital, for his kindly interest and encouragement, and to Dr F. B. Mallory and Dr Adolf Meyer for their valuable assistance in the identification of the various cell types, to Dr F. P. Gay for many valuable suggestions, and to our colleagues on the Staff of the Danvers Insane Hospital, and the assistants in the laboratory, who were always ready and willing to co-operate with us in this investigation.

Summary.

1. We cannot but regard Alzheimer's method as the best yet devised for the cytological study of the cerebro-spinal fluid, the good results depending upon rapid fixation of the cells and the subsequent treatment of them as if they were tissue.

2. A good differential count and a fair quantitative count are possible by this method.

3. The cells regarded by us as of greatest diagnostic importance are the plasma cell, the phagocytic endothelial cell, the fatty granule cell, and the lymphocyte if in excess.

4. In psychiatry the cell picture in general paralysis stands out distinctly from that in the other forms of insanity, the latter being considered by us as presenting nearly normal fluids.

A high cell count, with excess of lymphocytes, over 100 to 100 fields, the presence of plasma cells and perhaps phagocytes, in a case of suspected general paralysis, is the strongest evidence in favour of this diagnosis.

5. It is possible that other organic cerebral conditions may show a cell picture of diagnostic importance, as indicated by the finding of fatty-granule cells in these conditions post-mortem.

6. The origin of the cells in the fluid is without doubt in large measure, if not entirely, traced to the pia mater.

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Description of Plates.

Plates 15 and 16.—Photomicrographs of cells found in cerebro-spinal fluid. Pyronin stain : × 1500 diameters.

Fig. 1 A.—Lymphocyte. Note the absence of protoplasm and distinct chromatophilic granules, "clock-face" arrangement.

B 1, 2, 3.—Various types of endothelial cells.

B 1.—Large endothelial cell, the nucleus swollen, and taking up most of the cell. Very little protoplasm visible. The nucleus is folded upon itself, but the thin line between the halves does not show, and the nucleus has a round appearance.

B 2.—The usual type of endothelial cells. Horse-shoe shaped nucleus beset around the periphery of the cell, with very little protoplasm visible.

B 3.—Small type of endothelial cells, sharply indented nucleus. Very few chromatophilic granules. Note the absence of distinct granules in all nuclei of endothelial cells as compared with the nucleus of phagocytes.

Fig. 2.—Phagocyting endothelial cell with lymphocyte inclusion. The nucleus is flattened and crowded to the periphery. Note the light court around the lymphocyte and enormous swelling of the protoplasm of the endothelial cells.

Fig. 3.—Plasma cell. Rather indistinct, but dark staining nucleus with "clock-face" arrangement of granules can be made out, also the shape of protoplasm, with a brighter area in the lower part. Protoplasm a deep red and nucleus a deep blue. (See Plate II., 6, 7,8, 9.)

Fig. 4.—Cell showing mitotic figure in active state of karyokinesis. Difficult to determine to which type this cell belongs.

Fig. 5.—"Körnchen cell." The nucleus is hardly visible, but the fat droplets can be distinctly seen.

Fig. 6.—Low power field in case of general paralysis, showing the distribution and density of cells. The total cell count here was 900 to 100 fields. A normal field would show only one or two cells at the most.

PLATE 17.—Cells of cerebro-spinal fluid. Pyronin stain : drawn with camera lucida (No. 4 ocular and $\frac{1}{12}$ oil immersion).

Figs. 1, 2, 3.—Phagocytes. In 1 and 3 the inclusions are lymphocytes, but in fig. 2 the inclusion is apparently an endothelial cell, or perhaps a degenerated lymphocyte.

Figs. 4, 5.—Endothelial cells.

Figs. 6, 7, 8, 9.—Plasma cells.

Fig. 10.—Transitional form (?) between lymphocyte and plasma cell.

Fig. 11.—Lymphocyte.

Fig. 12.—Mitotic figure in cell, whether plasma or endothelial not decided.

Fig. 13.—"Körnchen" cell.

Fig. 14.—Fibroblast (?).

Fig. 15.—Polymorphonuclear lymphocyte. No protoplasm visible.

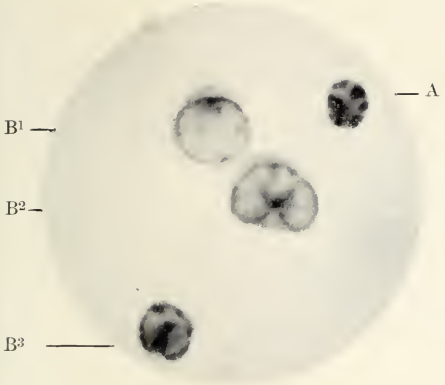

FIG. 1.

FIG. 2.

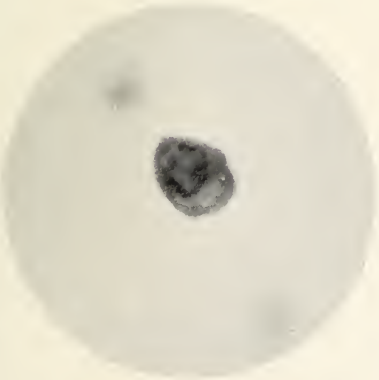

FIG. 3.

FIG. 4.

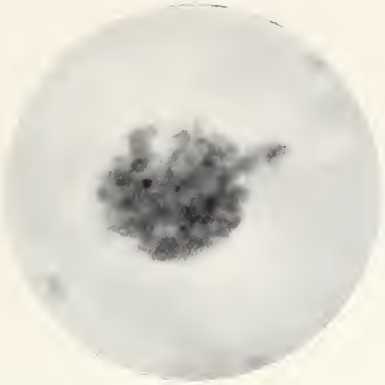

FIG. 5.

FIG. 6.

1, 2, 3. Phagocytes.
4, 5. Endothelial Cells.
6, 7, 8, 9. Plasma Cells.
10. Transitional Cell (?).
11. Lymphocyte.
12. Mitotic Figure (Plasma Cell?).
13. Kornchen Cell.
14. Fibroblast (?).
15. Polymorphonuclear Leucocyte.

All cells stained with pyronin-methyl green.

A CASE OF CENTRAL NEURITIS WITH AUTOPSY.*

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AND

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Introduction.

In 1897 Meyer, in describing various pathological changes in the Betz cells of the motor cortex, reported the findings in a case of melancholia of the involution or senile type, in which the alteration in the Betz cells, known as the axonal reaction, was present.[1] During the following three years, he was able to collect eight cases in which this reaction occurred, and he published these cases, with others found in the literature, under the title of "Parenchymatous systemic degenerations mainly in the central nervous system."[2] For this rather long and cumbrous title he substituted the name "Central Neuritis."

This condition, which was regarded as terminal, was found to occur in psychoses that were, as a rule, depressive in character at the onset. It occurred at the involution period, as well as in alcoholic-senile states and in alcoholic-phthisical-cachetic states. Banal cachexias and infections appear to have no direct relation to central neuritis, a fact that is verified by the rather rare occurrence of this condition in a great number of autopsies. The association of central neuritis with depressive mental states is striking but unexplained.

* Read at the annual meeting of the American Medico-Psychological Association, Cincinnati, Ohio, May 12-15, 1908.

[1] Adolf Meyer. Demonstration of various types of changes in the giant cells of the paracentral lobule. Am. Jr. Ins., Vol. LIV, October, 1897, No. 2.

[2] Adolf Meyer. Parenchymatous Systemic Degenerations Mainly in the Central Nervous System. Brain (Part XCIII, 1901).

The clinical symptoms are described as rather vague, occurring suddenly where no organic lesion was suspected; difficulty in locomotion, increased weakness of co-ordinated movements, at times jactitation of the limbs and rigidity, disorders of the reflexes, together with diarrhea and occasional febrile fluctuations. The mental condition in this terminal state is an anxious, perplexed agitation, delirium or stupor, not unlike a protracted delirium tremens.

The lesions in these described cases are distributed throughout the cortex, cerebellum, cord and spinal ganglia and also in the sympathetic ganglia. In some of the reported cases, peripheral neuritis was also present.

In two cases of polyneuritic delirium reported by Sims, axonal reaction was present in the anterior horn cells of the cord, Clarke's column, and many cranial nerve nuclei, and in one case this reaction was present in the Betz cells of the motor cortex.[3]

Aside from these cases, nothing has appeared in the literature in regard to this condition. Drs. Southard and Hodgkins [4] found the axonal reaction generalized in a case of epilepsy, and pointed out the striking reduction of consistence in the brain (encephalomacia autolytica).

That the condition (central neuritis) can be recognized from its symptoms and established anatomically is no longer in doubt and has been repeatedly demonstrated at the Worcester and Danvers insane hospitals.

The possibility of remissions during the course of this condition was suggested by Meyer and has been since observed.

Clinical History.[5]

E. S. H., æt. 40.

Family History.—Negative, except that father died of cancer.

Personal History.—Early development normal. No peculiarities known. No serious illness. Married æt. 20, and married life was happy until five years ago when husband's infidelity became known to the patient. Three

[3] F. Robertson Sims. Anatomical Findings in Two Cases of Korsakoff's Symptom-Complex. Jour. Nervous and Mental Diseases, March, 1905.

[4] Note on Cell Findings in Soft Brains. E. E. Southard and M. B. Hodgkins. Am. Jr. Ins., Vol. LXIV, No. 2, 1907.

[5] We are indebted to Dr. H. M. Swift of the Danvers Insane Hospital for the excellent initial mental and physical examination.

years ago husband brought home a woman from Porto Rico, which event completely upset the patient and she had some sort of a fit which lasted several hours. She was semi-stuporous for several days after this, and her mental trouble dates from this time. She brooded a great deal over the wrongs done her by her husband and gradually a change of disposition was noted. She neglected the children and seemed to lose interest in everything. Her son states that marked depression has been present for one year only. She was restless, walked the floor a great deal, wringing her hands. Delusions of persecution were prominent; she thought that everyone was against her, that her children were trying to kill her and that the neighbors were going to poison her. For two months before admission she became gradually worse. During the day she was inactive, refused to answer questions. At times she was much agitated and showed marked affect of fear. At other times she was sleepless at night. She thought something was going to happen to her children and was violent to her children without cause. Two days before admission she made a feeble attempt at suicide.

She was committed to the Danvers Insane Hospital September 10, 1906, and at time of admission she was somewhat depressed and agitated. She was restless, constantly rubbing her head with her hands and wringing her hands. She had an anxious, worried facial expression. Questions were answered relevantly and her conversation was coherent. She was willing to answer most questions, and was moderately communicative. She talked in a rather low tone and often slowly. During the tests for school knowledge she often asked examiner to stop as it was too much of an effort for her to think. She frequently repeated, "Oh dear me," but would not explain her agitation.

Consciousness and Orientation.—Patient's consciousness was not clouded and she was well oriented for time, place and persons. She had a good grasp upon her surroundings and a fair knowledge of current events.

Intellect.—Probably defective. Patient exhibits a rather scanty fund of information. School knowledge poorly retained. Calculating ability was defective. She was able to perform only the most elementary problems.

Memory.—Good for remote events, except for exact dates. Patient was able to give a consistent account of her life. Children's names and birthdays given correctly. For recent events her memory was fair. Retentive memory good.

Mental Attitude.—One of consistent depression with slight agitation. Spontaneous thought apparently sluggish. There was a suggestion of retardation as shown by some tests. She usually answered after a short pause. She spoke in a low tone and without animation, but not particularly slowly. She was able to count rapidly.

Attention.—Was difficult to obtain. Patient showed difficulty in concentrating her attention for problems, although she was able to count raps on the table when rapidly executed. No *hallucinations* could be demonstrated.

Delusions.—Depressive ideas and vague ideas of persecution were present. She maintained that she felt queer and that the neighbors might have poisoned her. No attempt at systematization. No true *insight* into her condition.

Physical Examination.—Height, 5 feet 4½ inches. Weight, 128 pounds. A fairly well-nourished woman. Complexion pale with lemonish tinge (hemaglobin found to be 50-60 per cent). Brown hair, streaked with gray. Dry scaly areas on inner side of left ankle and higher up on leg three small irregular scars.

Respiratory System.—Diminished breath sounds over the right side of the chest, both anteriorly and posteriorly. Slight dulness on percussion over the right lung posteriorly with increased fremitus.

Circulatory System.—Pulse regular, 70. Radial arteries not thickened. Apex beat is inside mamillary line. No enlargement of the heart.

Abdomen.—Negative.

Urine.—Slight trace of albumen. Specific gravity 1011. Slightly alkaline in reaction. No casts.

Neuromuscular Condition.—Negative.

Reflexes.—Knee-jerks and achilles brisk. Plantars and abdominals present. Forearm reflexes brisk.

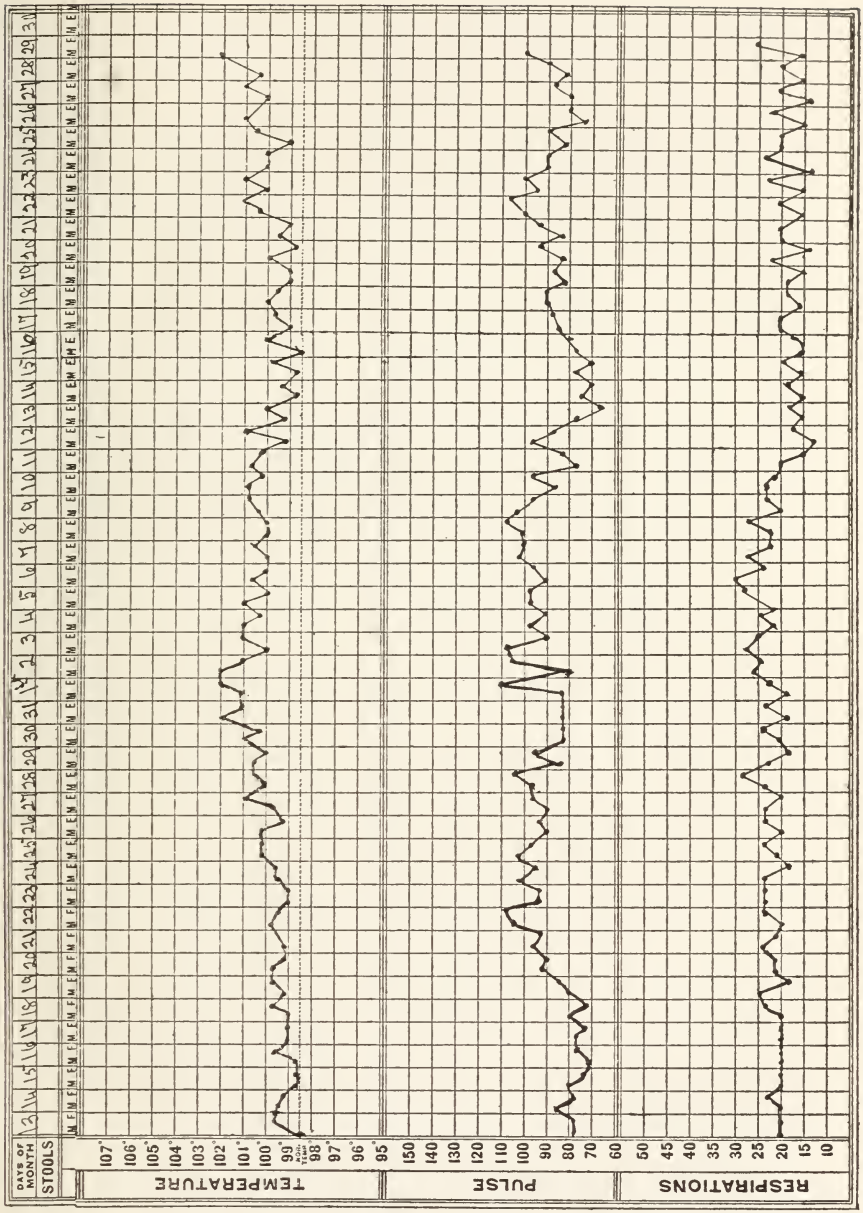
Pupils.—Equal, central and regular; react promptly to light and accommodation.

Progress of the Case.—Patient continued much depressed and emotional and was frequently found crying. Soon after admission she complained of great weakness, which she claimed was increasing. She was very inactive and this was probably due to weakness rather than retardation. On one occasion she vomited. She became more apprehensive and feared she would not recover. On September 24, she complained of having numerous loose movements. At this time her temperature began to rise. (See chart.)

October 15. Patient was put to bed because of general weakness. Twice during the night *she had fallen when going to the toilet room.* Once she was faint, and the nurse thought she was unconscious, but the other time she was not unconscious. She *maintained that her legs were too weak to hold her.* She was somewhat apprehensive and consciousness was quite clear. She had a good appetite. Urinary examination at this time negative. Appetite was very good. For a month patient continued to have loose movements day and night, but no pain accompanied them and no mucus or blood was present in the stools. Internal medication gave no relief. Mental condition much improved. She was less depressed and apprehensive and talked in a rational manner.

Blood Examination.—November 6. Reds, 3,757,705; whites, 4380; hemoglobin, 60 per cent.

November 17. A great change was noticed in patient. For several nights she had been delirious. Consciousness not altogether clear. Gives the date as December 20. Could not remember names of physicians. At this time a slight but rather constant twitching of the hands, fingers,


DATE October 13 - 1906 November
DAYS OF MONTH
STOOLS
TEMPERATURE
PULSE
RESPIRATIONS

lower jaw and toes was present and equal on both sides. Memory good. Gives the exact time of her hospital residence and time in bed. From the clinical symptoms present a diagnosis of "central neuritis" was made on this date.

November 19, 1906. For the past few days patient has been more or less delirious, especially when alone. However, upon questioning she can be brought to consciousness and gives evidence of being well oriented. At first says this is Lawrence, but upon being questioned, changes it to Danvers. Knows approximately the date and recognizes those about her, calling doctors and nurses by name. There has been almost constant fibrillary twitching of the hands, arms and legs for the past few days, jactitory in character, together with some stiffness in the neck muscles, backache and moderate stiffness of the arms and legs. Patient's diarrhea has been improved by warm irrigation and silver nitrate solution ordered for every day with salt solution enemas. Patient shows no marked depression except crying at times. There is no marked anxiety, but evidently some confusion. She has a good appetite and would eat all that was given her. Now takes only liquid diet; does not sleep well. Always more confused and delirious at night. When confused, calls out names of family. No evidence of hallucinations. Patient visited by daughter and friend yesterday. She recognized them, but refused to converse, often saying, however, she was glad to see them. Did not know her people at first. Now somewhat perplexed.

Vision.—Counts fingers at distance of one foot, but makes many mistakes at first.

Reflexes.—Elbow and forearm reflexes, knee-jerks and achilles exaggerated. Tendency to clonus. Considerable atrophy of the muscles of the arm, especially of ulnar muscles and fingers. Marked inco-ordination of hand movements, especially in touching nose. Tremors are increased in these tests. Left hand seems weaker in grasping. No true asterognosis in either hand. Patient's attention difficult to hold. Makes many mistakes, although many things are recognized.

November 20, 1906. To-day patient is somewhat worse, for the most part semi-conscious and very difficult to arouse. There is almost continuous twitching of the hands, feet and face, at times, with lower jaw drooped and lower lip considerably "caved in." Shows some difficulty in speaking. Recognizes physician and is oriented, although when first questioned shows marked confusion and perplexity. The last few days wrinkling of the forehead has been noticed, giving a very perplexed expression, becoming more frequent (omega contraction). Patient has very little to say voluntarily. No stools. Temperature to-day 99.6°, reaching normal in the morning.

November 21, 1906. Patient looks better this morning. Muscular twitching still present. Marked inco-ordination. She is a little brighter mentally and maintains she feels better. However, upon questioning, there seems to be some confusion. Has a good deal of difficulty in pronouncing words

intelligibly. When she becomes agitated over questioning, the face assumes the perplexed expression spoken of before. The patient does not talk voluntarily. Continually moves tongue about in her mouth and tongue takes part in the general muscular twitchings. Right pupil seems a trifle larger than the left.

Q. How do you feel? A. "Well." Q. Where are you now? A. "Danvers" (after much trying to pronounce name). Q. Do you know me? A. "Yes—no, Dr. Cotton." Q. How long have you been here? A. "Two days." Q. How long have you been here? Begins to cry and perplexed expression comes on. Q. Have you any pain? A. "No." Q. Do you feel comfortable? A. "Yes." When asked to shake hands patient takes hand from under the clothes, takes spread to give to physician, moves hands awkwardly about when command is repeated. Says, "I am—I am." Finally grasps physician's hand. In attempting to put finger on her nose shows some inco-ordination, brings finger within one inch of her nose, and holds it there as if she had accomplished the demand. Finally reaches the nose and keeps her hand there with some difficulty, since the twitchings increase very much, even extending to the eyes and all the facial muscles. When asked what she is doing, says, "Nothing," and takes hand down. Able to count fingers at a short distance. Q. Are you afraid of anything? A. "No." Q. Why do you look worried? A. "Oh, I don't know." Asked if she likes to have people talk to her, says, "Yes, I like to have company." *When patient is put on her feet she will collapse unless held.*

November 22, 1906. Patient gradually failing. To-day twitchings more frequent, with all muscles involved except abdominal. Patient is dull, stupid and has great difficulty in grasping questions and answering the same. Tongue twitches almost constantly. At irregular intervals patient's brow contracts and wrinkles, giving the *peculiar perplexed expression.* At these perplexed times, there is no more clouding of consciousness than at other times. Usually in a semi-dreamy state, patient when questioned, shows that she is fairly well oriented as to her surroundings. To-day her speech is hardly intelligible, and she often talks spontaneously in a sort of mutter. Occasionally looks upward at a corner of ceiling and waves hand as if grasping something. This may be a reaction to hallucinations, but the point is difficult to determine. Patient's attention is very difficult to obtain and cannot be held longer than a few minutes. To-day she reacts very sluggishly or not at all to pain stimuli. She scarcely ever winces when pricked. All reflexes much exaggerated. Slight touches bring out knee-jerks, arm and elbow reflexes. No Babinski. Organic reflexes apparently affected. Patient voids urine and feces without knowledge and does not appreciate any untidiness. Temperature, which has been lower the last few days, is higher to-day, reaching 102° in the afternoon. Patient seems much weaker. For three days she has had no diarrhea, apparently as the result of irrigation treatment. Abdomen smaller. Small enemas produced five loose movements during the night.

Electrical Reactions.—Pronounced diminution to Faradic stimulation in all muscles of forearms, hands and lower extremities. Difficult to accurately determine on account of almost continuous twitchings. Twitchings set up by the current and last several seconds afterwards. To galvanism there is also some diminution in all muscles tested, though not as marked as to Faradic. Patient showed to-day great difficulty in swallowing. The food was regurgitated and often choked her when she attempted to swallow. An attempt was made to get patient to try to walk, but she was unable even to stand alone. Absolute loss of co-ordination was shown also in other movements.

Blood Count.—Hemoglobin, 65 per cent; white count, 4840; red count, 3,912,000. Differential white count:

Polymorphonuclear leucocytes		56.5%
Large mononuclear leucocytes	26.0	43.5%
Small mononuclear leucocytes	2.5	
Transitional forms	15.0	

November 23, 1906. At first to-day patient seemed much worse. Made no attempt to answer questions and appeared unable to comprehend questions, or demands. Later, however, she answered a few questions, showing that she knew where she was. Unable to recall name of physician, but gave her own name and the name of the hospital. She took her nourishment better. Twitchings not so marked nor so frequent as yesterday. Perplexed expression not so frequent. Patient failed to sleep during the night, but was quiet and did not talk. To-day reacts somewhat to pin pricks, but is mentally so dull that tests are not accurate. Calls two fingers at first three fingers, later two fingers. A few days ago was able to count fingers fairly correctly. Patient complains of no pain. *Blood culture* sterile. All reflexes markedly exaggerated. Temperature 100.2°.

November 24, 1906. Patient seems a little better and takes nourishment. However, in the afternoon was much weaker and unable to swallow. Patient does not talk spontaneously and now cannot answer questions. Often lips move, but no audible sound is heard. Patient keeps eyes fixed usually in one position, but can follow finger when directed. Evidently hears when spoken to, but fails to understand. Twitchings not so frequent or general as at last note. Perplexed expression much less frequent. Neck stiff and head turned to left. Temperature 100° this p. m. Patient had four loose movements last night, one fairly normal movement to-day. Pulse weak and feeble.

November 25, 1906. Patient shows little change this morning. She had two movements during the night. No mucus or blood. Takes nourishment better. Speech very indistinct and thick. She recognizes those about her and asks for some hot drink. Twitchings of hands, fingers, tongue and lips more marked. Patient smiles, or attempts to smile, when told by physician, even when perplexed. Not apprehensive. This morning neck not so stiff. Patient calls out loudly at times, but what she says is unin-

telligible. She reacts to pin pricks, but in general, pain sense is much blunted and retarded. Occasionally takes hold of physician's hand as if frightened and talks indistinctly and fast. Knee-jerks equal and much exaggerated, and a slight tap produces marked reflex. Clonus in both ankles, but only a half-dozen beats and soon exhausted. Plantars are present and no Babinski.

Electrical reaction still diminished to both faradism and galvanism. Marked inco-ordination.

November 26, 1906. Patient slept little last night. Had frequent spells of fright probably in reaction to hallucinations (visual). She screamed, looked very much frightened and fingered imaginary things with her hands. This episode lasted only a few minutes, then she was quiet again. Night nurse states that patient has had such spells ever since she has been in this semi-conscious condition. Patient has slept little during the last three nights. Twitchings this morning more marked and now, aside from the minor jactitations, patient has developed a much coarser form of twitchings; these are almost convulsive in character and come at the same time as perplexed expression in face. The whole arm and head twitch, but not the feet. She is unable to form any words, but apparently makes the attempt. Continuous twitching of mouth and tongue. Great difficulty in swallowing. Patient has developed a beginning bed sore in spite of all care and attempts to prevent it. Voids her urine and feces frequently and involuntarily. Much rigidity of all the muscles this morning. Patient holds on to the bed clothes. All reflexes much exaggerated as formerly. Reacts very slightly to pin pricks, except on her face. Temperature, 101.4°. Slight ptosis of left eyelid.

November 27, 1906. Patient failing rapidly and now practically unconscious. Pays no attention to external impressions. Breathing rapid, pulse rapid and weak. Makes no attempt to articulate. Does not follow directions. Eyes open and staring. Pays no attention to pin pricks. Reflexes brisk, but there is marked rigidity of all the muscles, which accounts for less exaggeration. Ankle clonus only slight. Plantars normal. No Babinski. Head thrown back. Considerable rigidity of the neck. Twitchings almost continuous and at times stronger than at others. Expression blank, except for occasional furrowing of brow and perplexed expression. Temperature, 101.4°.

November 28, 1906. Patient did not rally after last note. She continued to fail. Almost constant twitchings of the extremities and facial muscles, also tongue and lips. Patient could not talk or form words at all. She died at 10 a. m.

Summary of Clinical History.

Psychosis appearing in a woman of 40, with negative family history and uneventful personal history. Onset of psychosis three years before admission following mental shock caused by husband bringing a strange woman to live at her home. Gradually increasing depression, resulting from

brooding over her wrongs. Vague delusions of persecution. Considerable apprehensiveness, agitation and sleeplessness. Violence towards children and suicidal tendencies. Admitted to Danvers Insane Hospital September 10, 1906.

Here, at first depressed, apprehensive and somewhat agitated. Clear consciousness, orientation and memory perfect. Intellect apparently slightly deteriorated. Sluggish stream of thought and suggestion of psycho-motor retardation. Delusions of persecution and depressive ideas prominent with strong reaction to the same. No insight into her condition.

Physical Examination.—Somewhat anæmic. Otherwise negative. Neurological examination negative.

Soon after admission appearance of general weakness. Became more apprehensive and depressed. One month later developed obstinate diarrhea, loose watery stools and no pain, mucus or blood. Slight rise in temperature. At this time unable to stand and fell on two occasions, once unconscious. Maintained that her legs were unable to hold her. Then one month with improvement of mental condition, but diarrhea resisted all internal medication. November 17 (two months after admission), so weak she was unable to stand. Slight bilateral twitchings, almost constant of arms, hands, fingers, toes and lower jaw. Consciousness somewhat clouded at times. Diarrhea improved and later checked by warm irrigations and nitrate of silver solution. Delirious when left alone, but could be roused by questions. Consciousness at times quite clear. In a few days twitchings were increased, and marked stiffness and rigidity of the muscles appeared with considerable pain when touched. Considerable exaggeration of reflexes and tendency to clonus. Marked atrophy and weakness of muscles of arms and legs. Marked inco-ordination in hand movements and tremor increased by voluntary movements. No astereognosis. Her physical condition became much worse and soon she was unable to speak intelligibly. Lower jaw was dropped and on November 20, occasionally a peculiar wrinkling of the forehead was noticed (omega contraction), showing marked anxiety and perplexity. No voluntary conversation.

Blood Examination.—Hemoglobin, 65 per cent; red, 3,912,000; white, 4840.

Differential Count:

Polymorphonuclear leucocytes		56.5%
Large mononuclear leucocytes	26.0	43.5%
Small mononuclear leucocytes	2.5	
Transitional forms	15.0	

Patient continued in a semi-delirious state, with constant twitchings of the muscles of the extremities, apparently visual hallucinations at times. Marked confusion and anxious perplexity as shown by peculiar "omega contraction" of skin of forehead.

Electrical Reactions.—Pronounced diminution to Faradic stimulation in all muscles of forearms, hands and lower extremities, also some diminution to galvanism. Reaction of degeneration not established. Constant twitchings made tests difficult.

Disturbance of cutaneous sensibilities developed later and marked exaggeration of reflexes and ankle clonus. Temperature chart shows various fluctuations, but temperature was above normal. Towards the last, involuntary passages of urine and feces. Inability to talk and swallow. Anxious, perplexed delirium became more profound and associated with vivid hallucinations and fear with occupation delirium.

Patient rallied a little but finally died November 28 of pulmonary thrombosis, eleven days after the appearance of the twitchings and inco-ordination. The terminal condition may be said to have lasted nearly two months and a half, if we date the onset at time of appearance of weakness with diarrhea and tendency to fall. The diagnosis of "central neuritis" was made on November 17, eleven days before death.

If we follow the course of this terminal condition, the first symptom to appear was a general weakness, then diarrhea, tendency to fall and inability to stand. Later, involuntary twitchings of the muscles of the extremities with atrophy, rigidity and pain on passive movements. The peculiar perplexed delirium occurred with the twitchings and became far more profound with progression of the other symptoms. Then inability to talk and swallow. Later, vivid hallucinations and considerable fright and occupation delirium.

Autopsy Findings.

The autopsy was performed three hours after death by the writers. The protocol is here presented in full on account of the possible interest which all the organs may attain in a case with such widespread lesions of the nervous system.

White female, age 40. Healed ulceration of left lower leg (varicose). Trivial area of sacral decubitus. Excoriations on inner surface of the right knee. Rigor and lividity absent. Abdomen lax. Pupils: left, 6; right, 4.5 mm. Abdominal fat, slight, orange yellow. Thoracic muscles of the usual appearance.

Peritoneal Cavity.—Parietal and visceral serosa normal. Intestinal vessels not injected. Contents of cavity normal. Omentum retracted, contains a little fat. Diaphragm arches to fifth interspace left; fourth rib right. Mesenteric nodes palpable, of a brownish gray tinge.

Pericardial Cavity.—Normal.

Pleural Cavities.—Show no adhesions.

Heart.—Weight, 285 grm. Sub-epicardial fat in considerable amount. Muscle firm, gray red. Faint fibrous mantling of wall of left ventricle near aortic valve. Faint nodular sclerosis of both coronary arteries.

Measurements.—T. V. 10.5, M. V. 9.0, L. V. 1.5, P. V. 6.0, A. V. 6.5, R. V. 0.3.

Lungs.—Left shows slight post-mortem congestion. General edema. Mural thrombus, 2.5 x 1.0 x 0.75 cm., mixed red and gray, granular and friable, attached to wall of branch of pulmonary artery leading to lower lobe (no infarction). Right shows thrombus, 4.0 x 1.0 x 0.75 cm., of similar character to thrombus of left lung, which has produced infarct 10 x 8 x 0.3 cm. deep upon outer surface of lower lobe.

Bronchi.—Normal. Bronchial lymph nodes small.

Spleen.—Weight, 245 grm. Capsule smooth, tense. Substance firm, cuts smoothly. Small hemorrhages 0.2-0.3 cm. in diameter in pulp. Malpighian bodies visible. Trabeculæ normal.

Gastro-intestinal Tract.—Explored throughout, shows no evidence of lesion beyond an occasional small spot of congestion. Contents, liquid, pale.

Liver.—Weight, 1845 grm. Border a trifle blunter. Substance gray red, cuts smoothly, takes thumbnail easily, shows lobulation very indistinctly and contains miliary and submiliary necroses.

Gall Bladder.—Not remarkable.

Pancreas, Adrenals.—Normal.

Kidneys.—Weight, 405 grm. Strip with difficulty from an uneven surface. Cortex not diminished in width. Markings evident. Centers of pyramids show a moderate fibrosis.

Pelves, Ureters, Bladder.—Not remarkable.

Genitalia.—Normal.

Aorta.—Shows nodular sclerosis of thoracic portion.

Organs of Neck.—Not remarkable.

Head, Scalp, Calvarium, Dura Mater.—Normal. Arachnoidal villi moderately developed.

Pia Mater.—Clear.

Brain.—Weight, 1405 grm. Soft and in large part moist. The consistence of the major part suggests the effect of a combined process of encephalomalacia and edema with the edema superficial and largely confined to the vertex. The left hemisphere is a bit firmer than the right. Both poles and the lower surface as far up as the inferior temporal gyri are firmer than the remainder of the brain. The orbital surfaces and the hippocampal gyri show the maximum consistence, the temporal gyri the minimum consistence in the hemispheres. The lower structures, including cerebellum, are softer than usual. Cerebellum, pons and bulb weight 175 grm.

Spinal Cord.—Consistence decreased. The roots are a trifle softer and perhaps moister than normal. No lesion can be observed in the root ganglia or in the Gasserian or abdominal sympathetic ganglia.

Anatomical Diagnosis.

General encephalo, myelo and neuromalacia; superficial edema of the cerebral tissues at the vertex; slight sacral decubitus; unequal pupils; pulmonary thrombosis in both lower lobes (recent); focal necrosis of the

liver; multiple small hemorrhages in spleen; chronic diffuse nephritis of moderate degree; slight coronary arteriosclerosis; nodular sclerosis of thoracic aorta; slight fibrous endocarditis of left ventricle; healed varicose ulceration of the left leg.

Chemistry.

Two portions of brain substance from the frontal pole and the central region of the left hemisphere were examined chemically by Dr. R. L. Emerson.[6]

Determinations were made of neurokeratin, alcoholic and ethereal extracts and of total phosphoric acid. The frontal portion gave a residue from 10 grm. of 0.17 grm. neurokeratin as against a residue of 0.1 grm. neurokeratin for the central region.

The alcoholic and ethereal extracts gave a residue from 10 grm. of 0.23 grm. for the frontal portion as against 0.31 grm. for the central portion. The frontal sample gave from 11 grm. of 0.16c. figured as P_2O_5 the central sample gave 0.12c. figured as P_2O_5.

Microscopic Findings.

The organs of the trunk and various parts of the nervous system were fixed in Zenker's fluid and stained by the eosin-methylene blue, anilin blue and phosphotungstic acid hematein methods. Various parts of the nervous system were fixed in alcohol and stained by Nissl's method. Similar parts were fixed in formaldehyde and prepared according to Weigert's myelin sheath method and the Marchi method. Preparations were also made according to Cajal's method for fibrils. Frozen sections were stained with Scharlach Roth.

Organs of the Trunk.—The examination of the organs of the trunk served in the main to confirm the gross diagnosis. The heart showed a minor degree of intimal sclerosis of small branches of the coronary arteries. A section from the left ventricle showed a considerable degree of interfascicular fibrosis, as well as several foci in which muscle fibers had been diminished in diameter or totally destroyed. A section from the right ventricle showed far less interfascicular fibrosis and no foci of muscular atrophy. It was also worthy of note that the right ventricle showed far less perinuclear pigmentation of the fibers constituting its walls than did the left ventricle.

Lungs.—Showed in the alveoli considerable number of pigmented phagocytic cells. The thrombus of a pulmonary branch described in the gross, however, had led to no infarction. Microscopic examination by several methods of the pulmonary arteries, showed an extensive sclerosis with deposit of lime salts, which recalls conditions found, as a rule, in the greater circulation. The zone of adhesion between the thrombus and the

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[6] Under a grant from the Proctor fund.

sclerotic wall showed very numerous pigmented cells imbedded in granulation tissue. The bronchi were normal.

Spleen.—Showed throughout the pulp numerous small hemorrhages of a recent character. A number of phagocytic cells can be demonstrated in various parts of the pulp, but phagocytosis cannot be said to be markedly active. There is an increase of fibrous tissue in the pulp. The Malpighian bodies are very generally dotted with mononuclear phagocytic cells which are actively digesting cells of the lymphocytic type. Most of the cells of the Malpighian bodies are small, of even diameter and provided with nuclei approaching the solid type. The Malpighian arterioles show a moderate amount of hyaline change.

Lymph Nodes.—From several sources show a moderate number of large mononuclear cells in the sinuses, but the sinuses themselves are not especially dilated. The cells of the lymphoid tissues of the lymph nodes present a certain difference from those of the Malpighian nodules of the spleen in that the nuclei of the lymphocytes in the lymph node, are rather more vesicular than those of the Malpighian lymphocytes. Moreover, there is a considerable tendency to the occurrence of cells resembling the plasma cells. There is nowhere any appearance suggesting invasion of perilymph-node tissue.

Bone Marrow of Right Femur.—The marrow is more cellular than usual. The capillaries are dilated with blood corpuscles. The cells of the tissue spaces are predominantly mononuclear. The mononuclear cells, as a rule, show large vesicular nuclei. The cytoplasm assumes a variety of shades both blue and red. A number of the nuclei of the mononuclear cells show indentation, with an occasional transition toward the polynuclear form. There is a certain number of cells with pyknotic nuclei about which it is impossible to say whether they are ill-preserved or degenerate. Cells of a frankly polynuclear type occur in about the proportion of one to ten of the mononuclear forms, although there are small foci in which polynuclear leucocytes are more frequent. Cells with large eosinophile granules are comparatively infrequent. They occur in about the proportion of one to twenty-five or more of the mononuclear forms. Many fields may be searched without results for eosinophile cells. The eosinophile cells are apt to be mononuclear or somewhat indented. The giant cells of the marrow are fairly frequent. They present the usual picture of multiple vesicular nuclei pulled out into various amœboid shapes. The cell bodies are rarely provided with prolongations.

Liver.—Microscopic findings confirm the gross diagnosis.

Adrenal.—Not remarkable.

Kidney.—Confirm gross diagnosis.

Intestinal Tract.—Several foci of the intestine showed intensely congested capillaries. These foci are minute and fail to be related with especially marked changes in nerve cells. The most important change found in the intestine, at least from the present point of view consisted in changes of two types found in the nerve cells of Auerbach's plexus. These changes

recall, on the one hand, the edema change as found frequently in the large nerve cells of the central nerve system, and, on the other hand, the axonal reaction of Nissl as found in the central nerve system upon section of the corresponding nerve fibers. We are unable to say definitely what relation these changes bore or could bear to the diarrhea. The second type of change, namely, that which resembles the axonal reaction of the central nervous system, may well be a sign that the lytic agent which has affected the nerve cells of the brain, spinal cord and dorsal root ganglia, has also taken effect in the sympathetic system. If so, this intestinal nerve cell change must be regarded as one of our best evidences that the condition with which we are dealing is a condition of general neuritis and not merely one of central neuritis.

The majority of cells show a reaction resembling the axonal reaction; that is to say, the cell body is rounded; the nucleus is pyknotic, somewhat shrunken and eccentric; and the contents of the cell body are homogeneous. (See Fig. 3, illustrating a change regarded as due to simple edema, and Fig. 4, showing the characteristic change in nerve cells of Auerbach's plexus.)

Numerous mitoses are found in the epithelium in various parts of the small intestine. It might be an attractive hypothesis to relate these mitoses of the epithelium in some ways to the nerve cell changes in the sympathetic system. There are not data enough by which to support this hypothesis.

Central Nervous System.—The examination of the central nervous system, like that of the organs of the trunk, serve, in the main, to confirm the gross diagnosis. We shall limit our description to points which we regard as related to the condition in hand. We relied upon the Nissl method in its original form for detection of the axonal reactions which the clinical symptoms had led us to expect. We examined numerous areas from both sides of the cerebrum, from several regions in both cerebellar hemispheres, and from three levels of the spinal cord by the Nissl method. Co-ordinately with these areas we examined adjacent blocks by the eosin and methylene blue, the anilin blue and the phosphotungstic acid hematein methods after Zenker fixation, as well as adjacent blocks fixed in formalin by the Marchi method for fat and the Weigert method for myelin sheaths. A certain number of sections were stained by the Bielschowsky and Cajal methods, as well as by the Scharlach R. method.

The essential changes of this disease are probably demonstrable by a combination of the results of the Nissl method with those of the Marchi method. Of course, the number of axonal reactions will in most cases fall short of the number of fatty fibers. This disparity in the results of the two methods is without doubt due to the fact that the Marchi mehod is better capable of demonstrating the changes than is the Nissl method. For the small cells fail to show characteristic axonal reactions under any circumstances.

The most difficult point to determine in such cases is how far post-mortem or agonal alterations are responsible for confusion in the gross diagnosis. Changes of the sort which we must regard as related either with edema or with post-mortem lysis were found in various places, but particularly in sections from the two superior frontal gyri and from the two gyri recti.

Far more common are the axonal reactions. These abounded in all regions in the large cells. The calcarine and hippocampal regions may be mentioned as especially rich therein. An increase of satellite cells with occasional apparent total replacement of nerve cells with cells of the satellite type was found particularly in sections from the two superior frontal gyri.

The white matter in most regions shows a moderate amount of green pigmentation in phagocytic cells of the perivascular sheaths. This pigmentation was slightly more prominent in the motor areas, and could be found in very few vessels of the gyri recti.

A certain disparity in the cell proportions was noted on the two sides of the cerebrum in the motor area. As these changes seem to bear no relation to the disease in question, we shall postpone their consideration to another context. Of importance in the present connection seems to be the fact that the nerve cells show relatively the same proportion of axonal reaction on the two sides.

The Marchi reactions of the various areas are of note in that they suggest certain differences in the severity of the fatty degeneration in various parts. Thus, we have noticed that the superior frontal gyri, the right calcarine and right hippocampal gyri show slight Marchi changes. The right gyrus rectus appears to show considerable more fatty degeneration than does the left. The left leg area shows extensive changes; but these are less marked than those of the right leg. We have noted that the left hippocampal gyrus and the right leg area show the maximal changes found in this case. It seems impossible to correlate these variations with known characters of the lytic process. It must be remembered that except in marked instances the fiber methods for fatty degeneration are for technical reasons more qualitative than quantitative. It is difficult to control the thickness of sections and the degree of penetrability of the osmic acid-Muller mixture.

We have stated above the number of cells showing the axonal reaction will fall short of the number of fatty fibers. This is true if the Nissl method alone is used to demonstrate the changes in the nerve cells. However, the sections stained by the Scharlach R. method, which is fairly accurate for showing fatty pigmentation of the cells, or better, fatty degeneration, exhibits many nerve cells affected, and usually these are smaller cells, which show apparently little or no change by the Nissl method. Hence, there is little disparity between the proportion of degenerated fibers and affected cells. In some respects the Marchi method for fat and the Scharlach method show similar pictures; but fatty pigmentation is demonstrated better in the cells by the latter method, which

method does not stain the degenerated myelin sheaths so well. By the Scharlach method the tissue is hardened in formaline, and does not go through solutions that tend to extract the fat, and for that reason a more accurate picture can be obtained. In the large Betz cells of the motor area, both methods will demonstrate the fatty degeneration. In cells slightly affected, as in Fig. 2, the fatty pigmentation seems to surround the chromatolyzed area, and while in cells where the process of degeneration is further advanced, the whole of the chromatolyzed area is filled with fat. In the smaller cells, however, a great many show a well-advanced type of degeneration; the whole cell is filled with fat, and in some instances the axis cylinder shows the same picture, while a small amount of fatty pigment may be considered normal in cells at certain periods of life, when it is present in the amount shown here, we can well believe that it is pathological.

This process is distributed unevenly throughout the cortex, some areas showing a large majority of cells so affected, while in other regions the process is less marked. Cells in the same section will also show the same variation.

Cells stained by the method of Cajal and Bielshowsky for neurofibrils were not altogether satisfactory, but in a few instances a definite change in the fibrils within the chromatolyzed area were observed.

Spinal Cord.—The great majority of large cells show characteristic axonal reactions by the Nissl method. The Marchi method showing scattered degeneration in all parts.

Cerebellum.—The cerebellum shows few changes by the Nissl method which could be related to a lytic process. Nevertheless, a few Purkinje cells show an approximation to the axonal reaction with, however, a preservation of Nissl bodies. The Marchi reaction shows marked fatty degeneration of a scattered type in the white matter. It seems difficult to deny that some of the fibers related with Purkinje cells must have undergone fatty changes. Further study seems desirable to discover what peculiarity permits the Purkinje cells to resist to all appearances the lytic process.

Peripheral Nervous System.—The nerve roots and nerves examined show a general fatty degeneration of a moderate scattered type. The nerve roots opposite their origin at the spinal cord show the same degree of change which is shown by the adjacent fibers of the cord itself. The root ganglia exhibit a majority of cells which are either quite normal or slightly pigmented. A certain number, however, of the root ganglion cells show axonal reactions of an exquisite and wholly characteristic type. Enumeration shows that about one in fifteen of these cells shows the axonal reaction. The reacting cells occur in small groups as a rule.

Bacteriology.

Blood culture one week before death proved sterile.

Culture from the *heart's blood at autopsy* was sterile. The *cerebrospinal*

fluid contained *Bacillus coli communis.* A few staphylococcus colonies grew from a plate taken from the left inferior frontal convolution.[1]

Summary and Conclusions.

The present case is a fresh example of Adolf Meyer's central neuritis and shows, as did some of Meyer's cases, an involvement of the peripheral and sympathetic nervous system, together with the central nervous system, in a condition of severe and extensive lytic change. These lytic changes are exhibited in characteristic Marchi degenerations of the medullated fibers and in the axonal reaction of Nissl in certain nerve cell types.

These fiber and cell changes are, it is probable, only the evident fraction of a large series of changes of a lytic nature, most of which cannot be demonstrated by present histological methods. Thus the Marchi degenerations invariably surpass in amount the axonal reactions, doubtless because many of the fibers which show fat drops are connected with cells that are too small or too scantily supplied with Nissl bodies to exhibit the axonal reaction of Nissl. As shown by the Scharlach method the small cells have undergone a serious form of degeneration and are filled with fatty pigment.

Another evidence of the universality of these changes is the characteristic reduction of consistence on the part of both the encephalon and the cord. Attention has been called to this alteration of consistence by Southard and Hodgkins. In the case reported by them, the reduction was striking in all parts except an area of sclerosis in one hemisphere. Examination of the tissues by the Marchi and Nissl methods showed that the preserved nerve cells and fibers in the sclerotic area exhibited the same changes as the cells and fibers elsewhere. The disease, therefore, seemed due to some lytic agent differential for nerve elements, possibly an autolytic agent. The present case again illustrates the generalized reduction of consistence of central nerve tissues (general encephalomalacia and myelomalacia), together with some indication of the process in the peripheral elements, the result, perhaps, of a lysis or autolysis yet more general (neuromalacia).

[1] We are obliged to Dr. F. P. Gay, bacteriologist to the Danvers Insane Hospital, for these findings and several suggestions.

The question may well arise whether the cells or the fibers are the first to be involved in the lysis. Despite the extent and severity of the Marchi degenerations in the medullated fibers, it is nevertheless probable that the lysis primarily affects the nervous elements rather than the myelin investments. This point is borne out by the extensive changes, simulating the axonal reaction, in the nerve cells of Auerbach's plexus in the present case. Reasoning from this finding to the interpretation of central nervous findings, it seems possible to argue that the hypothetical lytic agent attacks elements largely proteid in character. The Cajal fibril preparations, so far as decisive, are consistent with this hypothesis. The nerve cells, stained with Scharlach Roth, show no accumulations of fat within the central or chromatolyzed area in the first stages of degeneration, but later as degeneration proceeds, the whole cell is filled with fatty pigment.

When such cytolytic changes prove to be so extensive as in the present case, involving various groups of axis-cylinders and eventually various nerve cell bodies and nuclei, as well as myelin sheaths in many regions, it may well be that the change here particularized is only an expression of a still more general lysis or autolysis which will be best attacked along chemical lines.

DESCRIPTION OF PLATES.

FIG. 1.—Betz cell from motor cortex (after Adolf Meyer), showing typical axonal reaction by Nissl method. Note the dislocation of the nucleus, and homogeneous degeneration of center of cell and of part of the apical process; Nissl bodies almost entirely destroyed. From a case of central neuritis, reported by Dr. Meyer, and reproduced by his kind permission.

FIG. 2.—Betz cell from motor cortex, showing axonal reaction, stained with Scharlach R., and counterstained by hematoxylin. Fat stained red, and surrounds chromatolyzed area. As degeneration advances, the fatty substance encroaches on center of the area until finally it fills the entire cell.

FIG. 3.—Similar cell stained with osmic acid and counterstained with saffronin. Fatty pigment stained black. The central portion shows no fat.

FIGS. 1, 2, 3, drawn with No. 4 ocular and 1/12 oil immersion.

FIG. 4.—Photomicrograph of the nerve cell characteristically found in Auerbach's plexus in our case of central neuritis. ×1000. The cell body is almost homogeneous and stains moderately deeply. The nucleus is shrunken pyknotic and eccentrically set. The adjacent non-nervous cells and the tissue at large exhibit no striking alterations, and fail to suggest general lysis. The appearances in the nerve cell suggest those found in central nerve cells when the axones have been cut or otherwise destroyed (the axonal reaction of Nissl).

FIG. 5.—Photomicrograph of nerve cell from Auerbach's plexus. ×1000. To illustrate the effect of *simple edema.* The central oval space is partially filled with a large nerve cell with ragged edges and a vague spongy cell-body. Note that the nucleus is vesicular and preserves a central position. There is a somewhat wide light zone about the nucleus, recalling the appearances described by Hoch for edematous cells of the central nervous system.

We are indebted to Mrs. Henry A. Cotton for the drawings of Figs. 2 and 3.

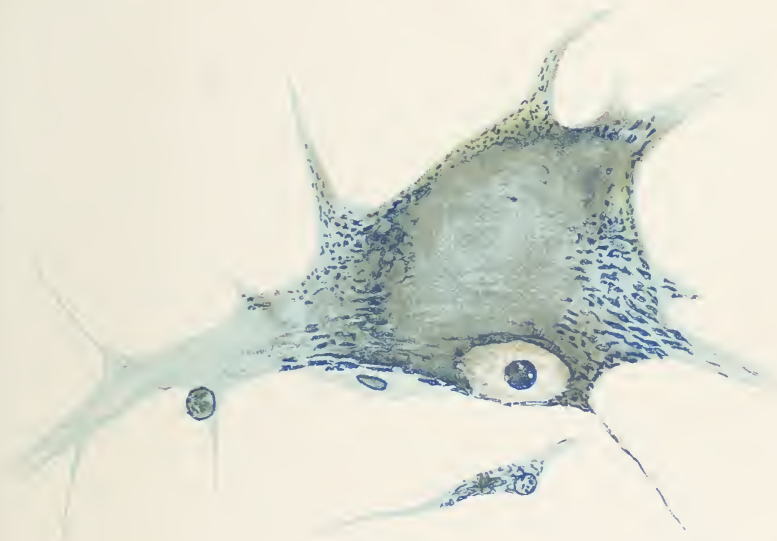

FIG. 1.

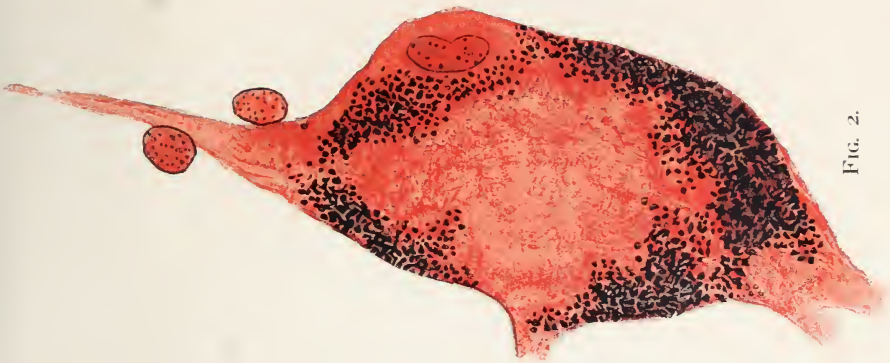

FIG. 2.

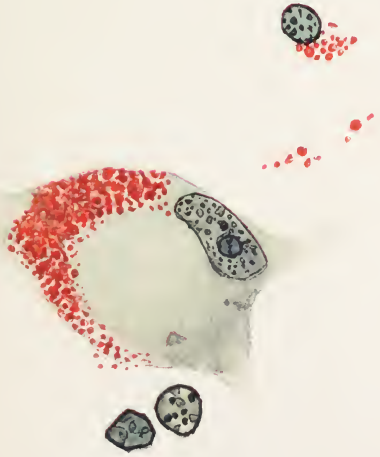

FIG. 3.

FIG. 4.

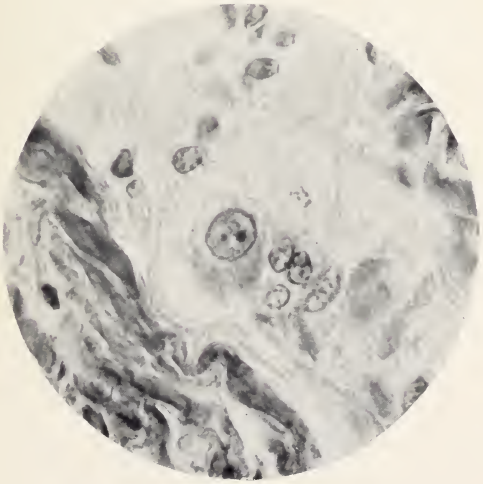

FIG. 5.

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CARDIO-GENETIC PSYCHOSES.*

REPORT OF CASE WITH AUTOPSY.

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We have been accused by investigators in other fields of medicine, of exerting all our energies in the quest for diagnosis, and that classification has occupied our attention to the exclusion of other subjects in psychiatry, and while this criticism may be justified to some extent, it must be admitted that only by clearly differentiating various types can we expect to offer a basis for curative and preventative measures. One fact has been clearly demonstrated by this quest for diagnosis, that is, we have obtained a more accurate symptomatology of mental diseases, and more complete histories have brought to light new factors in etiology, which factors would have remained unknown but for this zeal in diagnosis.

Another fact is evident to those engaged in studying symptomatology and symptom complexes that the more careful and accurate our observations and analyses become, the more difficult it is to place all cases or types into a hard and fixed classification, and more difficult becomes the problem of identifying all cases, or dismissing them with a "one-word" diagnosis. Some cases defy all attempts to place them in any special scheme and can only be given a descriptive diagnosis. It is far better to let them remain unclassified or undiagnosticated than to force these obscure cases into groups where they do not rightly belong. If so placed they complicate matters, and render more obscure our ideas of various

*Read at the sixty-sixth annual meeting of the American Medico-Psychological Association, Washington, D. C., May 3-6, 1910.

groups, and that the recognition of these unclassifiable cases as such, rather than indicating defects of knowledge, denote a clearer insight into the realm of mental disorders.

A more careful observation and recording of symptoms will tend to clear up these diagnostic difficulties.

The epoch-making work of Kraepelin has given us a ground work for further advance. But we should not fall into the error of thinking that Kraepelin has offered a finished scheme in his work of classification, for that is accepting more than Kraepelin himself would claim.

Recently Alzheimer, in a timely article, has called attention to the diagnostic difficulties in psychiatry, and although a staunch supporter of Kraepelin, he, however, maintains that there exists a necessity for further separating from well defined and clearly established groups, types which evidently do not belong there. And while we recognize the harm which can come from advocating new types to add to our classification, we feel that in spite of any criticism which might arise on that score, an attempt should be made, if we have sufficient clinical and anatomical evidence, to more fully differentiate such a type.

In the field of so-called functional disorders, where a majority of cases present a clinical picture which permits a logical classification, there is, nevertheless, a certain number of mental disorders, especially those of a fatal termination, which do not satisfactorily conform to any one type. This is especially noticeable among the depressions. It is well recognized that in the so-called organic group often obscure cases will be cleared up at autopsy, and where a diagnosis based upon anatomical findings is possible, one does not meet with unsurmountable difficulties as is apt to be the case in the functional group.

It is for this reason, then, that any group which might furnish a rational anatomical basis for diagnosis and differentiation is worthy of the fullest investigation. It is a step forward in the transformation of the so-called functional into the organic group; not, however, losing sight of the psycho-genetic factors which operate throughout the entire domain of mental disorders. It is only by the most careful observation of symptoms in such cases, and correlation of clinical symptoms with anatomical findings that this result can be accomplished, as exemplified in the instance of the now definitely established "Central Neuritis."

But as distinguished from organic diseases originating in the brain per se, must be considered other types essentially organic in their cerebral effects, but in which the cerebral changes result from an organic process which exerts itself primarily in organs other than the brain. The best known, and, perhaps most widely accepted explanation of the effects of such organic diseases upon the central nervous system has practically, up to the present time, dealt exclusively with the effect on the psychic centers of substances essentially toxic in nature, elaborated in organically altered tissue. And in this the effects of various anæmias, the intoxication from renal and hepatic disease and altered thyroid function are exemplified.

As distinguished from such purely toxic conditions the effect of a wholly mechanical interference with cortical nutrition, originating in a definite cardiac deficiency is in this instance considered, and the condition designated in accordance with its underlying causation as a cardio-genetic psychosis.

Review of Previous Work.

Although reference to circulatory psychosis is frequently made in the literature, and numerous monographs have appeared, some as early as 1806, still the work of Alfons Jakob, published in September, 1908 (Journal für Psychologie and Neurologie) may be considered the most exhaustive work, review of literature, detailed description of cases and discussion of the subject. Attention should be called to the fact that in publications previous to that of Jakob, the crucial point of the whole question was referred to the heart disease as such, while the theme before us is more exactly concerned with a disturbance of circulation resulting from heart disease. In reviewing the literature the point of chief defect is that the various investigators reached the most divergent opinions and results, and Jakob rightly considers this divergence of opinion as responsible for lack of attention to the etiology of psychic disturbance accompanied by heart lesions. It is significant to note that even modern books on psychiatry treat the subject in a very superficial manner. Kraepelin has very little to say upon the subject, and is inclined to consider heart lesions accompanying psychic disorders merely coincident and that they have no causative relation. But in view of the excellent clinical

histories and anatomical work of Jakob one is not justified in thus dismissing the subject. Jakob recognizes the complicated problems connected with cardiac psychoses and propounds several queries which he considers he has answered in his work.

"When do circulatory disturbance give rise to psychic changes? Why not in every case? What phenomena are presented by these psychic disorders? What process lies at the base? Will perhaps the microscope be able to furnish the solution as to what happened, and how it happened?"

In order to present the subject from all sides, Jakob examined 25 cases of heart disease in patients not considered insane for symptoms of psychic disturbance with special reference to the definite points of orientation, attention, instantaneous perception and variation in the emotions. Slight changes were noticed in all but one case of myocarditis and four cases of mitral insufficiency. But in none of these cases was it possible to demonstrate grave disturbances such as hallucinations and delusions or delirious conditions. In five cases of broken compensation, however, some psychic changes were noted. In one difficulty in directing attention and thoughts, and poor memory. In another frequent changes in mood, often ill natured, excitable; another showed time and place disorientation, states of excitement, especially at night, mistaken identity of persons and hallucinations. However, this case was arteriosclerotic and had softenings. Still another case was very irritable, and a fifth case showed clouding of consciousness. He concludes that "no parallel is to be drawn between the psychic symptoms and the degree of broken compensation. That these circulatory disturbances must indeed encounter wholly special cerebral conditions to call forth peculiar psychic disorders."

Jakob includes in his investigation primarily such disturbances of the circulation which assure the purest material, viz., hypertrophy of the heart and heart failure, and eliminates as far as possible cases complicated with other conditions.

He divides his cases into two groups:

1. Cases with characteristic psychic disturbances extending over a considerable period of time before the fatal termination; and 2d, those cases in which these phenomena developed shortly before heart failure and death.

The second group of cases, while interesting, are for our pur-

pose to be dismissed with but a few words. They usually come from general hospitals, and the mental phenomena consist in certain delirious episodes which ensue just prior to death. Probably the numbers of such cases would be large, but such material is not available for those engaged in insane hospital work.

Our attention and interest is directed principally to the first group, of which Jakob reports five cases. As a brief description of the cardinal features of this form of psychosis by which it may be recognized, in general it may be said to bear a recognizable, although modified resemblance to certain phases of the various forms of atypical anxious depressions with hallucinations, to the toxic exhaustive group of psychoses and states of anxious delirium; and that, broadly speaking, this psychosis is characterized by an even greater irregularity of course, and by an even greater display of atypical manifestations than are the conditions mentioned and from which it must be differentiated. Although the chief feature perhaps is the complex of anxious depression interrupted by delirious episodes with fatal termination. The fuller symptomatology, because of its marked variability and irregularity, must be given more in detail, if a correct understanding of this group is to be acquired.

The age of the patients does not seem to be of any significance. (The cases of Jakob vary from 18 to 64 years) but, of course the differential diagnosis varies considerably according to the age.

The previous condition of the patients is also of little importance. They are usually normal or even above the normal in intellect, and no predisposing psychic factors in make-up appear to be present or necessary. Heredity plays a negative role.

Following the appearance of organic heart lesions, psychic phenomena supervene; whether the lesion is purely myocardial or endocardial in character does not seem to be of moment. The precipitating factor which seems to be necessary in practically all cases is a severe emotional shock. Aside from the cardiac lesion, the psycho-genetic factor seems to hold a prominent place in the etiology, where its effect upon the heart may be as great as its emotional effect upon the mind. These two factors of heart lesion and emotional shock appear to be necessary to produce distinct cardio-genetic psychoses, for while the psychic factors are not absolutely essential, the majority of the reported cases show its presence.

As this group has to be differentiated from certain well established types, the symptomatology will be considered along with differential diagnosis, in order to emphasize the prominent symptoms.

The onset is usually sudden, and hereby resembles other acute functional disorders, especially the toxic-exhaustive delirium, and also, it is important to note that the disturbance reaches a climax in a few days. The first symptoms noted are, depression with agitation, apprehensiveness and anxiety. Quickly follow delusions of auto-, allo- and somato-psychic character. Here the differentiation from manic depressive insanity, depressed phase, or mixed phase, or involution depression is extremely difficult, especially if the patient is, during periods, free from delirium. The depressed attitude with agitation, self accusation, somato-psychic delusions, and fear of impending danger would suggest any of the above diagnoses. However, elements of a pure depression are absent, and there is no true retardation or inhibition, on the other hand marked psycho-motor restlessness is always present, with no retardation in speech or ideation. At times during the agitation, patient will smile and even joke, and present elements of a mixed condition. But coupled with these symptoms is found clouding of consciousness, varying in intensity and degree, according to the severity of delirium. Disorientation is not always complete, so that one gets several impressions during the same conversation. Disorientation for time seems more constant on account of difficulty of concentration and lack of attention. Accompanying these symptoms are vivid hallucinations and illusions, especially more marked at night, with strong reaction, affect of fear and sleeplessness. At times, patients in such a state resemble delirium tremens. During the day delirium is always milder, and when spoken to patients become quiet and react for a while in a normal manner; they soon relapse, however, and give voice to depressive delusions. Attention, while difficult to obtain, is always fixable (with great effort at times) if even for a few minutes. There is difficulty of diverting the depressing stream of thought, but seldom is incoherence a prominent symptom. The marked motor disturbances are also accompanied by severe general tremors, over the whole body, which become more marked under the emotional strains of hallucinations and delusions. The tremors are so

marked at times as to suggest organic brain disease, especially general paralysis, but they are not accompanied by other physical signs of that disease and the character of the mental disturbance, such as the absence of ethical or intellectual failure further differentiates the two disorders.

Marked disturbance of concentration and lack of attention, stand in close relation to the impairment of memory for recent events with deceptions and fabrications. In sharp contrast to this memory defect, stands the clear and unimpaired memory for remote events. The irregularity of the delirious state, which is present at times, especially at night, often absent during the day, and for periods of several days at a time, seems to differentiate between cardio-genetic psychosis and delirium due to whatever cause.

Another important feature of this group is the improvement in mental symptoms which accompany an improvement in the heart lesion, under treatment. Often for days or weeks patients may be quite clear mentally, with no abnormal conduct and have good insight into delirious episodes, but with failure of heart action again supervenes the mental disturbance. Finally the fatal termination, usually with characteristic symptoms up to the last, when coma or unconsciousness precedes death, gives one of the distinctive features of the group. Of course, under the microscope such conditions as general paralysis, arteriosclerotic brain disease, and other organic conditions can be easily differentiated, and the presence of certain histologic changes in cardiac cases would rule out the purely functional group of psychoses.

Pathogenesis of Cardio-Genetic Psychoses.

This question is discussed at length by Jakob, and it may not be out of place to mention some of the points made by him to substantiate the theory of the causative relation of a heart lesion to a definite psychosis. "A great many attempts have been made to explain functional disorders by circulatory disturbance. Thus, Grislain found in mania, that the cerebral convolutions are almost obliterated by pressure of the brain against the cranium, while in melancholia the brain had sunken together in itself, which he conceives as the expression of a relative increase and decrease of the influx of the blood in proportion to the cranial pressure."

There is no doubt enough evidence of the effect of altered circulation in the brain producing psychic effects, so that a detailed discussion of the theories of various authors is unnecessary. These various theories of the causation of mental disorders by circulatory diseases are interesting, but nevertheless the difficulty experienced in attempting to attribute all these pathological changes to one uniform cause, is unmistakable. In the last analysis the same effect is produced, viz., damage of the nervous elements. So even in considering the mechanical effect of circulatory disturbance in the brain, the chemical factor must not be ignored. With the lowering of the cardiac power and the subsidence of the circulation and the condition of stagnation in the lungs thereby superinduced, the acid content of the blood increases to a noticeable degree, and this overloading with carbonic acid of the venous blood already accumulating in excess will always exert an influence upon the functional activity of the central nervous system.

In closest connection with this mechanism stands the demonstration that the disturbance of the circulation effects a diminution of the supply of nutriment to the brain, which supply is assuredly indispensable to the maintenance of its highest functional activity.

And it cannot be disputed, that as a consequence of diminished power of the cardiac muscle and the resulting anæmia of the brain the physiological activities of the highest nerve centers are correspondingly disturbed.

Clinical History of I. H.

Anamnesis given by brother, an intelligent colored man.

Family History.—Grandparents lived to old age, and were temperate. Father, a sober and industrious man, lived to over 80 years. He was a slave in Maryland and bought his freedom. Mother was free born negro woman, living at age 78 years. Patient had four brothers and two sisters. Two of her brothers died in childhood. Other brother and sister living and in good health; all married. One brother held a responsible position in State House. This brother died on the 13th of October, suddenly, supposed cause, heart disease or apoplexy. He was a heavy drinker. No known heredity or neuroses in family.

Personal History.—Patient was born in Trenton, November 22, 1854. Early development essentially normal. She attended school between ages of six to sixteen years, was a bright student, and passed examination as public school teacher in that city where she taught for 35 years.

Illnesses.—She had the usual diseases of childhood, but never had typhoid, diphtheria, and no serious accident.

Habits and Occupation.—Patient was extremely temperate in her habits, and was of religious disposition. She taught school for 35 years, till 1907, when she had an attack of nervous prostration following ill health and overwork of teaching. This attack lasted for six weeks, and she was treated at home. This attack was of a rather milder character than the present one. Patient showed many neurasthenic symptoms, and displayed some tendency to self accusation as well. She was depressed, claimed that she was going to hell. She probably had hallucinations, claimed to see the devil, and said her food tasted bad. Patient improved, but frequently she was in a mild semi-delirious condition. At times was disoriented for time, place and person, but this was not constant. Neither were her delusions constant. She was in very poor physical condition. (Dr. Cort attended her, but could not find his notes of the case at that time.) It is difficult to form an idea of the character of this attack, and no diagnosis is possible with the data at hand. It may have been profound neurasthenia or symptomatic depression due to her ill health. No heart lesion was noted at this time, but it is possible that it may have been overlooked.

She recovered gradually, and after three months was as well as usual, but she did not take up active teaching again, as her health was not good. She was made assistant truant officer and looked after colored truant scholars. She also assisted in the housework at home.

About six weeks before the onset of the present attack, patient went to Dr. Cort for treatment as she was in poor physical condition. Dr. Cort reported that the patient at the time was suffering mainly from organic heart disease. The pulse was feeble and the heart sounds so weak as to be scarcely audible. She seemed to improve under treatment. No murmurs were found upon examination.

Onset of Present Attack.—Sudden. Her brother died suddenly on the 13th of October, supposed cause, heart disease or apoplexy. He had been drinking heavily for some months, which worried his sister, the patient. In order to cure him of his drinking habits she had obtained some patent cure which she secretly administered to him. At the time of his death she was greatly affected. She worried much, and imagined that her own actions were accountable for his death. Two days following she became nervous, restless and sleepless. She was depressed and accused herself of committing the unpardonable sin, and of killing her brother. She claimed to be possessed of the devil, and was going to kill her mother, also said she was going to hell and take all her family with her. She refused to take food or medicine. She was dominated by her delusions of self accusation and would talk of nothing else. She claimed people accused her of killing her brother, and of being cruel to her old mother. She did not sleep at night, but wandered aimlessly about her room, talking constantly in this strain. She was apprehensive at times. Two days before admission she was sent to St. Francis Hospital, but was too much disturbed to remain there, so she was admitted to the New Jersey State Hospital at Trenton, upon the certificates of Drs. Clark and Cort, October 23, 1909.

On admission patient was somewhat restless and talkative. She was oriented for place, but only fairly well oriented for time; knew it was fall, but could not give exact day and date. At times appeared somewhat agitated, wringing her hands, and crying, "Lord, oh, Lord."

PHYSICAL EXAMINATION.

General Type, Appearance and Condition.—Patient is a light colored mulatto woman, 55 years of age, of good frame and muscular development. Her head is well shaped, face and features of African type. Forehead well developed, hair long and kinky, and abundant in quantity. Eyes brown, nose flat, has lost all her upper teeth and uses an artificial plate instead. Has all her front teeth below and they are in good condition. Palate moderately high and arched, chin normal, ears moderate in size, adherent lobules. General complexion, light mulatto. No malformation or stigmata.

General Nutrition.—Good. Height, five feet, three inches, weight, 141 pounds. Temperature normal, pulse 84, respirations 22-24 per minute. Patient is well nourished, sub-cutaneous tissue present in considerable amount. Muscles well developed and moderately firm, mucous membranes moist. No fractures or deformities, no anæmia, jaundice or dropsy. Has some bruises on her body.

Evidence of Acute or Chronic Constitutional Disorders.—None. No evidence of syphilis, no ostitis gumose, no enlargement of the glands of the elbow or groins. No evidence of gout, rheumatism or infectious diseases. General temperature normal.

Nervous System: General and Subjective Sensations.—Has a general feeling of weakness and debility. Does not complain of headaches or vertigo. Owing to lack of co-operation, it cannot be ascertained whether she has præcordial, intercostal or sciatic pains.

Smell.—Does not seem to be impaired, cannot be tested. Says the test solutions smell like hell, that they are different, some smell worse than others.

Taste.—Does not seem to be impaired. Says that sugar is sweet, salt is sour, vinegar bitter and quinine tastes like the devil.

Eyes.—Expression rather sad and uneasy. Lids—No deformities. No ptosis or spasms. Conjunctiva congested, eyeballs moderately protruded, no arcus senilis. No scars on the cornea. Pupils equal, central and regular, respond to light and accommodation.

Mastication Segment.—Normal.

Sensibility and motility of the jaw good.

Ears.—No subjective complaints. Hears a watch tick at about 18 inches from either ear. Condition of auditory canal normal. No growths or discharges.

Cutaneous Sensibility.—Sometimes she says that she has had a feeling of numbness in her hands and feet, and at other times denies it. Owing to her resistiveness and refusal to co-operate, it is difficult to ascertain whether she has areas of hyperæsthesia or not. She recognizes the difference be-

tween hot and cold water bottles and seems to be sensitive to touch, temperature and pain.

Stereognostic Sense.—Cannot be tested. Does not seem to have any tenderness over deep nerve trunks or muscles.

Vasomotor and Trophic Conditions.—Skin is dry and rough. Dermatographia is not well marked.

Reflexes.—Elbow and wrist normal. Knee reflexes equal and somewhat exaggerated. No ankle clonus. Achilles tendon normal. Pharyngeal and plantar reflexes normal. No Babinsky.

Motor Functions.—Movements of the facial muscles are symmetrical and under control. Co-ordinate movements are performed fairly well. Hand grips strong. Strength of flexor and extensor muscles good. Gait unsteady, station erect. Considerable swaying in Romberg position. No evidence of hemiplegia, local palsies or spinal paralysis. No cataleptic conditions.

Tremor: Has tremors of tongue, fingers and extremities. Fibrillary twitchings of her whole body.

Speech: Hesitating, but no slurring. Repeats test words and phrases.

Organic Reflexes and Their Control.—Bladder and rectum under control when she makes an effort, but frequently passes her urine involuntarily.

Convulsions.—No history of convulsions. No hysterical attacks.

Sleep.—Poor.

Dreams.—Not ascertained.

Thoracic Organs.—Chest: Well developed, 33 inches.

Clavicles, sternum and ribs normal, sub-cutaneous tissue in considerable amount. No deformities.

Lungs: No subjective complaints of pain, dyspnœa, cough, expectoration or hemorrhages. Expansion fair and equal, respirations 22-44. Percussion and auscultation negative. Difference between forced inspiration and expiration 1¾ inches.

Circulatory Organs.—Heart: Subjective complaints of palpitation, pain and abnormal sensations present.

Percussion: Area of dullness in about the usual limits. Apex beat seen and felt in the fifth interspace inside the nipple line. Auscultation: No abnormal sounds or bruits discovered. Radial pulse fairly regular, about 84 per minute. Moderately strong. No arterio sclerosis.

Abdominal and Digestive Organs.—Has to be urged to take food. No abnormal thirst, nausea or vomiting. Mouth, pharynx and tonsils—mucous membrane moist and clean. Tongue clean. Abdomen full, walls are thick, no pain, tenderness or rigidity. Stomach, liver, spleen and kidneys in normal position.

Urinary Apparatus.—Bladder: No subjective complaints. Micturition normal. Urine analysis: Color—dark straw, turbid. Sp. gr.—1025. Reaction—acid. Albumin—good trace. Sugar—negative. Few hyaline casts. Squamous epithelium.

Genital Organs.—Not examined. No history of specific disease.

MENTAL STATUS (OCT. 28, 1909).

Demeanor.—On and since admission, patient was restless, apprehensive and resistive. She would not remain in bed during either night or day. She walked aimlessly about her room, screaming and pounding on the door and frequently calling out "they are murdering me." This apprehension was always more marked towards evening and during the night. On days when she was quiet, the following night she became agitated and apprehensive. When questioned she would often answer at random, but when pressed to give accurate answers she usually could pull herself together long enough to answer correctly. When on the ward patient wandered aimlessly about, and did not appear to know what she wanted, or where she was going. The greater part of the time patient seemed confused and bewildered, but when spoken to, the confusion could be temporarily controlled. The patient showed constant trembling and tremors of the whole body were marked. The facial expression was variable. At times it was sad and worried, but when talking it became brighter, and sometimes she would almost smile or assume a somewhat joking expression. Occasional hallucinatory attitudes were noted.

She was untidy in her habits and careless of her personal appearance. She had to be dressed and undressed, and when put to bed refused to remain there.

Stream of Thought.—Somewhat shallow and disconnected. Cannot give a clear connected account of her trouble. It is frequently interrupted by her depressive ideas and self-accusations. She is restless and agitated during the interview. Claims she is in hell and her sisters are there also. She does not give spontaneously any hallucinations but probably these are present from her attitude.

"How long since you quit teaching?" "I have not taught any since 1907." "Is that the time you were first sick?" "Yes. I had nervous prostration at that time. I was in bed for six weeks, and had a doctor and a trained nurse." "What were the names of your physician and nurse?" "Dr. Cort attended me and the trained nurse was from Douglass Hospital in Philadelphia." "What was her name?" "Miss Bowne." "What did you pay her?" "They paid her twenty dollars a week for six weeks." "How much would that be altogether?" "One hundred and twenty dollars, but she threw five dollars off. "How long since this last attack came on?" Here she becomes confused, says the family are not all crazy. "My sister is in hell, I am already there." "How long since you came here?" Here she commences to mumble about something else and does not answer. "I want to know when you came here?" "I haven't been here at all, in the asylum, that was an awful thing to do, it was all a mistake." She gets up and walks around and the attendant has to bring her back and put her in the chair. Says she is dead, that she is in the wrong place, that it is the devil's business. "What is the devil's business?" "Taking all the coons and my sister and putting them down in an awful place." "What is this building here?" "It is called the New Jersey State

Hospital. I am not insane, but dead. I killed my brother." "What was your brother's name?" Gives correct name. "What happened to him?" "He is supposed to be dead. I am talking, I thought he was dead." "What did he die of?" "Some said he died of heart disease and others said he died of apoplexy." "How old was he?" "Fifty-two." "When was he born?" "January 22, 1852." "What was the cause of your nervousness?" "Because I feel responsible to God for not having five hundred children." "Is your present condition like it was in 1907?" "Something like it was then. I thought I was a devil and I tried to make people uncomfortable." "How long since you came here?" "I don't know, I can't tell, this is awful. I am in hell."

Moods and Emotional States.—Patient depressed and apprehensive, and at times agitated, wringing her hands and exclaiming how terrible she is. Marked self accusations. At times her mood is not in harmony with her ideas; frequently she assumes a somewhat joking attitude, but maintains a depressed expression.

"How do you feel?" "I do not feel well, I feel as though I had not done right and am much ashamed of it. All these people who are ugly looking are looking at me and claim to be my children. My poor mother has no place to sleep to-night. I pray to my father, the devil. I do not enjoy these noises around here, it makes me feel terrible." "Are you sad or depressed?" "I am ashamed of what I have done, I have been shamming, said I was the devil and could run the universe. There is my dear mother now bidding me good-bye. It is awful, I don't know what to do."

Paranoid Trends.—None elicited. She does not think that any one has treated her badly or that she has been peculiar. Denies that there has been any conspiracy against her.

Delusional Developments, Non-Paranoid.—Patient has many fleeting and some partially fixed delusions, and marked self-accusation. Claims she has sent her family down to perdition, and has collected all the "coons" together and sent them to hell. That she is responsible for all the colored children and in that way is the mother of them (probably explained because of the fact that she was a truant officer for colored children). That she is unworthy and has committed a mortal sin.

She asks constantly about children. She thinks she is responsible for not having any children. That because she has no children of her own she is responsible for all the children of the colored race, and in that sense is the mother of them all.

All these delusions are shifting and unstable and none of them seem to be fixed.

Ideas of Negation.—Somato-psychic in character, prominent. Claims that her body is dead; that she is dead; that her passages have stopped; that she is in hell, etc.

Somatic Sense Deceptions.—Present. Claims that she has queer sensations in her body, claims her heart stops beating. That there is nothing left of her. Also complains frequently about her heart.

Hallucination. Auditory hallucinations probably present.—Patient assumes hallucinatory attitudes, and claims to hear the voices of brother and sister. At times mistakes the noises on the ward, and is easily frightened by these noises.

Visual Hallucinations.—Probable. At times shows some affect of fear in reaction to these hallucinations. She claims she can see the various members of her family, also sees "all kinds of people and sees all kinds of pictures."

Both auditory and visual hallucinations are more marked at night, and the reaction to same is more vivid.

MENTAL ORGANIZATION.

Orientation and Grasp Surroundings.—Variable, and at times very poor. At other times she is well oriented for place and persons, but always poorly so for time. She is able to give her own name; often claims this is hell, but in reality she knows it is a hospital for insane people; often claims that all the people here are devils with horns, but recognizes physician. At times marked clouding of consciousness, especially at night; she is then in a semi-delirious condition and completely disoriented.

"What is your name?" "I—— H——, of 25 Lamberton Street, Trenton, N. J." "What place is this?" "It is an awful place. Let me go, I haven't yet. This place Dr. Cort says is a hospital." Says she don't know the day or date, but finally says "Saturday." "What month is it?" "Oh, that is awful, an awful thing, it's twenty-five days." "What month is it?" January." She says it is winter, that people around are all devils with horns, that the place is for insane patients.

Data of Personal Identification.—Only fair. Can give account of remote events fairly accurately, but recalls recent events very poorly. Constantly refers to her somatic ideas and her illness. No change in personality.

"Where were you born?" "Trenton, N. J." "When?" "November 24, 1854." "How old are you?" "Fifty-seven years." "Between what ages did you go to school?" Repeats the question and does not answer. "Where did you go to school?" "I used to teach." Then she says that she went to common school and the State Normal. Says she did not graduate there. Then says, "I graduated on Lamberton Street." "Where did you teach?" "I can't talk because my heart and lungs are not in my body." "Did you ever have any children?" "No, I never had any children, but I thought I was responsible for a million of children's souls." "What illness did you have?" "I was sick with melancholia in 1907, that is all. Dr. Cort and a trained nurse attended me."

Memory for Immediate Past.—Very poor. Patient is unable to tell about her admission to the hospital or when she came here. Refuses to tell how many meals she had to-day and what she had at meal time.

Retention.—Defective. Patient will not co-operate in tests because of her agitation and apprehensiveness. Recalls number 387 after a few minutes, and two colors, blue and purple. She refuses to attempt three numbers.

Grasp upon School Knowledge and General Experience.—Patient is confused, and does not co-operate well. She can repeat the alphabet, months of year, days of week, the Lord's prayer, the United States. She knows the President, his predecessor, also some historical data. Tests interrupted by her moaning because she is in hell.

Calculation.—Fair. No retardation. Counts from 1 to 20 in five seconds. Will not co-operate in all tests. Refuses to subtract continuous 7's from 100. Multiplication good. Will not add or subtract.

Reading.—Not defective, but she is careless and indifferent.

Writing.—Poor. Shows marked tremor and misspelled words, defective and not in keeping with her education.

Insight and Judgment.—For the most part defective. At times apparently realizes that she is not right in her mind and has insight into her attack of prostration in 1907. Her judgment is defective.

SUBSEQUENT HISTORY OF THE PATIENT.

November 3, 1909. Preliminary presentation before staff by Dr. Felty.

Patient continues depressed, agitated and apprehensive. At night she is always much worse, constantly pounding on door, claiming she is being murdered. During the day she sits alone, at times becoming agitated, and when agitated there is marked tremor over whole body. Frequently much confused, and at times in a delirious condition. She often refuses her food because it is the "devil" or her dead brother that she is eating; takes food with persuasion. Thinks this is a punishment because of the powders she gave her brother, which killed him. She often puts her finger down her throat in order to vomit, because of having eaten her dead brother. At times refuses medicine because it is the "devil's blood." She has many somatic delusions. She claims her insides are dropping out. That she hasn't any brains. Claims her hair has all been cut off; all her bones have been broken. That the devil has her vitals; her breasts are all gone.

During the interview this morning she was restless and agitated. Frequently disturbed by noises in the hall, misinterpreting them and showing much fear and apprehension. Patient is oriented for place, as she knows this is an insane hospital, although she often calls it a jail, and says that she is here to be murdered. Memory is defective, and at times there is marked clouding of consciousness. Often expresses insight, says she is suffering from insanity, "because the more I want to talk the less I can talk." She claims to feel "as if I had no brains," also that she has no veins and no blood in her veins. Self-accusation also present. Claims she has done wrong to the rest of the family. When she hears a noise in the hall, misinterprets the same, claims that "they are banging their heads together out there."

Patient's Conversation.—"Good morning?" "Good morning, Doctor." "Do you know where you are?" "I am in an insane hospital." "How long have you been here?" "I don't know." "Why are you here?" "Because I was suffering from insomnia." "Have you ever seen me before?"

"Don't remember you." "What happened to upset you?" "Bones are getting broken." "Do you feel worried or sad?" "Oh, they make me a helpless maniac, suffering from insomnia. I couldn't eat before, then the shooting began." "What do you mean by shooting?" "Yesterday I was there." "Broke my bones, they are upside down now." "How do you mean?" "There are no veins, there is no blood in my veins." "What are you suffering from now, outside of your insomnia?" "I suppose insanity, because the more I want to talk, the less I can talk." "Do you feel confused?" "I feel as if I hadn't any brains." "Are you sad, do you feel worried?" "I have been suffering from melancholia." (Looks at picture.) "There, that's my mother." "Are you afraid of anything?" "I am afraid of having done wrong to the rest of the family." (Hears a noise.) "They are banging their heads out there, too." (Doctor knocks on table.) "No wonder they are insane if they have their heads banged against the wall like that." "Do you feel sick?" "They had my hair all cut off. Every bone in my body is broken, What is my name? I don't know. There goes the heads (hears a noise). That was a cruel thing to do, too. High oppression, Doctor, it is too intense." "What is this about going to hell and sending your family there?" "I haven't sent them all there." (Doctor knocks.) "The devil's got my vitals, my heart, that's all gone."

Dec. 4, 1909. Second presentation before staff by Dr. Felty.

There has been but little change in patient since last note. She is still apprehensive, depressed, agitated, resistive, and at times nervous, and tears her clothing. On the 19th of November took hold of a violent patient, shook her and shouted, "help me to undo the past." The latter patient struck her a blow on the nose which caused it to bleed, and patient said she was glad as it was the devil's blood coming out. Patient is always more disturbed and apprehensive at night. She is usually sleepless, pounding on door, screaming. Shows much fear at night, and often reacts to hallucinations. Some days she is better than others and more easily managed. Often it will take several nurses to dress her, because of resistiveness, but when she comes in a room with her company she is able to control herself for a while and talk, but in the same depressed strain, showing self-accusation and absurd delusions. In her better moods she admits that her ideas are all imagination and untrue, that she has never harmed any one. At times she takes some interest in her surroundings, talks to nurses, and goes to other wards to visit. But she is usually much disturbed at night. During this time her temperature could not be taken, but her pulse was usually irregular and weak. (To-day brought before staff meeting.) She was talkative, but productions are somewhat incoherent and disconnected at times. She jumps from one subject to another, but productions are always along depressive lines, and self-accusation prominent. Occasionally confused, and there is clouding of consciousness. Claims she is in jail, is in the sky. She claims she hears people say she has committed a great many vulgar crimes. Has ideas of negation. At times shows some insight. Claims she has been taken from prison to prison.

Patient's Conversation.—"Ah, what a shame, being murdered and electrocuted, these are gentlemen that I don't know, such creatures, accusing me of all kinds of crimes, I have been moved from jail to jail." "Where are you now?" "I must be in an asylum, I have been traveling around from place to place, do you remember my sister, do you remember my mother and father." "What about your brother?" "My brother died, I imagined I murdered him, because I gave him a powder for the drink habit, and the coroner said an inquest was not necessary. It is the race hatred, they say I commit all kinds of crimes, every horrible crime that is committed they say that I—— H—— committed it, three or four women keep me under their control. Do you suppose I could commit such awful sin that they accuse me of? They say they were committed up in the sky, very vulgar crimes." "Were you up in the sky?" "I suppose I was. Do my family still exist, are my people all killed?" "Are you afraid of anything?" "I am awfully afraid of these women, they haul me around and drag my hair out by the roots. I have been taken from post to pillar. I have been electrocuted. Where is my doctor? Where is Dr. Cort? They accuse me of all sorts of brutal murders and robberies; every crime that is committed they say I—— H—— committed it. Where are the people? Have they been burned to death? Has the town been burned? What a shame," etc.

Subsequent History.—Patient changed but little for a few weeks; she then began to fail in her physical condition. She was usually restless, agitated and apprehensive, and at night she was always worse. Slept but little, even when given medicine. When visited by friends she knew them, but made many contradictory statements. For example, at one time told about her being struck on the nose and accused nurse of beating her. Another time told her sister that her brother struck her on the nose. Patient did not take sufficient nourishment, as she claimed her food was poisoned. Frequently had spells of agitation and fear, in which she ran aimlessly about the ward and screamed, confused and delirious. She would blindly resist everything that the nurses did for her.

On the 19th of January seemed to be worse. She would not sleep for fear she would not wake up, and seemed afraid that she was going to die. She got up and dressed herself, and took her breakfast, a glass of milk and cup of coffee, and ate some food. At 8 a. m., she asked for a comb and brush, and wanted to fix up and go down town to see a lawyer about her will, as she wanted to leave all her money to the churches. A little later she fell heavily to the floor in syncope. Some slight twitchings, but no paralysis. This lasted until 10 o'clock, when she felt better. Her temperature was 96; pulse, 56-60, very weak and irregular. After this heart stroke she was more feeble and very weak. Unable to stand on her feet, would fall down when making the attempt. At times she could scarcely swallow, and the next day had to be tube fed by Dr. Felty. On the 20th, urinary analysis showed Sp. Gr. 1022, acid and small trace of albumin. No casts. She appeared almost unconscious. Could not swal-

low. Patient trembled in all muscles and there were fibrillary twitchings, but not more marked than previously noted. No ejactations and no mental symptoms at this time to suggest central neuritis. Patient was unable to talk. Temperature continued 96; pulse, 56-60, very weak.

On Jan. 21st her condition had not changed. She was visited by her brother, and called for him after he left. Her temperature was 97. Heart beats, 56; pulse could not be felt. She pulled on bed clothes, tried to talk, but could not make any intelligible sounds. Temperature in the evening, 96. Heart beats, 50-54. No diarrhea, no muscular twitchings of ejactatory type. She became stuporous and unable to recognize any one. She died 7.20 a. m., January 23, 1910, of degenerative myocarditis.

Synopsis of Clinical History.

We have here to deal with a psychosis in a single negro woman, aet. 55, with no heredity known of. Mental development above the average of her race. Successful school teacher for thirty-five years. No peculiarities or evidence of mental abnormalities until 1907, over two years before her last illness. Following close application to school work, with rather poor health, and at period of menopause, the patient suffers a breakdown, probably a profound type of nervous prostration, with evidences of depression, but exact character of attack at that time unknown. She spent six weeks in bed, and after a few months recovered entirely mentally, but on account of poor physical condition she did not return to teaching, but assisted truant officer in looking after colored school children and assisted with house work at home. Following first recovery no peculiarities were noticed in the patient until present attack. Six weeks, however, before the onset of last attack she was in poor physical health, and was treated by Dr. Cort for organic heart disease. He states no murmurs were detected, but that symptoms of organic myocardial disease were present. This improved somewhat under treatment.

Onset of Present Attack.—Was sudden, and followed the sudden death of brother from heart failure or apoplexy. Patient worried because she had secretly given brother patent medicine to cure the drink habit. Thought this might have caused his death. Two days after death of brother shows the first mental symptoms. She was restless, sleepless, worried continually over her actions in giving the powder. She became more depressed, agitated, apprehensive, and developed ideas of self-accusation, claimed she had committed the unpardonable sin, had killed her

brother, was possessed of the devil. She refused food and medicine. She would not sleep at night, and probably had auditory hallucinations. Six days later she was sent to St. Francis Hospital, but could not be kept there, and was then admitted to the New Jersey State Hospital at Trenton on October 23, 1909, eight days after appearance of mental symptoms.

On admission patient showed marked motor restlessness, depression, agitation and apprehensiveness. Her attitude was variable. Oriented for place, but poorly so for time and persons.

Physical examination, made a few days later, showed a light colored mulatto of good frame and muscular development, typical African features and kinky hair. No stigmata or malformation. General nutrition good. Height, 5 ft. 3 in. Weight, 141 lbs. Temperature was normal; pulse, 80-84. Well nourished. No evidence of acute or chronic constitutional diseases.

Nervous System.—General feeling of weakness and debility. No disturbance of taste or smell. Eyes moderately protruded, pupils normal. Vision normal. Hearing normal.

Cutaneous Sensibilities.—Not accurately tested owing to patient's lack of co-operation, but no abnormalities found in coarse tests; pain and touch sense found to be normal.

Reflexes.—Knee-jerks somewhat exaggerated, but no other abnormality of reflexes.

Motor Functions.—Facial movements symmetrical. Co-ordination good. General muscularity fair. Gait somewhat unsteady. No evidence of hemiplegia or paralysis.

Tremor.—Marked tremors of all muscles of body, due to her emotionally disturbed condition. Marked fibrillary twitchings of tongue, lips and fingers.

Speech.—No slurring, but some hesitancy.

Organic Reflexes.—Under control, but frequently passes urine involuntarily. No *convulsions* or hysterical attacks.

Lungs.—Not abnormal.

Heart.—Subjective complaints of palpitation. She frequently spoke of pain about heart. Pulse irregular, 84 per minute, and rather weak. No arterio-sclerosis. No murmurs heard, but heart sounds are weak. Abdominal organs negative.

Urine.—On October 24, turbid, Sp. Gr. 1025, acid, albumin, good trace. Hyaline casts. No sugar.

Summary of Mental Status.—Patient's mental condition was extremely variable, and hardly ever presented the same picture for any considerable length of time. At first the delirious state was more prominent, with extreme apprehension, and affect of fear in reaction to hallucinations and illusions. Coupled with this was an anxious mood with much agitation and motor and psychomotor restlessness. Her condition during the day was usually better than at night when she was more apprehensive and reacted more vividly to auditory and visual hallucinations. Delirium was also more profound. Disorientation varied often during the same interview, when she would claim she was in prison, or in hell, but when pressed further, would give the name of the hospital. Her time orientation was more constantly impaired, as also her memory for recent events. Although attention was always difficult to obtain and could be held only for a few minutes, there were intervals during which rational answers could be obtained, orientation became clear, and delirium with clouding of consciousness disappeared. Immediately following such intervals, however, the patient would become again disoriented by her affect of fear, depressive ideas, ideas of unreality and motor agitation. The abrupt alternation of these states, and the transitory character of the delirium was a marked feature, and one that obscured the diagnosis. At times the patient presented a typical anxiety psychosis, but this was liable to be succeeded by traits of a manic character, as shown in her pert references to the physicians, and distractibility of a modified character. At times even a tendency toward a flight of ideas was present. However, the predominating symptoms were the anxious and agitated depressed state. At no time was retardation or inhibition noted. Although she would occasionally sit alone on the ward, she would again wander aimlessly about appealing to other patients, or getting into bed with them. Often she was aimlessly resistive, through fear rather than negativism. The stream of thought was often wandering, shallow and disconnected, but here again, as in general demeanor, abrupt alternations were frequent. One constant symptom was the marked disturbance at night. Usually the patient was sleepless, agitated and noisy, pounding on door and screaming. Vivid reaction to hallucinations were present. Ideas of unreality, in the allo-, auto-, and somato-psychic fields were present, but not con-

stant or fixed. These ideas changed constantly. At times she was in hell, all about her were devils; again she was drinking devil's blood, her veins had no blood in them, or had no veins and no body; that her heart stopped beating. During apprehensive episodes, and at other times there were marked self-accusations, occasionally based upon hallucinations. She maintained people accused her of various crimes; that she had killed her brother; sent her family to hell; committed mortal sin.

Instead of the fixed immobile expression of depression, the patient exhibited an extremely mobile expression, rapidly changing from anxious, worried, bewildered, to one somewhat sarcastic or even half smiling.

Memory, usually good for remote events when her attention could be obtained, was defective for recent events and retention, and frequent fabrications were present.

School knowledge and calculation could not be accurately tested, as patient was seldom able to concentrate sufficiently to answer correctly. No retardation in counting. Counted 1-20 in five seconds.

Insight and judgment defective according to the degree and intensity of the delirium and agitation. Occasionally recognized that she was insane, but this insight also showed marked changes.

Subsequent course resembled largely her condition as described above, with daily variations, and sleeplessness and apprehensiveness at night. Hardly a night's sleep without hypnotics. Her physical condition became progressively worse. She lost weight from 141 lbs. to 125 lbs. Sudden attack of syncope four days before death marked the beginning of the terminal stage, and following this patient had to be kept in bed on account of weakness. She refused food, and could not articulate, but no ejactatory twitchings or other symptoms of central neuritis were observed. For a week before death her temperature was subnormal, 96-97, and heart action weak and irregular, 56-60. No pulse could be felt, and she died in coma January 23, 1910, three months after admission.

It is worthy of note that the albuminuria with hyaline casts which was present on admission, was absent on later examination, and that the mental condition did not improve coincidentally with the kidney condition.

Discussion of Symptoms.

The differential diagnosis in the case presented many difficulties, and so varied and atypical were the symptoms that no agreement as to the diagnosis was reached, as shown by the staff conference notes.

The age (past the menopause), apprehensiveness, anxiety, self-accusation, and ideas of negation, somatic sense deceptions, delusions and melancholic features, would stamp the case as one of involution melancholia, or a depression of the involution period. However, the delirious states, variability of the symptoms, and transitory clouding of consciousness, more marked at night, would speak for something more than a depression of involutional type.

Toxic delirium was the next diagnosis suggested from the presence of albumin in the urine, probably originating from kidney disturbance. But while there were undoubtedly delirious episodes, there were also *other features* of fear, anxiety, depression and apprehensiveness, that would not fit altogether in that diagnosis.

Manic depressive insanity must be carefully considered, and more especially a mixed state. The marked depressed ideas, without retardation, but with agitation, fear and marked motor and psycho-motor restlessness, and a tendency to joke at times, speak very strongly for such a consideration. Also the history of an attack in 1907, two and a half years ago. But the extreme apprehensiveness, with fear and clouding of consciousness and vivid auditory and visual hallucinations would be extremely atypical, also the subsequent history of the case helps to rule out such a diagnosis. For the prognosis in this case, when considered as a manic depressive insanity, even the mixed phase should have been good, and the prospect of death in three months would certainly not be thought of. It must be admitted that the prognosis was considered fair in this case, and it was with much chagrin that it was noticed that the patient was steadily failing instead of improving under the treatment.

There were no focal symptoms present and no neurological symptoms by which the case could be diagnosed, either general paralysis of arterio-sclerotic brain disease. Later a lumbar puncture was taken, but was negative for general paralysis.

At first no particular attention was paid to the fact that the patient had been treated for organic heart disease, or that she

was suffering from that trouble at the time of admission. The seriousness of the heart trouble was first shown at the autopsy, when a severe myocardial degeneration was found. The absence of murmurs was probably responsible for the fact that the heart lesion was not more fully considered.

So, while a tentative diagnosis of mixed phase of manic depressive insanity, with delirium, was made, the case was considered in the end unclassified delirium, and neither diagnosis was satisfactory. However, the autopsy in the case was the means of clearing up the diagnosis and of explaining the rapid decline and death of the patient, when the prognosis at first was considered fair and prospects of recovery good. The absence of any acute febrile or infectious disease prior to the onset of the psychosis is significant, and would rule out the various deliria of infection and febrile origin as well as collapse delirium.

The symptomatology and outcome of this case resemble in most particulars the typical cases reported in detail and discussed by Jakob, whose timely work has been of immense benefit in clearing up the diagnosis in this class of cases. (Of the histo-pathology we will speak later, but will mention here that in the principal features this case closely corresponds to Jakob's cases.)

A work here as to the etiology is important in this case. In view of the symptomatology, outcome and autopsy findings, we must consider that the organic heart disease doubtless played a very important role in the causation of the psychosis. And we can believe that the heart lesion preceded the onset of the psychosis by at least two or three years. Not only is this shown in the history, but the character of the lesions leads one to believe that it was of chronic type and well advanced long before the psychosis appeared. The nervous breakdown in 1907, with symptoms somewhat similar to the present attack, would lead one to suggest this as the onset of the psychosis and heart lesion, but through treatment, mainly rest in bed, the heart condition improved, and later, the cessation from teaching, and living a more equable and quiet life, was responsible for great improvement and cessation of any untoward symptoms until six weeks before the last onset.

But, coupled with the heart lesion, we have also evidence of a severe mental and emotional shock, the sudden death of a beloved brother, and the bare possibility that his death might have been

caused by patent medicine given him by the patient to cure the drink habit. As pointed out by Jakob, the combination of a heart lesion and a psycho-genetic factor is common in most cases of circulatory psychoses, and was present in the majority of the cases reported by him. The resemblance of the mental symptoms to those of a functional psychosis does not rule out a psychosis due to organic lesions, as we have the well recognized fact of the manic complex in general paralysis and depression in arterio-sclerotic brain disease which cannot always be differentiated from the true functional types.

The histological findings in the case, which resemble closely those of central neuritis, make it imperative to differentiate it from that complex. But the terminal condition did not show any similarity to central neuritis. The only points in common were, the anxious depression with delirium and hallucinations, which is also a prominent feature of central neuritis. Although mentally there were similar symptoms the physical phenomena characteristic of central neuritis were absent, viz., disturbance of reflexes, ejactatory twitchings, muscular rigidity, pain and tenderness over muscles, neurotic symptoms, and diarrhea. The terminal condition of central neuritis is so characteristic that it has been seldom overlooked in this hospital, and certainly no such symptom complex was observed. One symptom which may be confused with those of central neuritis was the tremors, but these were present throughout the time of her residence in the hospital, were general and constant, more marked when patient was agitated and apprehensive, and more of an ejactatory character.

Anatomical Findings.

Autopsy three hours after death.

Body with well-developed muscles and without essential wasting. Pupils moderately dilated; distinct œdema of ankles.

Internal examination of the head shows no detectable changes in the dura; in the pia a very trifling degree of turbidity along the longitudinal fissure only. The dural and cranial sinuses negative.

The walls of the basal vessels are a trifle opaque but in neither the major trunks, primary or secondary divisions are there any indications of atheroma or sclerosis of any significance.

Brain weight, 1100 gms., moderately small in size but in general appearance and consistency shows no departure from the normal. There is no atrophy of the convolutions and no increase in fluid. The ependyma is clear. No focal lesions were detected on subsequent dissection.

With the exception of the heart the anatomical and histological findings in the organs of the trunk were not highly significant.

Anatomical diagnosis confirmed by microscopic examination:

Marked myocardial degeneration.

Chronic sclerotic mitral endocarditis.

Subacute adhesive pericarditis.

Chronic bilateral pleural adhesions.

Moderate bilateral hydrothorax.

Marked bilateral pulmonary œdema.

Moderate aortic atheroma.

Slight chronic degenerative nephritis.

Cause of death, myocardial degeneration and pulmonary œdema.

Heart findings in full: Externally the pericardial sac shows nothing of note; on attempt at incision, the parietal and visceral layers are closely interadherent; the membranes are dry and tough and can be separated only with difficulty. The pericardial sac is completely obliterated.

The heart appears small in proportion to the other organs; depth of left ventricle, 7 cm.; circumference at base, 23 cm.; weight, 250 gms.

The subepicardial fat is notably increased, particularly over the right ventricle where it forms a large part of the wall.

The pulmonary and tricuspid valves do not appear unusual; the aortic valve segments show general opacity; the mitral leaflets are dull white in color; to the touch they are thickened and stiff.

The heart muscle of both ventricles is flabby and of very poor consistency, it is a turbid brownish-red in color.

The wall of the right ventricle is .4 cm. in thickness, and consists largely of the subepicardial fat; the muscle is very thin and ill defined and is transversed by delicate yellowish lines.

The wall of the left ventricle is .6 cm. in thickness, the muscle does not show the yellowish streaks seen on the right side.

The coronary vessels present nothing of significance.

Microscopically by paraffin sections and hematoxylin and eosin

there is no demonstrable alteration in the interstitial connective tissue and the vessel walls show only a very trifling degree of thickening affecting the individual coats about equally.

The subepicardial fat of the right ventricle forms nearly half the thickness of the wall and from it occasional small strands of fatty tissue extend inward between the muscle bundles.

The muscle striations are indistinct.

In the individual fibers are considerable accumulations of brownish pigment granules, for the most part situated about the nucleus, and with weak illumination a number of minute vacuoles in the muscle substance can be distinguished.

By Marchi there is a heavy accumulation of blackened granules in practically every muscle cell of the myocardium.

The granules are for the most part of minute size and are best seen with oil emersion and high illumination. They are diffusely distributed throughout the muscle fibers, those of larger size usually lying in proximity of the nucleus.

They are most abundant in cells nearest the endocardium, here an occasional cell is seen in which their numbers obscure both striations and nucleus.

No relation between the location of vessels and distribution of blackening in the muscle cells can be distinguished.

The picture is one of severe generalized myocardial fatty degeneration.

Technique of Examination of Brain.

Blocks of fresh tissue were removed from the first frontal convolution, the paracentral lobules, gyri recti, first occipital, first temporal, from the region of the calcarine fissure and from the cornu ammonis and cerebellum. Duplicate block from each area were fixed in 95 per cent alcohol, corrosive sublimate and 10 per cent formal, respectively.

A portion of the alcohol material was cut unembedded and stained by the original Nissl method, and the remaining portion embeddel in celloidin and stained with toluiden blue.

Blocks from the sublimate solution were embedded in paraffin, cut at a thickness of six microns and stained with hematoxylin and eosin, eosin and thionin and Van Gieson's stain.

The formalin material was taken for Marchi's, Pal's and Mallory's phosphotungstic acid hematoxylin stains and for frozen sections stained by Herxheimer's scharlach fat stain and Bielchowski's method for neurofibrils.

Histologic Findings of the Brain.

To general observation it is at once evident that the sections of the different areas present no indications of focal destructive change. The stratification is everywhere apparently normal; there is no architectural nerve cell loss or massive glia replacement.

The pia is everywhere comparatively thin and contains no cellular infiltration.

The vessels of the pia, not structurally noteworthy, are chiefly remarkable for a quite noticeable engorgement affecting the veins.

These are quite generally filled with well-preserved red corpuscles and, in contrast to the arteries, are moderately dilated.

At certain points a limited number of grouped red cells are found lying free in the pial meshes.

Beneath the pia the superficial fibrillary glia in Mallory preparations appears everywhere as a thin zone of delicate fibers. Occasionally at the bottoms of sulci the glia belt is a trifle increased, but nowhere does it show notable overgrowth.

The cortical vessels, as a rule, are without alterations of importance, the walls are of normal thickness and the individual cell nuclei of their coats well stained.

Occasionally among the long medullary vessels, certain elements are rendered conspicuous by the presence of a relatively large number of deeply stained nuclei in and about their walls.

A limited number of these cells are of the spindle shaped adventitial type; the greater number, however, are endothelial elements possessing slightly enlarged nuclei which are chiefly conspicuous for their slightly distorted shape and large amount of chromatin which they contain.

It is probably correct to regard such elements as hypertrophic and as exhibiting mildly proliferative tendencies, but since their occurrence is limited to comparatively few of the cortical vessels no particular significance can be attached to their presence.

Further study of the Mallory glia preparations and of sections stained by Weigert-Pal furnishes no additional data to the histo-

logical picture and alterations of essential importance are found wholly in the individual elements of the cortex.

These changes, since they present fundamental differences in type and distribution for descriptive purposes at least, are best considered as separate processes; one affecting the large elements of the deep cortical strata and the other the small and medium-sized pyramids of the outer cell layers.

As seen in Nissl preparations the alteration in the larger elements affects most severely the large Betz cells of the paracentral lobules. These cells, with but occasional exceptions, show very typically the central glassy dissolution of Nissl granules and peripheral nuclear displacement of an axonal reaction remarkable for the severity of alteration and number of cells involved. To a less degree among the large cells of other areas cellular reactions of similar general type occur and together with the more evident changes in the Betz cells constitute one very readily distinguished form of cell alteration, which were it not for the presence of an equally marked, though less conspicuous, alteration of another type, would largely overshadow the entire histological picture.

In the medium and smaller-sized pyramids, however, changes of different type are presented and the alterations as seen in such cells, while of much less individual prominence, constitute by their wide distribution and frequency of occurrence an essential part of the histological picture.

As distinguished from the axonal changes, the alterations affecting the cells of lesser size are apparently of more chronic type, and, as differing from the swollen globular cell bodies and little altered processes of the larger cells, these frequently present small shrunken bodies and prominent tortuous prolongation (Plate I).

The staining reaction of the entire substance of such cells is either increased or diminished so that in the fields they appear as diffusely colored pyramids with little demarcation between nucleus and cell body, or, having lost their affinity for the stain, as faintly stained elements with difficulty distinguished from the surrounding ground substance.

On close examination in cells of the latter type the cytoplasm is seen to have assumed a lightly stained and loosely reticulated appearence and in still more severely affected elements this has given place to a finely granular debris surrounding the still darkly

colored nucleus (Plate I). Cells presenting a shriveled, shrunken appearance with vacuoles in the protoplasm are also not infrequently encountered.

In some places, occupying the upper layers of the cortex, there are found occasional small fields in which with few exceptions all the nerve elements show varying stages of similar alterations.

Pigment deposits in these cell types, as shown by the scharlach stain, are peculiarly irregular in distribution.

Many cells, immediately adjoining others in which no scharlach reaction is visible, are filled with well-marked accumulations of small-sized granules or are occupied by large dark red clumps of similar material situated beside a normally staining nucleus.

A point not without importance in connection with the alterations in the cells of the outer layers is their distribution, for the occurrence of the affected small and medium-sized pyramids is not limited to any particular brain area. By comparison, both in intensity of the alterations themselves and number of cells affected, no differences can be detected between areas in which marked axonal reactions are displayed and in those with few cells of sufficient size for its demonstration; whereas, in no area showing axonal changes are the more chronic alterations among the small cells absent, and many regions are encountered in which the latter type of change is the only one presented.

The glia reaction by which the ganglion cell alterations are accompanied, while perhaps not quantitatively remarkable, is worthy of note. Occasionally about comparatively normal, as well as altered, ganglion cells a moderate increase in the satellite glia nuclei is noticeable and in a limited number of instances there is some tendency to replacement about certain of the more regressive small and medium-sized pyramids.

The individual glia elements concerned in this appearance, as well as in a similar increase noted along a number of the smaller vessels, are for the most part of progressive type; the nuclei are sharply stained and contain a number of very distinct chromatin granules somewhat resembling those of lymphocytes in distribution.

As shown in Nissl preparations the amount of protoplasma surrounding the glia nuclei in these situations is small and does not constitute an essential feature of the picture. Nor, as shown by

the Herxheimer stain, can fatty deposits in the glia be said to be a finding of importance.

The most notable alteration in the cellular glia, is the presence of certain peculiar individual elements; nuclei of altered shape, oval or bean shaped, having an indentation on one side, or even occasionally presenting a spindle-shaped outline. The latter elements, those of more elongated form, in addition show, at the nuclear poles, the faintest suggestion of protoplasmic prolongations and in general appearance resemble, to some degree, the "stäbchenzellen" of general paralysis.

That in this instance such cells are true glia elements is clearly indicated by the presence of many transition forms. Elements in various stages between the usual type of round glia cell and the oval or spindle-shaped nuclei of the modified cells.

The distribution of these altered glia types shows no relation to the presence of vessels or occurrence of axonal reaction, but are seen in greatest number among the more chronically altered small and medium-sized pyramids of the outer cortical layers where their presence is doubtless another indication of the same chronic degenerative process displayed among the nervous elements.

The amount and distribution of fatty pigments, as shown by the Marchi and Herxheimer methods, varies somewhat with particular cortical areas examined.

By Marchi is shown a characteristic and rather heavy-black dotting of the white substance throughout the white matter of the para-central lobules and similarly, but to a notably less degree in the myelin of other regions as well.

With the scharlach stain the distribution rather than the amount of fatty pigment is chiefly noteworthy. Among the larger elements and those showing axonal changes, and in the glia as well, many elements, perhaps the majority, show pigment deposits that are notably small and not infrequently are such deposits even absent.

The most notable reaction of this type is observed in the smaller cells of the outer layers and even as seen in these cells the intracellular distribution of the fatty pigment is not such that of itself causes any considerable alteration in the cell form, as in cells affected with senile change, but rather as deposits which conform in shape to that of the altered and shrunken cell body (Plate II).

Although even in this situation the number of cells essentially altered by fatty change only is not sufficient to warrant the assignment of a too great importance to this change alone it is worthy of note that while no relation can be established between the reaction in the smaller cells and points of maximum Marchi reaction in the myelin, the distribution of the chronically shrunken degenerated small pyramids of Nissl preparations corresponds accurately in location with the maximum fat deposits demonstrated by the scharlach stain.

In Bielchowsky preparations the two types of alteration among the ganglion cells shown by other methods is even more plainly evident.

Among the Betz cells and larger motor pyramids where in Nissl preparations axonal changes are demonstrated, corresponding fibril pictures are seen, and with great distinctness is shown the abrupt termination of the fibrils within the cell and their complete disintegration into the dust-like particles and glassy homogeneous material with which the excentrically displaced nucleus is surrounded. The unusual severity of such changes in the large cells is apparent from the large number of cells in which hardly a trace of original fibril structure is retained (Plate IV).

Of equal significance, however, is the second type of alteration, which, in the small and medium-sized ganglion cells of the second and third layers is displayed alike in motor areas and general cortex throughout. As seen particularly well in fibril preparations, alterations of this second variety, among the smaller elements, are subject to a noticeable gradation of severity, which seemingly corresponds more or less closely to the size of the elements affected, and in certain cells of larger size their interpretation cannot be definitely established.

In these larger cells (the medium-sized pyramids of the third layer) the fibrils have retained a fair degree of usual arrangement, and in the processes and peripheral areas of the cell body are relatively intact and unaltered save that they are somewhat closely placed.

In the centers of such cells, however, about the nucleus, with few exceptions well-preserved fibrils are absent and the nucleus is surrounded by a well-marked light-colored area in which the remnant of normal fibrillar structure is represented by either a hardly

distinguishable web-like arrangement of complexly interwoven delicate broken wavy fibrils, or by merely a collection of fine dust-like particles (Plate V).

Whether the changes in such cells are associated in origin with axonal alterations or whether they belong to other changes of more chronic nature affecting the smaller cells cannot be decided. The situation of the broken fibrils in the center of the cell about the nucleus possibly indicates the so-called central chromatolysis of axonal reaction, while on the other hand the unaltered central location of the nucleus and the resemblance in other respects which these alterations bear to those of small cell type suggests the possibility of their being the milder expression of a similar process affecting chiefly the cells of smaller size.

The changes in the latter elements, whatever doubt may be justified in those in the other cells, are shown by fibril methods to be such as are readily separable from those of other type present and by both severity and frequency they constitute a part of the picture equal at least in importance to the more conspicuous axonal changes among the larger elements.

So wide spread in distribution and so frequent in occurrence are the pronounced alterations among these smaller cells that technical errors are only excluded by the similarity of all sections prepared and the uniformity with which the changes appear in the special locations mentioned.

On detailed examination a fair number of small cells are found in which the intracellular fibril arrangement is comparatively but little altered and the cell in a fair state of preservation, but as a rule the small cells, in contrast to elements of larger size, appear as ill defined "cell shadows," so that even in darker colored preparations many are distinguished with difficulty, and the occurrence of partially normal appearing cells among whole fields of intensely degenerated elements strikingly emphasizes the altered appearance of those affected.

In the latter the usual appearance of intracellular fibril arrangement throughout the cell has disappeared and is replaced by pictures of varying grades of destruction. In some the fibrils entering from the processes appears to terminate in a more or less orderly net work, the open spaces of which are seen as small refractile points probably representing pigment granules (Plate VI B).

In others showing no indications of pigment, an appearance resembling a coarse open lattice with large spaces is assumed, or a greater part of the cell body may be occupied by large multiple vacuoles and no fibrils visible (Plate VI A, C and D).

In still other elements, with darkly impregnated nuclei, a different picture of degeneration even yet more marked is present. Cells in which neither straight fibrils, lattice work or vacuoles are seen, but in which the fibrils on entering are immediately broken up into short filamentous threads, in some instances dark and irregularly swollen, in others thin and delicate, but always poorly stained and which without definite arrangement lying thickly scattered throughout the cell and constituting the sole remnants of the intracellular fibril structure (Plate VI; E).

In both type and location these functionally dead cells of the fibril preparations correspond definitely to the same process less strikingly demonstrated in Nissl sections and definitely indicate the presence of a severe and well-advanced process of cellular decay among the cells of small and medium size in the outer layers of the cortex.

Summary and Discussion of Histologic Findings.

Study of the preparations by all methods employed as well as the gross examination shows that arterio-sclerosis, general paralysis, glia scleroses and other lesions of a like coarse nature are definitely excluded, and that likewise changes such as would result from an organically senile state do not enter into the make-up of the histological picture.

Aside from the detectable engagement of the veins in the pia and the presence of occasional minute hemorrhage in the same location the changes are confined almost wholly to the parenchymatous elements of the cortex.

The character of the changes occurring in the nerve elements, for descriptive purposes justifies their diversion into two types. These affect the Betz cells and other deeply placed larger elements and the small pyramids of the outer layers respectively.

In the alteration in the larger cells all the characteristics of the axonal reaction are displayed and are accompanied by the usual Marchi degeneration in the myelin of the para central regions.

The second type of alteration displayed in the outer layers throughout the cortex among the smaller cells is apparently of different nature and possibly of longer duration than that affecting the larger cells.

It is characterized by a more chronic form of degeneration in which the affected cells by a process of shrinkage and decay are reduced to distorted vacuolated elements of ones showing but remnants of granular debris.

One point of importance by which changes of the latter type are distinguished from the axonal alterations may be mentioned the distribution of the two changes. For while the cells showing most characteristically the axonal reaction together with the accompanying Marchi degeneration are most numerous in the paracentral regions, the other set of changes shows no predilection for any one region and occurs with equal frequency and severity in the outer layers of all areas alike.

A similar condition obtains in the distribution of fatty pigment among the cells as shown by the Herxheimer method, for there again this does not correspond to axonal reaction changes.

In cells showing the latter, fatty deposits are as a rule strikingly small, and while even among the smaller outer layers this alteration is not unduly prominent, still it is among these elements that the maximum fatty deposits occur.

The Bielchowski method emphasizes more clearly than any other the changes in the small cells and shows plainly the differences between these and the axonal reaction. As in Nissl preparations, but here more strikingly shown, the majority of the small cells are essentially altered and in a relatively large number even complete disintegration of the intracellular fibrils into coarse lattice work, granular debris or disorderly recticulum is distinctly evident.

The glia reaction, which is qualitative rather than quantitative and characterized by the occurrence of certain peculiar cells of irregular oval or spindle-shaped form, is shown only with any degree of prominence in the outer cortical zones of small cells.

To summarize in brief we have as the principal characteristics of the histological picture the presence of engorged and dilated veins and minute hemorrhages in the pia, a marked axonal reaction in the large cells of the paracentral region; and a severe,

and perhaps chronic, degenerative alteration in the smaller cells of the second and third layers (accompanied by qualitative glia reaction) throughout the cortex.

In attempting to correlate these changes with those hitherto demonstrated in connection with psychoses of circulatory origin the point offering the greatest difficulty perhaps is the interpretation of the presence of the axonal reaction.

It must be noted that in the first systematic histologic investigations of the histologic alterations present in psychoses thought to be based on circulatory disturbances, Jakob gives prominence to a change among the Betz cells referred to by him as "Central Chromatolysis." From both descriptions and drawings it is evident that this change is identical with the axonal reaction (Fig. 6).

In such case the question naturally suggested is whether in his cases Jakob is in reality dealing with a condition of central neuritis, or whether in these instances the axonal reaction forms merely a part of a series of specific changes of another process. Or, on the other hand, are these cases instances of central neuritis with a special etiology?

The previously reported cases of central neuritis cannot be said to show records of heart conditions sufficiently severe or characteristic to justify a positive conclusion on this point, but since even mechanical circulatory interferences must in the end exert their deleterious influence on the nervous elements through chemical action, a supposition that the changes of central neuritis may in certain instances result from such mechanical action does not conflict with the previous conception of its toxic origin.

But aside from the change in the large cells which must be conceded to be at least of central neuritis type, are those present in the elements of smaller size. It is realized that the changes of central neuritis are of a wide-spread character and that in the presence of changes among the larger elements by which it is characterized, additional changes in other cells must be interpreted with caution. But here again we must recognize the fact that such changes in the small cells in the present instance correspond to those in the cases of circulatory psychoses clinically observed and histologically examined by Jakob and the subject again reverts to the original question:

Do the findings in this and other similar instances indicate a

central neuritis with a special etiology or may they be regarded as indicating some other special process to which at some point of evolution the features of central neuritis are added? The determination of this point can only await the results of subsequent observations.

Conclusions.

1. Previous successful attempts to further differentiate certain unsatisfactorily classified conditions and to place them in separate categories indicates that if a sufficient basis of fully recorded clinical facts and anatomical findings can be obtained, further efforts in this direction are justifiable.

2. The achievements most desirable in this direction are those in which a chain of events can be traced between definite etiological factors, clinical features and anatomical findings.

3. In separating from an indefinite class of atypical depressions and undifferentiated deliriums, a type of mental disorder etiologically related to definite organic heart affections, a desirable step in the further necessary elucidation of such conditions is accomplished.

4. The principal clinical feature of such "cardiac" or "circulatory" psychoses is the complex of anxious depression with sudden onset and extremely irregular course with principally nocturnal delirious episodes, vivid reaction to hallucinations and early fatal termination.

5. The conditions from which cardiac psychoses must be particularly differentiated are toxic exhaustive delirium, mixed manic depressive insanity and terminal central neuritis.

6. The histologic cortex findings in the present case are such that the question of their relation to central neuritis and to cardiac psychoses on one hand, and the possible connection between cardiac lesions and changes of central neuritis on the other must be determined by further observation.

PLATE II.—HERXHEIMER STAIN.

Small cells of the second cell layer showing maximum pigment deposits. Compare the relative amount of pigment in these elements with that in the Betz cells.

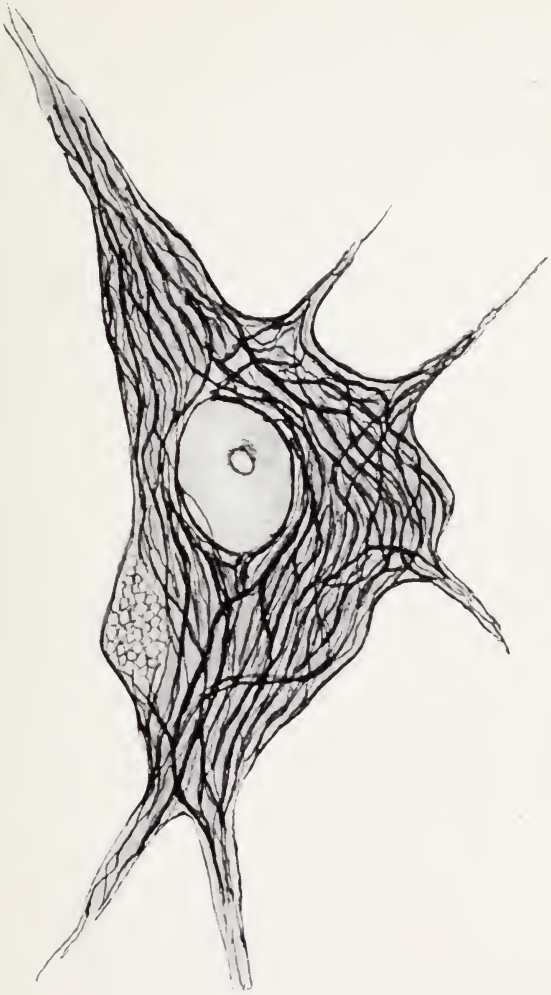

PLATE III.—BIELCHOWSKY.
Normal Betz cell with intracellular fibrils intact.

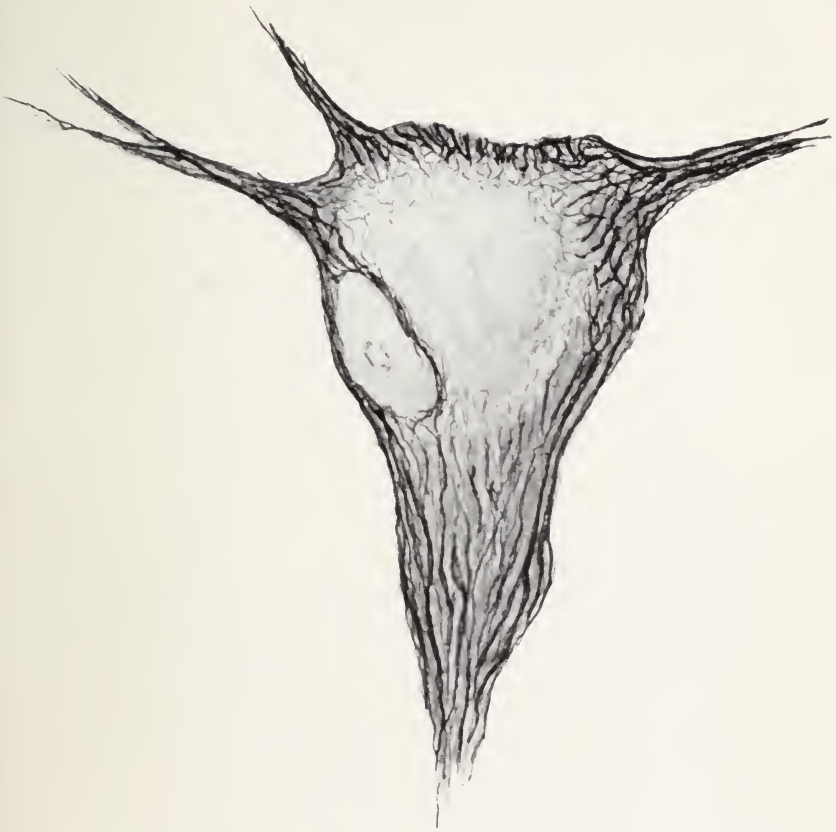

PLATE IV.

Betz cell with axonal reaction showing breaking up of fibrils and complete absence of even fibrillary fragments in the homogeneous zone adjoining the nucleus.

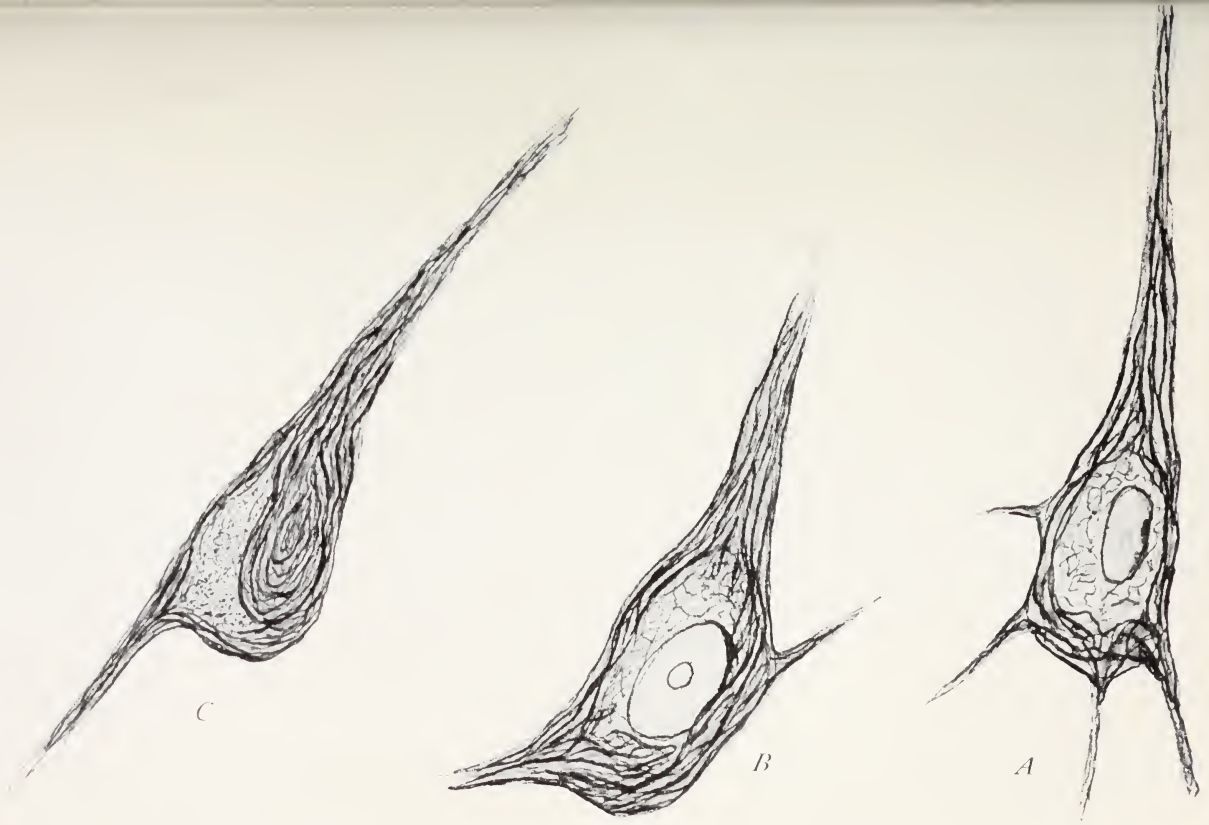

PLATE V.—BIELCHOWSKI. MEDIUM SIZED PYRAMIDS OF THE THIRD LAYER.

The nature of the alterations in these cells is indefinite. Whether they are due to axonal reaction or to the more chronic type of degeneration affecting the small cells cannot be decided.

In *A* and *B* the clear zones about the nucleus in which fine interlaced thread like filaments appear may represent the "Central Chromatolysis" of axonal change, but the position of the nucleus is unaltered.

C shows a peculiar vortex arrangement of the fibrils with a relatively large area of granular debris in which no fibrils are present. The nucleus is not seen.

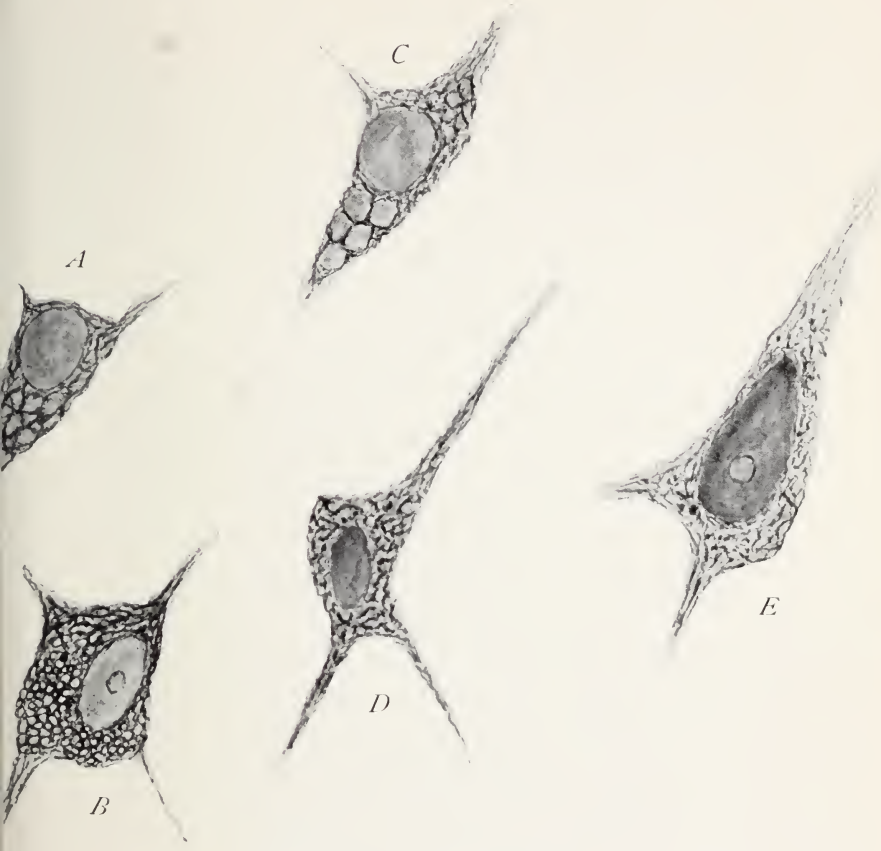

PLATE VI.—BIELCHOWSKI.

Chronically degenerated small cells of the second layers showing various types of fibril alteration. In *A* and *B* the usual intracellular fibril structure is replaced by a reticulum. In the lower element the meshes are small and probably enclose pigment granules. The cell above the mesh work is coarse and the apical process appears as if broken off. *C* shows the prominent vacuole formation with even greater distinctness than in Nissl preparations. In *D* and *E* the fibrils are in the end stages of disintegration; no unbroken fibrils remain. In *D* there remains a dark but indistinct and imperfect reticulum of broken short swollen filaments which fill the cells. In *E* even this has disappeared and the only indication of fibrils remaining is the almost unstained and hardly distinguishable filaments which lie promiscuously scattered about the darkly impregnated nucleus.

PLATE VII.—AFTER JAKOB. NISSL STAIN.

Betz cells of paracentral lobule showing the change referred to by Jakob as "Central Chromatolysis." The similarity of this change to the axonal reaction is readily seen.

SOME PROBLEMS IN THE TREATMENT AND PREVENTION OF MENTAL DISEASES.*

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In presenting this subject for your consideration, I realize the tendency of the specialist to see no further than his own field, and to exaggerate the importance of his own work. And to many practitioners it may appear that they have little in common with psychiatrists, and that their duty toward this branch of medicine is a negligible quantity. However, I wish to present some facts gleaned from recent work in this department of medicine, and I also hope to show that a grave responsibility rests with the general practitioner, not so much in the treatment or cure of mental diseases, as in their prevention.

Unfortunately, physicians as well as laymen have been accustomed to take a too fatalistic attitude toward insanity and the insane. To regard the insane as a class, rather than to differentiate types or forms, is an error that could be excused a few

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years ago. But to-day there is no reason why physicians should not become informed upon this subject and keep abreast of the progress that is being made, and assist materially in the work of the hospital physicians.

It must be admitted that in the past there were few opportunities for the average physician to become acquainted with this subject, even with the rudiments which were necessary in order to commit a patient to the insane hospitals. And we must also admit that in a large measure the hospital physicians were to blame for this state of affairs. But they were victims of circumstances, and cannot be criticized for their unenviable position among physicians in general.

The lack of any particular instruction in psychiatry in the medical schools places the hospital physicians as well as the general practitioner at a tremendous disadvantage Aside from this the former were over-burdened with executive work, and those who had the inclination toward scientific work saw the hopelessness of their situation, and either left the service or resigned themselves to their fate. But whatever our difficulties and shortcomings in the past, today at least we cannot be criticized because of any lack of industry or ambition to solve the difficult problems with which we are confronted.

Unfortunately, much of the work accomplished by the hospital physicians appears in official or special journals, and sel-

dom reaches the general practitioner, unless he makes a special effort to secure this information, so I may be pardoned if I give a brief resume of the period of activity in psychiatry, which began about eighteen years ago. I am speaking specifically of this country, for psychiatry was much further advanced in Europe, especially in Germany, than here and it is not surprising to find that we owe this awakening spoken of above to the Germans. Psychiatric clinics had been established in connection with the medical schools, and for years well-trained workers under skilled professors were engaged in research work. The science of psychiatry, however, in Germany as well as in this country, was dominated by tradition and dogma, and this influence was felt, not alone in the field of classification, symptomatology and diagnosis, but in the care and treatment of the insane.

To Professor Kraepelin, of Heidelberg, we are indebted, not only for our advanced knowledge of the subject, but for the stimulus he has imparted to the scientific study of psychiatry the world over. He was brave enough to overthrow existing tradition and dogmas, and formulate a more comprehensive system, based upon painstaking and systematic observations of cases, and also upon individual experimental work in the domain of normal and abnormal psychology. He brought to bear his knowledge, gained from these sources and from the work of others, upon the subject, and

at last a little light began to dawn where before had only been chaos and confusion. Although we cannot say that his work is complete, or that it cannot be improved upon, still we must give him full credit for establishing a groundwork for future progress, without which we would probably still be floundering in the dark.

In this country we cannot speak of the recent progress of psychiatry without mentioning the work of Adolf Meyer. He inaugurated systematic and organized work in the State Hospital in Worcester, Mass., and later organized the scientific work of all the insane hospitals of the State of New York.

He saw the need of training men for this special line of work, and through his efforts, not only have the State hospitals become centres of activity, but in Illinois and New York, and lately in Maryland, psychiatric clinics have been established in connection with the universities and central institutes, which are not only centres of research, but places of training and equipping physicians for this special work.

So that within a scant fifteen years a great change has taken place in the character of our insane hospitals. Formerly, the main function of these hospitals was custodial, and the public and profession were satisfied when patients, who were dangerous to themselves or the community, were properly safeguarded. Of the treatment of the insane under the old condition I will say but little, as you are all familiar with the methods. But to-day a well regulated

and organized hospital bears little resemblance to the asylums of olden times, or even recent years. Restraint has given place in many institutions to rational methods of treatment, and the abolishment of this one method alone I consider ample reward for those who have been responsible for these newer methods. In a recent paper, "The Problem of the State in the Care of the Insane," Dr. Meyer gives some very practical suggestions, and in the following pages I will frequently make use of his suggestions, as I can give you no better authority upon the subject.

The hospitals to-day have ceased to be mere State boarding-houses, but are now centres of curative activity which is not confined to the limits of the hospital by any means.

It is incumbent upon these hospitals to have an efficient medical staff, capable and ambitious, who not only visit the wards and prescribe for intercurrent affections among the insane, but who are well trained in psychiatry and capable of engaging in research work of a high character; well-equipped laboratories for clinical as well as anatomical work, and the members of the staff should be given opportunities to engage in the work. And it is obvious that complete libraries with current literature are a necessary adjunct to this work. In many hospitals to-day we can find such opportunities as have been described, but they are still too few.

The economic problem connected with

this subject should be discussed here. For years the standard of economy has been a false one, and the State has been satisfied with a system that maintained its insane at as low a figure as possible. It is obvious to any one that the criterion of efficiency should not be, how cheaply we can care for the insane, but how efficient is the care they are receiving, and how efficient is the organization to cope with problems of prevention rather than mere temporary maintenance. It is far better for the State to spend money in investigation with an aim toward prevention, than to pay out large increasing sums annually for maintenance. High standards of efficiency should take the place of temporary expediency, if the best results for the future are to be accomplished.

We cannot expect that society will be rid entirely of insanity, any more than it would be rid of vice, crime and disease, but we do feel that much can be done in prevention; and that along such lines the problem is best attacked.

In order to do this work, it is necessary for the hospital physicians to go beyond the confines of the hospital. Knowledge obtained by them should be imparted to the general practitioner and the public, and a campaign of education waged similar to that now being waged on tuberculosis. And we must look primarily to the general practitioners as the active agents in such a campaign. They are the ones who first see insane patients, often knowing them intimate-

ly before any symptoms of insanity have become apparent, and who observe mental disorders in their incipient stages. How often are they perplexed in the treatment of such cases even at the onset. They are hindered in many ways. Frequently they have to combat the family who will not consent to hospital treatment until such patients become dangerous to themselves and others, and often this stage marks the onset of chronicity, so that when they are received by the hospital physicians, all hope for remedial measures has vanished. Hence, we can only say what the results might have been if certain treatment had been instituted. So then we see that the hospital physicians have a responsibility that cannot be overlooked or slighted, and should be in very close touch with the general practitioner, and a hearty co-operation between them is essential if any practical results are to be obtained. On the other hand, it behooves the practitioner to pay more attention to this somewhat neglected subject, and to pay more attention to diagnosis, to look upon the insane not simply as a general class, but to regard them as made up of definite types to be treated in different ways. Also they must realize that their responsibility is great, not only for the outcome of individual cases, but in the whole problem and prevention of mental diseases.

Not only in prophylaxis, but in the after care of patients who leave the hospital, has the physician a very important sphere of activity. In the latter work his advice and

supervision of discharged patients will be an important factor in enabling these patients to resume their proper spheres of activity and position in the community, and will prevent recurrences and necessity for recommitment. Their influence is necessary in organizing "after care work" in their communities; and that they will be amply repaid for their interest by the results accomplished, has been clearly proven by the work in the State of New York where "after care" of discharged patients has reached a high state of efficiency.

So you see that not only is the physician in charge of the insane hospitals charged with an important responsibility, for he must not only organize the efficient medical and business arrangements of the hospitals, but his activities must extend throughout his district, if the work of prevention is to be accomplished. My contention is that such work as I have been describing is imperative in our hospitals, and I know that you will agree with me. As in other branches of medicine, your hearty co-operation can be depended upon when we are in a position to give the necessary information. And by dissemination of such knowledge I believe a great many of the preventable forms of insanity can be eliminated. Different communities will present different problems, as, for example, the urban and country districts. Different race types and nationalities will also present different problems in prophylaxis.

CLASSIFICATION OF THE INSANE.

I will briefly outline some of the forms of insanity with which we have to deal, grouping them mainly in three groups (as suggested by Dr. Meyer):

The *first group* consists of forms of congenital mental defects, or defects from birth, that present a stationary type which does not progress. They cannot be said to have an active mental trouble, and come to the hospital when they are unable to care for themselves, or when they get into trouble with the community. Very often they are able to remain at home, if properly safeguarded. In this class we find the imbeciles, and they are not difficult to recognize. The causes usually of such forms of insanity, due to arrested development, is hereditary—not necessarily insanity in the family—but the inheritance which comes from excessive indulgence in alcohol, and, second, certain physical diseases that cause the arrest of development in the unborn child.

The prevention of such cases must be chiefly considered from the side of the antecedents, their health, morals and habits. When this effect is better understood, no doubt, many cases that are now considered accidental and unexplainable can be prevented. Fortunately, they do not occur in a large proportion among our patients in insane hospitals, because this State maintains a home for feeble-minded children.

In the *second group* are classified the forms due to physical causes, extra psycho-

logical (or not due to mental conditions), such as intoxication (alcohol, drugs) delirium following infectious diseases and exhaustive conditions, such as childbirth, and forms associated with specific diseases of the nervous system, general paralysis, arteriosclerosis and senile dementia.

A part of this group are largely avoidable, such as forms due to alcohol and drugs. These comprise about twenty per cent. of the male admissions to our hospitals. It is needless to say that if such persons whose mental disorder depends on these factors, would abstain from their use and abuse, a notable decrease in our admissions would be the result.

We may consider mental disturbances the result of physical disease, such as that due to fever following childbirth, as rather rare, and, fortunately, such cases usually recover, so that from our present knowledge we may consider such types as unavoidable.

Another form in the second group to be considered, is general paralysis or paresis. It is one of our most hopeless maladies, but one of the forms of which we know to a certainty the cause, and that cause dependent entirely upon the habits and morals of the persons attacked. I refer to syphilitic infection. No other moral lapse carries a penalty that is so sure and certain. Usually the men attacked, after years in which their disease may be forgotten, just in the prime of life, are rendered in a few years hopeless dements, and then die after three or four years spent in total mental obscurity.

These cases amount to about ten per cent. of our admissions.

The simple senile dementia, or old age, can, to some degree, be considered normal except when it is premature, in such cases where arteriosclerosis occurs, rendering the person affected prematurely demented. Various are the causes for this condition, among which alcohol plays an important role. This class furnishes about ten per cent. of our admissions, of which about half could be cared for at home, and no doubt many such cases, with friends and relatives, do not come to the hospital at all. We see that thirty per cent. of our admissions, and probably more, come from this group, and are entirely avoidable, if the moral and physical laws are not broken.

In the *third group* we put forms of mental trouble which are essentially disorders in the mental sphere alone, where such factors as affect the mental equilibrium are concerned in the production of insanity.

Their mental trouble may depend upon an inherited intellectual weakness, or on acquired mental states, or on factors that are mentally upsetting in the normal, such as grief, disappointment, worry, etc. In normal individuals we have these factors frequently occurring, and the mental reaction is profound, but it does not cause them to lose their mental balance; but in certain types these disorders are not so easily overcome, and they seem unable to readjust themselves in the face of adversity, or to maintain a proper equilibrium. About ten

per cent. of our admissions belong to one class of this group, composed of those who are not so profoundly affected mentally, or who are better endowed with recuperative powers, and who finally recover their equilibrium after longer or shorter periods of mental trouble. These cases are merely exaggerations of normal states, such as depression on the one hand, and states of exhilaration, with over confidence and talkativeness on the other. The profoundness of the attack varies greatly in individuals. Some go very slightly over the border line, and it is often difficult to call them really insane. After they recover from an attack the main thing to be considered is to prevent subsequent attacks. This can be accomplished by adopting a regular mode of life, usually taking up rural outdoor pursuits, and giving up a life of stress and competition. A proper understanding by friends and relatives of such a patient's needs, and dangers to be avoided, goes a long way toward preventing a recurrence of the mental trouble.

Another class of cases in this group, unfortunately, does not recover its equilibrium so quickly, and this class constitutes the permanent residents of our hospitals. They furnish about thirty per cent. of our admissions, and it is very important to consider them with a view toward applying measures for prevention. Formerly, the view was generally prevalent that such cases, by reason of hereditary endowment and mental deficiency, were predestined to

become insane. This fatalistic attitude by physicians, as well as by the public, cannot be too strongly condemned.

This opinion was largely based upon statistics of such cases, which ignored the valuable criterion as to whether anything had been done for them before the onset of their mental disturbance at a time when the trouble was merely incipient or threatened, to prevent the oncoming dementia. Experience has shown us that symptoms were overlooked, or considered too trifling or inconsequential to be noted, which, perhaps if properly understood and treated, could have prevented the trouble that appeared later. Not until all means suggested have been tried during the incipiency of these forms, are we justified in assuming that fatalistic attitude spoken of above. I am inclined to be optimistic in viewing the possibilities in this unfortunate class of cases. And the fight to be effective will, to a large extent, be waged in the youthful age of these cases, principally during school years and the period of adolescence.

Certain traits and tendencies in school children, which are in the light of later developments, *i. e.*, at the time they are classed as insane and studied in our hospitals, are neglected through ignorance of parents, teachers, and often physicians, so that instead of helping the child over these obstacles during this difficult period, often they are forced along in directly the opposite way from that which would eliminate these traits. And, finally, unable longer to

readjust themselves to their environment, a mental failure supervenes which is followed by deterioration. Psychology has helped us somewhat in understanding the complicated mechanism of habit and reaction to our surroundings. The mechanism by which a mental balance is maintained can be lessened in effectiveness when persistently abused, and like other organs of our body, finally fail to respond in a proper measure, and readjustment does not take place as formerly. Meyer has justly termed these forms "habit deteriorations." And here it is well to speak of the warning uttered by Meyer, that the appearance of such traits as day dreaming, seclusiveness, listlessness, abnormal bashfulness, are not always an indication of inevitable failure. Also that no one symptom can be taken as a criterion, but all must be taken together before one can conclude that radical measures should be adopted. But these peculiar traits, when persistent, and carried to the point of interference with a child's proper reaction to every-day life, should be heeded as grave warnings, and an effort made to ascertain the true cause for such deviations, and, if possible, remove them and correct the habits.

An important class of this type is composed of the cases which in early life show true hysterical outbreaks or tantrums, which are grave warnings of a future breakdown, unless the cause of such tantrums is removed and the subsequent life so ordered to avoid these mental pitfalls. The

energies of such patients should be directed into a congenial environment where encouragement shall take the place of bickerings and distasteful competition. We frequently find in the histories of these cases of deterioration, that in their early life distinct hysterical elements were present, which were, unfortunately, overlooked, and finally resulted in the incurable form of insanity.

A very important phase of this question is the relation of these cases to the schools and methods of teaching. At present we have in many places a very necessary supervision of school children by physicians who correct physical disabilities, such as eyesight, and diseases incident to those years of life. This is a very praiseworthy effort, and is to be highly recommended. But does such a system go far enough? Is not the mental condition of school children of as much importance as physical disabilities? In the first place, the question of tire or fatigue must be thoroughly understood by the teachers and those who mold the curricula of public schools. In regard to the mental recuperation from fatigue or brain fag, children will show great variations. Children well trained from infancy seem to stand increasing strain without serious embarrassment, but those untrained show a tendency to break down under the stress of keeping abreast of other children, and of prolonged mental work. And this brings up the question in regard to the capacity for work of different children.

Often an ill-directed ambition will seriously overtax a child incapable of undertaking such studies, and result in a later breakdown. Especially is this true during a later period of life, when one takes up more advanced work without proper preparation and finds that it is necessary to overtax one's mental capacity to keep up with one's studies.

It would seem that a healthy outdoor life for children, who are perhaps somewhat abnormal, would tend to alleviate their condition, and prevent a breakdown from overtaxing the mental faculties by too close application to study. Added to this, a plentiful amount of health exercise should be insisted upon, but not flavored too much by competition or carried to the point of fatigue.

Especially in the case of young girls at the critical period of their development, should all mental strain be avoided. Rather have them discontinue their studies for a year, than to damage them to such an extent mentally that they may not recover their normal mental poise, especially, if in such cases, physical ailments are also present.

And here it must be emphasized that a proper guarding of the sexual instincts and functions by acquainting children of these matters and truths about themselves, will often prevent a serious mental shock when such truths are learned through other sources, often distorted, and in an objectionable manner. Often more harm is

done by brooding over secret sins, and continually thinking of such matters, than by the actual physical acts themselves.

Frequently we meet certain patients who belong to the class of sexual neurasthenics, whose trouble is brought about directly by brooding over their habits. Such brooding usually is the result of reading patent medicine literature regarding "lost manhood," "sexual excesses," etc., which is at times spread broadcast and comes into the possession of young persons. Only too frequently these cases do not end favorably, for these broodings, if not checked, lead to permanent mental derangement. The gravity of such habits should be explained by the family physician, and all fear engendered by the pernicious literature noted above, eliminated.

LEGISLATION.

We are extremely fortunate in New Jersey in our laws regarding the commitment of the insane, and I think the procedure is far in advance of the procedure in most States, and we feel proud of the men who framed such laws. The main reason of their superiority lies in the fact that it is only necessary for two physicians to certify as to a person's insanity, and the legal commitment comes later. This allows physicians to bring patients at once to the hospital without the necessity of waiting for other legal steps, the patient meanwhile being confined in the jail or some equally undesirable place.

But, good as our laws are, they do not go

quite far enough, for they do not allow voluntary commitments, a procedure that is in vogue in many States. The odium of having been declared insane is still very unpleasant to most people, and to avoid this patients are kept from the hospital at a time when remedial measures would be effective. But if such patients, often on the border line of insanity, could avail themselves of the privilege of applying for admission themselves and feel that they were not detained against their will, frequently they will come into the hospital and receive the benefit of early treatment. A class of patients which we group as cases of neurasthenia, hysteria, psychæsthenia, etc., who could not legally be declared insane, would be benefited by such a form of commitment.

An attempt was made during the session of the last Legislature to get such a bill passed, but was not successful. And I want to thank the chairman of the Legislative Committee for his valuable assistance and interest, and hope that the next Legislature will favor constructive legislation to a much larger degree than the one just past.

But the members of the profession in general can and do exert a great deal of influence in these matters of legislation, and by constant and persistent effort will accomplish the needed results, I am sure.

COUNTY ASYLUMS.

Another matter of which I want to speak briefly, is in regard to the county asylums in some of the counties of this State. In

the first place, there should be no institution for the insane under the control of counties, for many reasons. County asylums are a thing of the past in many States, and are fast being deposed in others.

At the present time it is useless to think of doing away with them entirely, but we certainly can ask for, and insist upon a reorganization of these asylums. And I do not mean to cast any reflection upon the management of the county asylums, some of which are admirably conducted. But the principle of having a layman in charge of the acute insane is entirely wrong. As we said at the outset, the public and the profession should not be content with mere custodial care of this class of patients, no matter how good that custodial care may be. It is true that these asylums have attending physicians, but they have little voice in the policy or control of the hospital, and no matter what they think should be done, they can be overruled by those in charge and their advice disregarded. But I think that by concerted action of the medical profession, the freeholders could be induced to change their policy.

In visiting the county institutions last fall I was struck with the low per capita cost—$2.50 to $3.50 a week in most asylums. As the State pays $2 per week, it is easily seen where the responsibility for the condition I have described exists. Here again, temporary expediency and economy

are the only standards, and the freeholders should be enlightened as to their error.

I have barely touched upon the more important themes of this problem, but if I have aroused your interest in this subject I consider that the object of this paper has been, in a measure, attained.

In conclusion, I want to emphasize again the important role of the family physician in the solution of these problems. They are much better acquainted with the modes of life, peculiarities, characteristics and general "make up" of both the patients and their families, and often have the opportunity of observing the development of individuals. At such times well-timed advice and counsel would do much in correcting the life of such patients, and it is to these physicans we look for their assistance and co-operation in dealing with this complex subject.

That the hospital physicians can do a great deal more than has been done toward securing the valuable co-operation of practitioners is too true, but we look for the dawn of better conditions. We are ready to accept any suggestion as to how this relationship can be made close and each benefited materially thereby.

SCARLET FEVER AS AN ETIOLOGICAL FACTOR IN THE PSYCHOSES.

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A glance at the evolution of psychiatry is sufficient to impress one with the fact that etiology has held a prominent place with psychologists from the mythical era to the present time. It is also noticeable that at different periods, different causes were considered sufficient to produce a psychosis. Certain forms of insanity have come down through the ages unchanged, but etiology has oscillated from the heavens to its antipodes. With this oscillation of the real or supposed cause, care and treatment has followed in a most natural order of sequence. When the aberrations were attributed to the smile of the gods, the favored one was looked upon as supernatural and venerated. When possessed of the devil, praying, singing of hymns, violent exorcisms and magical formulæ prevailed. Only when the etiology came within the confines of physical causes and human reason can we discern any real progress. It is said that Galen, the last of the great ones of the golden age, who wrote at the beginning of the third century, did credit to a twentieth century text-book. During the dark ages which followed, the science of medicine degenerated into an elaborate system of empiricism and mysticism, and demonology was reinstated as a controlling element in life. "The world seemed to be like a large mad-house for witches and devils to play their antics in."

We foster the modern view: a human being sick: physical causes; a hospital, light, airy, clean and comfortable; suitable and abundant nourishment, trained nurses, kindness, non-restraint, reason, liberty. But let us not be deluded. "The cost of giving the treatment has been materially increased, the recovery rate remains unchanged" (Bancroft).

The scientific study and treatment of the insane has met with signal achievement, but the results are far from gratifying.

The ever increasing percentage of insanity tends to turn our atten-

tion to that genius, Dr. Pliny Earle, of 30 years ago, who said, "Very clearly, if insanity is to be diminished it must be by prevention and not by cure." The old adage is also quite appropriate: "He who cures a disease may be the skilfullest, but he who prevents it is the safest physician." *As etiology necessarily precedes prophylaxis,* so a careful study of each *known* and *probable* cause seems worthy of consideration.

Where scarlet fever originated is not known; descriptions are given of it by medical writers before the Christian era. To Sydenham we owe the name and its differentiation from measles. It is very generally disseminated, it has been studied in all parts of the civilized world. No race is immune. Whether it is due to the streptococcus scarlatinæ of Klein and Gordon, or the streptococcus conglomeratus of Kurth, or an organism resembling the meningococcus as isolated by Wadsworth, has not been determined. Mallory would seem to demonstrate that the cause of the disease is probably a protozoon. Age does not confer immunity; susceptibility, however, is in inverse ratio to the age, the greatest incidence being from four to eight years of age.

Hospital care of scarlet fever cases has greatly reduced both morbidity and mortality, 23.48 and 1.56 respectively, per ten thousand population, in the Boston City Hospital. The mortality for the State of New Jersey during the past five years is given as 2.49 per ten thousand. The percentage of mortality varies, with age and epidemics, from 33 per cent to 1.33 per cent. The death rate in the Municipal Hospital of Philadelphia in 5,213 cases was 9.72 per cent.

Although the mortality and morbidity has been considerably reduced, yet with hospital care and modern treatment, complications and sequelæ that may lead to permanent physical or mental impairment continues very high, estimated at over 90 per cent in some epidemics. Albuminuria accompanies nearly all cases of severe scarlet fever, often with interstitial changes especially marked. McCullom finds a mitral systolic murmur in 187 of 1,000 cases analyzed. Otitis varies from 10 to 75 per cent. This in turn has been the direct cause of 10 per cent of deaf-mutism in the State of New York, in Great Britain 23.5 per cent.

The nervous system also receives no little portion of the damage done by this disease. Convulsions are not infrequent at the onset of the disease in children, which indicates a sudden and severe disturbance of the physical equilibrium, or they may occur late as a result of uremia. It may be well to state in this connection that in many cases of

epilepsy the initial convulsion occurred at the time of an attack of scarlet fever. Weildermuth reports 12 cases in a series of 187.

"More cases of epilepsy are consecutive to scarlet fever (apart from the influence of nephritis) than all the other acute diseases put together." "This together with the fact that optic neuritis may follow scarlet fever, without any organic change in the brain to cause it, seems to show that the scarlet fever poison has a special action on the nervous system" (Gowers).

The writer has found, in a series of 122 cases of epilepsy, 11 (more than 9 per cent) with a history of scarlet fever, the initial convulsion occurring at the time of the disease or as a result of some complication or sequelæ. Other factors, however, such as heredity, alcoholism and imbecility, were not excluded.

Meningitis, paralysis, embolism, hemiplegia and cholea have also been reported during the past year.

In regard to the relation of scarlet fever to the psychoses: The author has reviewed the literature at his disposal, but has failed to find much that treats it specifically, and no statistics bearing upon the subject except in an indirect way. It is also difficult to handle the information that has been gathered in a manner that would benefit those not already familiar with the subject. At the present time it shall be the attempt of this paper to bring together only such isolated facts as seem worthy of consideration; and if, by so doing, I assist anyone in any manner or shall have offered a suggestion that will lead toward the establishing of scarlet fever in its proper place as an etiological factor in the psychoses, then compensation will have been sufficient.

The question might well be raised here. Does the specific poison (or organism) of scarlet fever have a predilection for the nervous system, or, are its toxins more apt to affect the nervous system than the toxins of any other acute infectious disease?

To the first part of the above question with the light of modern research no definite answer can be given. Some would lead us to the view that scarlet fever poison has a special action upon the nervous system, while others prefer to explain its attack upon an anatomical basis —continuity and contiguity of tissue. The former view seems to receive some support by the fact that optic neuritis may follow scarlet fever without any organic changes in the brain to cause it.

To the latter part of the above question there is also some ground for

discussion. For those who would oppose the view that the specific poison (or organism) of scarlet fever has no predilection for the nervous system, there must be some explanation of its effects other than anatomical relations, especially in those cases in which no complications were recognized, the patient, apparently, not having had a severe attack. It is not uncommon to get a history of an ordinary attack of scarlet fever followed by a change in disposition, defective memory or arrested development. Furthermore, it has been observed that more cases of nervous disease are consecutive to scarlet fever than all the other acute infectious diseases put together.

In dealing with the psychoses alone, it seems most natural to place them in two groups. First, those in which scarlet fever is a *direct* cause; and second, those in which it is an *indirect* cause.

In the first group are placed such forms as manic-depressive insanity, fever delirium, post-febrile psychoses, exhaustive psychoses and dementia præcox.

The first form is passed briefly as it occurs but rarely. The second form does not differ essentially from the fever delirium caused by the toxins of other acute infectious diseases. It follows rather closely the clinical course of the fever, and in a measure depends upon it. The clinical picture presents four different grades corresponding to the intensity of the toxic action upon the cortical neurons, varying from moderate irritation to paralysis and finally to complete destruction of the same. This form of psychosis is of short duration and in favorable cases subsides with the temperature. A few cases emerge from the fever delirium into an exhaustion psychosis or become the starting-point of other psychoses.

The third form of mental derangement in which scarlet fever is recognized as a direct cause is that known as post-febrile psychosis. This, as its name indicates, is found usually following the fever and is apt to lead to permanent mental impairment. Because of this tendency some of its symptoms deserve mention. The mildest form is represented by those cases in which, after the subsidence of the fever, the patients fail to show their former physical and mental energy, they are dull and sluggish, very susceptible to fatigue; they cannot collect their thoughts and find it difficult to occupy themselves; are indifferent to their surroundings and let things go as they will. In emotional attitude they are sad and troubled, sometimes irritable, and occasionally

at night they suddenly develop a state of great anxiety. In the severe types hallucinations of all the senses may be present, disorientation with confusion of thought, fantastic delusions and active excitement with anxiety. Emotionally, dejected and at times ill-humored, obstinate and resistive. Physically there is faulty nutrition and insomnia. It may be differentiated from dementia præcox by greater affect and disturbance of apprehension and orientation at the onset of the disease, and by the absence of negativism and stereotype movements; from the depressive phase of manic-depressive insanity by the absence of psychomotor retardation and the presence of faulty memory. The prognosis is unfavorable; after months of institution treatment, only one-half of the cases recover; the other cases improve gradually, but present as residuals weakness of intellect, poor judgment, inability to keep up with their classes, take up their former occupation, or provide for themselves

A few cases are reported that seem to come quite properly under the heading exhaustion psychoses, as they apparently arise from excessive exhaustion or insufficient restoration of the nervous elements in the cerebral cortex. There is usually a history of a severe attack of scarlet fever, and evidence of a radical change of the physical organism. But even here one cannot always exclude the possibility of toxemia arising from the destruction of tissue.

Last, but not least, the relation of scarlet fever to dementia præcox must be considered, especially in view of the fact that so seldom can a definite or satisfactory cause for dementia præcox be ascertained. It is conceded, by good authorities, that, now and then, it follows very closely an attack of scarlet fever and bears a direct relationship to the same, but more often it is consecutive to some form of psychosis previously mentioned. It is the *indirect* relationship of scarlet fever to dementia præcox that suggests any ground for discussion. Years may have intervened between the attack of scarlet fever and the onset of the psychosis. Cases have come under our observation at the New Jersey State Hospital at Trenton with intervals ranging from 7 months to 31 years, with an unquestionable history of the fever indirectly influencing the psychosis.

The disease may have been forgotton or recalled only after careful and specific questioning; at the same time we find a history of convulsions, a delirium, physical weakness, otitis, loss of energy, long or final absence from school or arrested development. Too often the papers

committing these cases to the psychopathic hospitals contain no statements whatever indicating the etiology of the psychosis; or such statements as overwork, mental strain, masturbation, intemperance, ill-health, cigarette smoking, a fever, feeblemindedness, etc. On the other hand the examining physician encounters much ignorance on the part of the parents regarding the diseases their children have had. Such statements as "a fever" or "a rising in the head" are only suggestive, not to mention the great number of aliens committed to our hospitals who are practically out of the question.

Kraepelin, in his study of the etiology of dementia præcox, has found that in 10 per cent of the cases there is a previous history of some severe acute illness, particularly typhoid or scarlet fever, from which time the patient has exhibited some change, as increased irritability, susceptibility to fatigue, or impairment of the full mental capacity. From the records of the Trenton State Hospital, we find a case corresponding identically with this view.

Case No. 1.—F. C., male, white, single, age 24 years; occupation, laborer. Birth and infancy normal, strong and bright until six years of age, then had scarlet fever. Apparently good recovery, except mental dullness, more noticeable in his school work. Never independent of his parents, but earned wages. Admitted May 1, 1908. A year before admission a change in disposition occurred; he became seclusive and apprehensive; later suspicious of food, showed peculiar attitudes and mannerisms, was afraid to go to bed at night, had hallucinations of sight and hearing, at times untidy; disorientation and deterioration decided at the present time.

It will also be observed that the history of this case, prior to the onset of the psychosis, is practically the same as we find in those of arrested development or acquired imbecility, varying in degree rather than in symptoms. The following case illustrates this point:

Case No. 2.—W. C., female, single, age 63 years. Family history negative. Personal history: Not unusual until eight years of age; then had an attack of scarlet fever with convulsions. Went to school very irregularly after this on account of her delicate physical condition. She could not keep up with her classes, became discouraged, lost interest in her studies and preferred to stay at home with her parents. After her first menstruation she became stronger in body, but her mental state remained impaired; never self-supporting, but a good helper in her own home. She continued on through life without any essential change except that now and then she had irritable and contrary spells. During the past year, symptoms of senile deterioration were observed. She would wander aimlessly about the house or away from home. Meddled with fire and matches, imagined she was going to starve, and had no clothing to wear; up and about her room at night, accumulating numerous and worthless articles. Committed to State Hospital October, 1908.

Again the question might arise, Why should the first case become one of precocious dementia, while the second continues a high-grade imbecile until arriving within the period of senile deterioration?

I might enumerate cases indefinitely, but that would simply add tedium without compensation. There is yet one condition that seems sufficiently important to justify a few additional remarks. As stated in the early part of this paper, otitis as a complication in scarlet fever has been recorded as high as 75 per cent in some epidemics, with deaf-mutism as high as 23.5 per cent, which makes a population surprisingly large and particularly susceptible to episodes which cause them to be sent to our hospitals.

Case No. 3 illustrates this class. W. S. B., male, white, single, age 30 years; occupation painter.

Born at full term, labor normal, fifth in line of birth, breast-fed; cut teeth, walked and talked at usual time. Strong and healthy child until about five years of age, when he had an attack of scarlet fever, discharge from both ears, lost sense of hearing, gradually lost his speech; later attended school for the deaf, learned the sign language and painter's trade, and was employed as carriage painter for four years in his home town; laid off because of slack work, became suspicious, irritable and threatening, homicidal and suicidal, carried razors and attempted arson; arrested and committed to the State Hospital. No deterioration. A prompt recovery.

In conclusion, first, allow me to repeat the words of Dr. Earles. "If insanity is to be diminished it must be by prevention and not by cure." Second, that scarlet fever is an etiological factor in the psychoses and worthy of more consideration. Third, that it is more apt to be followed by complications and sequelæ and impair the future usefulness of the individual when it occurs during the evolution period; hence a most rigid quarantine should be instituted in each and every case of the disease and prophylaxis should be the "battle-cry".

STUDIES IN HEREDITY WITH EXAMPLES.

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Heredity has long been recognized as an important etiological factor in mental disease. The term, however, has been loosely applied and indefinitely stated. It is usually considered sufficient to state the percentage in which hereditary influences appear in the different psychoses without any attempt to specify the character of these defects. In the present paper an attempt is made to determine more definitely what psychoses or peculiarities are found in the families of a series of cases in the institution with which the writer is connected.

At the very onset it is well to consider the difficulties encountered in such a study. The hospital records constitute one of the important sources of information. One who has had any experience with old asylum histories, however, need not be told that these are often meagre and valueless. Moreover, when an honest effort is made to obtain useful data the informant is frequently unreliable. He may be ignorant or may purposely distort or conceal the real facts. Even if the informant be reliable, yet there is no standard in measuring mental conditions. One must consider also the education of the individual, his environment, opportunities, and so forth, before an equitable judgment of his mentality can be made. Again it is difficult to decide the relation of the peculiarity in ancestors to the psychosis in the case at hand. The fact that a history of insanity or peculiarity may be obtained, after careful search, in the families of many normal individuals must be borne in mind, and the danger of a *post hoc propter hoc* argument avoided.

The biologists are accomplishing much, which will doubtless help to solve the problems of the hereditary etiology of mental disease. A number of analogies may be found between the unit characters of the anatomical and those of the mental make-up. The time may come when, as Prof. Davenport has said, if the

characters of the parents are known, it will be possible to predict the kind of children.

In this regard it is important to make careful and minute studies of individuals in families in respect to certain traits or unit characters and their transmission, disappearance, or change in successive generations. In order to eliminate, so far as possible, the element of difference in education, environment, and opportunities, Strohmayer suggests that the families studied should be from a small little-fluctuating community.

The problem then is extremely complex. The present examination scheme, as usually followed, is not sufficient to collect really valuable data to establish the influence of heredity. To one in search of facts, even the so-called well-worked-up records are exceedingly disappointing.

Besides studying the psychoses in relatives and endeavoring to show in this way a real hereditary influence, it is also well to consider to what extent acquired conditions may affect the descendants. Although some writers dispute the possibility of the transmission of acquired characters, yet it must be acknowledged that such habits as alcoholism in the ascendants leave their mark upon the inheritors. Alcoholism in the parents, especially at the time of conception, has been shown, by more than one authority, to result in the propagation of defectives.

In the examination of the present series of three hundred and eighty-six cases, two hundred and twenty-nine men and one hundred and fifty-seven women, special attention has been paid to the psychoses, peculiarities or toxic habits in paternal and maternal grandparents, uncles and aunts, parents, brothers and sisters. Many of the statistical findings are not greatly different from those of numerous writers on the subject. Of the three hundred and eighty-six cases, one hundred were in the manic depressive group, sixty-eight dementia præcox, fifty-two alcoholic insanity, eighteen general paresis, twenty-three epileptics, six narcotic inebriety, nine imbeciles and one hundred and ten cases in which there was found to be apparently very little hereditary influence and which are grouped together. Ninety-five cases, or a percentage of 24.61 of the whole number, showed undoubted heredity, such as psychoses or eccentricity in ancestors. If those

cases were added which gave a family history of alcoholism only the percentage becomes 35.

STATISTICS OF HEREDITY.

Form of Insanity.	No. of cases.			No. showing heredity.			Heredity percentage.		
	Male.	Female.	Total.	Male.	Female.	Total.	Male.	Female.	Total.
Manic Depressive	47	53	100	19	10	29	40+	18.8	29
Dementia Præcox	43	25	68	13	4	17	30+	16	25
Alcoholic Insanity	46	6	52	15	0	15	32.6	0	28.8
General Paresis	13	5	18	7	0	7	53.8	0	38.8
Epilepsy	17	6	23	7	1	8	41+	16.6	34.7
Narcotic Inebriety	6	0	6	4	0	4	66.6	0	66.6
Imbecility	6	3	9	4	0	4	66.6	0	44.4
Other Psychoses	51	59	110	3	8	11	5.8	13.5	10
Grand Totals	229	157	386	72	23	95	31+	14.6	24.6

In the manic depressive group, one hundred cases, forty-seven men and fifty-three women, there was an hereditary taint of 40.42 per cent in the former and 18.86 per cent in the latter, or a total of 29 per cent. While most observers agree that the male cases show a greater percentage of heredity than the female, yet the difference is not usually so marked as in the present series.

As has already been said, it is impossible always to state even the probable diagnosis in the cases of insanity in the relatives. A number, however, show evidences of manic depressive insanity, both by individual symptoms, namely depression or excitement with recovery, and by recurrence of the attack. Five were suicides, very likely constituting depression. One case had a maternal grandmother who had a psychosis following childbirth from which she died. His mother was twice admitted with maniacal symptoms, recovering completely from the first attack and staying out of the hospital for eighteen years. Her second hospital residence has been of twenty years' duration, and now she seems to be a senile dement. His sister is also of the manic depressive group. There were seven other probable cases of manic depressive in the relatives, eight of apoplexy or paralysis, a few nervous, neurotic or deficient, two epileptics, several senile dements, a number classed as simply "insane." It is interesting and important to record a well-marked case of dementia præcox,

brother of a female manic depressive—the præcox exhibits the characteristic apathy, dementia, mutism and resistance.

In eight male cases, or 17 per cent, a history of alcoholism with no psychosis was found. If this is added to the percentage already obtained, a total of 57.44 per cent among the males results and a grand total of 37 per cent. Comparing these figures with those usually given the difference is marked. Paton gives the percentage as between 80 and 90; Diefendorf, 70 to 80.

Of the sixty-eight dementia præcox cases, seventeen, or 25 per cent, showed evidence of heredity. There were forty-three men with 30.23 per cent and twenty-five women with 16 per cent hereditary influences. Twelve out of the seventeen cases showing heredity have relatives who are designated as neurotic, peculiar, queer, defective, or as having the same psychosis. In seven there was no psychosis, only the peculiarity or eccentricity. In one case, there was a history of brain abscess in paternal grandfather, paralysis in paternal grandmother, excitement, with recovery, in maternal grandmother and paternal uncle, the latter two possibly manic depressive cases. Some doubt was cast upon the diagnosis of dementia præcox, however, by the complete disappearance in a few days after admission of all symptoms. Some favored a diagnosis of hysterical insanity, others a remission in a præcox. In two instances it was impossible to determine the form of insanity in the relative, one being the father, the other the maternal uncle of the patient. A maternal uncle of one female patient was twice an inmate of this hospital. The records state he was always considered queer. He remained only five months the first time, his age being forty-five. The second admission occurred six years later and from that time until his death, twenty-four years afterwards, he was confined in the hospital. His death was supposed to be from cerebral hemorrhage (post-mortem examination not being allowed). The records state he showed gradual deterioration with dementia towards the end.

There seems, therefore, to be some basis for the statement that in dementia præcox the hereditary influence in the ancestors is frequently a peculiarity, eccentricity or defect causing the persons to be designated as neurotic or queer. Also that the same psychosis is apt to appear in the relatives.

As in the manic depressive group, so also in dementia præcox,

alcoholism in the family history seems to be quite common. There were eight cases which showed alcoholism only in relatives. If these be added to the cases showing insanity or peculiarity the total percentage of heredity is 36.76. There were four cases giving a family history of insanity which also had alcoholic relatives. Most of the alcoholic taint came through the father.

All those cases in which the psychosis or trouble was some form of alcoholism have been placed in the alcoholic insanity group. Thus, chronic alcoholism, alcoholic hallucinosis, alcoholic paranoia and delirium tremens are grouped together.

There were fifty-two cases, forty-six men, six women. Fifteen of the men, or 32.6 per cent, showed some form of insanity or peculiarity in relatives. None of the women gave any evidence of heredity. There were among the relatives three cases of senile dementia, three of paralysis or apoplexy, two of epilepsy or convulsions, five nervous, hysterical or eccentric, five depressions, one being a suicide. The above calculations leave out of consideration any alcoholism in relatives. Nineteen showed alcoholism only in ancestors, eight alcoholism and insanity. The percentage of alcoholism above added to that of psychosis or peculiarity brings the average up to 73.9 per cent.

There seems to be nothing striking or characteristic about the kind of psychoses in relatives of cases of alcoholic insanity. The percentage of alcoholism in ancestors, however, is large and should serve to emphasize the importance of this etiological factor in mental disease.

General paralysis is commonly thought of as a disease in which heredity is of little importance as an etiological factor. Wiglesworth concluded that paresis has less hereditary causation than other forms of insanity. Diefendorf, on the other hand, gives an heredity of 50 per cent. Paton states that the consensus of opinion " favors the view that the family history indicates the existence of nervous or mental trouble in the ancestors in at least 45 per cent of all cases."

In this series there were only eighteen cases of paresis, thirteen men, five women. The latter showed no hereditary influences—the former, 53.84 per cent. If the female cases are included the total percentage becomes 38.88. The specific instances of insanity or peculiarity in the relatives, however, were rather scat-

tered and perhaps difficult to connect with the paretic cases. For instance there were found alcoholism in the father and paralysis in the maternal aunt in one case, queerness in father and depression in brother in another, senile dementia in maternal uncle in still another, alcoholism in father and brother, insanity in maternal grandfather, insanity in brother and lastly apoplexy in father. When one takes into consideration the mass of evidence supporting the syphilitic etiology of paresis, such hereditary influences as have been found in these cases probably play a minor part.

The epileptic group, twenty-three cases, seventeen men and six women, have eight cases (seven men, one woman) showing hereditary influences in the men, 41.17 per cent; in the women, 16.66 per cent, a total of 34.78 per cent.

Among the psychoses or peculiarities of the relatives there were five insane, one maternal grandmother, two maternal grandfathers, two mothers, form of psychosis unknown, one insane brother, a well-marked catatonic præcox, three cases of paralysis—two in fathers and one in mother—one alcoholic dementia in father and one extremely irritable, alcoholic mother. In one case there was a sister diagnosed as arrested development. In two others, there was alcohol in father and mother alone, bringing the total percentage of heredity up to 43.47. Six cases showed some alcoholic relatives, four of these being accompanied by a history of some psychosis or peculiarity.

Six cases of narcotic inebriety, morphinism, all males, gave a high percentage of heredity. Every one of these showed some peculiarity in relatives, either psychoses, alcohol or drug habit. Four, or 66.66 per cent, had relatives with some form of mental disease. One had a maternal aunt and a sister in the institution, both recovering, the form of psychosis in the aunt unknown, that of sister being manic depressive—depressed phase. The father of another was a hemiplegiac and the maternal aunt insane, form unknown. In a third case there was apoplexy in the father, the mother nervous, maternal uncle a suicide, a brother paralyzed and a morphine habitué, the sister nervous. The fourth case showed apoplexy in maternal grandfather and paternal uncle, the father and mother being nervous. Four cases showed also an alcoholic and morphine history in relatives, that being the sole peculiarity in two cases.

The nine imbeciles likewise gave a high percentage of hereditary taint. There were six men and three women, the latter giving negative family histories. Four of the men, or 66.66 per cent, showed actual psychosis or peculiarity. In one the father was markedly eccentric. A second, the maternal grandfather was insane, form unknown. A third showed senile dementia in father, neurotic mother. A fourth, a half-brother was a deaf mute and a sister neurotic. Besides these, two more gave evidence of alcoholism, one in both parents, the other in father only. The total percentage showing psychoses or peculiarities was, therefore, 44.44 per cent, or if those are included which gave an alcoholic family history only, 66.66 per cent.

Under the heading, "Other Psychoses," a number of conditions are grouped, which have not given such a large percentage of heredity, or of which there are only a few cases. These are paranoid condition, senile dementia, arterio-sclerosis, constitutional inferiority, hysterical insanity and unclassified—a total of one hundred and ten cases, fifty-one men and fifty-nine women. Three of the men, cases of constitutional inferiority, showed psychoses or peculiarities in relatives. One, diagnosed as hereditary cerebellar ataxia, gave evidence of the same disease in mother and brother. A second had an alcoholic paternal grandfather and father, and a maternal aunt who had a psychosis from which she recovered. A third had a neurotic father and paternal uncle, and an insane maternal uncle, form unknown.

Eight of the women showed heredity. One, a case of delirium, had a sister an apoplectic. A case of hysterical insanity had a mother insane, the psychosis being a recurrent type. The father and sister of a constitutional inferiority with hysterical complexes were insane, form unknown. A senile dement had an insane sister, form unknown. An arterio-sclerotic, with hemiplegia, showed mother and paternal uncle insane, form unknown. A case of involutional insanity had a brother and a sister insane, with recovery. Two paranoid conditions showed heredity, one had two præcox brothers and a feeble-minded brother, the other a sister having a recurrent form of insanity.

Returning to a general consideration of the findings, one is led to conclude from the present series of cases that the percentage of hereditary influences is much lower than that usually given.

MANIC-DEPRESSIVE GROUP.

Name.	P. Gr-Fa.	P. Gr-Mo.	M. Gr-Fa.	M. Gr-Mo.	Fath
Male—					
A. C.				In. fol. c. b.	
A. J.				Stroke.	
G. S.					
C. V. C.			Apoplexy.		Al. Pa
P. P. W.					
E. B.					
C. C. S.					Dep. S
L. J. D.					Paraly
F. G.					
M. H.	Insane.				
H. H.					Alcoh
F. B.			Ins. Sui.		Alcoh
E. B. L.					Insane
N. M.					
R. P.					Neuro
T. C.					
T. P.					Insane
H. M.					M. D.
W. E. C.					
Female—					
M. S.		Insane.			
I. S.					Rec. I
A. H.	S. D.	Insane.			Alcoh
A. L.					Alcoh
M. A.					Insan
A. N.				Insane.	
J. M.	S. D.	Relig. Ins.			Alcoh
K. P.					
K. K.					
L. V.					
Alcoholism only (all male cases):					
J. A.					Alcoh
J. M.					Mod.
H. R.					Alcoh
J. D.					Alcoh
J. R.					Alcoh
G. S.					Alcoh
H. B.					Alcoh
A. K.					Alcoh
DEMENTIA PRÆCOX.					
Male—					
C. J.	Peculiar.				M. D.
M. G.					Alcoh
G. E.					
P. H.	Br. Abscess.	Paralysis.		Insane.	
P. O.					
N. E.					Pecu
J. O.					Alcoh
M. K.		Stroke.		Insane.	
C. J.	Alcoholic.				Alcoh
J. R.					Al. H
C. B.					
J. DeF.					
F. S.					Defe
A. W.	Insane.				Ecce
Female—					
J. W.					Insa
A. B.			Insane.		
A. LaR.					
E. A.					D. P.
Alcoholism in relatives only (all male cases):					
H. B.					Alco
J. D.					Alco
A. S.					Alco
J. K.					Alco
F. J.					Alco
S. R.					Alco
U. P.					Alco
I. F.					Alco
ALCOHOLIC INSANITY.					
G. G.					
J. MacM.					Alco
M. L.					
F. R.					
P. D.					
A. T.					
W. F.	Alcoholic.		Alcoholic.		Alco
S. G.	Demented.				Alco
C. V.					Mel
C. D.					

MANIC-DEPRESSIVE GROUP.

her.	Pat. Uncle.	Pat. Aunt.	Mat. Uncle.	Mat. Aunt.	Brother.	Sister.
3. D.						M. D.
ui.					2 Alcoholic.	
exy.		Insane.	M. D.			
us.						
	2 Paral.					
	2 Insane.				M. D.	
	Br. Ab. Sui.					
			Insane.			
					Insane.	
tic.					Peculiar.	Peculiar.
					Defective.	
		Insane.				
					Ins. Fb. Md.	Ins. Sui.
					Rec. Ins.	
						Insane.
Nerv.						Rec. Ins.
nt.					Epilepsy.	Nervous.
				Insane.		
				Insane.	D. P.	

DEMENTIA PRÆCOX.

			Insane.			
Pec.						
	Insane.					
c.						
ar.						
ar.						Queer.
ic.						
is.	Alcoholic.					
					D. P.	
					D. P.	
					Defective.	Defective.
	Insane.					
		Defective.	Defective.			
				Insane.		
	Alcoholic.				2 Alcoholic.	
lic.						
					Alcoholic.	

ALCOHOLIC INSANITY.

					Insane.	
	Insane.					
			Eccentric.			
is.						
			Epileptic.		Alcoholic.	
			Convulsions.			
is.			Sui. Ins.	Insane.		
ric.			Alcoholic.			

ALCOHOLIC INSANITY—Continued.

Name.	P. Gr-Fa.	P. Gr-Mo.	M. Gr-Fa.	M. Gr-Mo.	Fath
J. H.					Al. Par
A. C.		Apoplexy.	Sen. Dem.	Nervous.	
J. H.					Alcohol
L. C.					
Alcoholism only:					
T. B.					Alcoho
J. MacM.					Alcoho
T. R.					Alcoho
C. S.					Alcoho
L. U.					Alcoho
F. C.	Alcoholic.				
T. MacC.					
I. H.					Alcoho
J. K.					Alcoho
F. L.					Alcoho
T. A.					Alcoho
N. G.					Alcoho
T. P.					Alcoho
W. F.					Alcoho
T. L. C.					Alcoho
T. B.					Alcoho
S. P.					Alcoho
T. K.					
N. N. H.					Alcoho
GENERAL PARESIS.					
J. C.					Alcoho
H. S.					Queer.
H. M.					
J. D.			Insane.		
T. C.					
E. B.					Apople
T. P.					Alcoho
EPILEPSY.					
W. K.				Insane.	
S. B.					Al. De
D. W.					
C. H.					Paraly
D. C.					Alcoho
R. E.			Insane.		
A. L.			Insane.		
C. W.					Alcoho
W. C.					
A. Van c. F.					Paraly
NARCOTIC INEBRIETY.					
W. B.					Mod. A
H. C.					Hemip
U. S.					Al. Ap
G. S.			Apoplexy.		Nervo
A. T.					Alcoh
J. L.					
IMBECILITY.					
F. S.					Eccen
W. B.			Insane.		
F. P.					S. D.
G. H.					Alcoh
C. H.					Alcoh
OTHER PSYCHOSES.					
Constitutional Inferiority:					
F. M.					
W. C.					Neuro
A. M.	Alcoholic.				Alcoh
Paranoid Condition:					
M. L.					
R. N.					
Involutional Psychosis. Arterio-sclerosis:					
N. W.					
Arterio-sclerosis. Hemiplegia:					
E. A.					
Senile Dementia:					
M. C.					
Hysteria:					
A. S.					Insan
M. P.					
Delirium:					
M. Z.					

ALCOHOLIC INSANITY—Continued.

...ler.	Pat. Uncle.	Pat. Aunt.	Mat. Uncle.	Mat. Aunt.	Brother.	Sister.
.....	.....	.....	.....	.....	.....	Insane.
...ea.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	Insane.
...ep.	.....	.....	.....	.....	Ins. Dep.	Ins. Dep.
.....	Alcoholic.	.....	.....	.....	Alcoholic.	.....
...lc.	.....	.....	.....	.....	.....	.....
.....	Alcoholic.	.....	.....	.....	.....	.....
.....	Alcoholic.	.....	.....	.....	Alcoholic.	.....
.....	Alcoholic.	.....	.....	.....	.....	.....
.....	Alcoholic.	.....	.....	.....	.....	.....
.....	Alcoholic.	.....	.....	.....	Alcoholic.	.....
.....	.....	.....	.....	.....	.....	.....
.....	Alc. Several.	.....	.....	.....	Alc. Sev.	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	Mod. Alc.	.....
.....	.....	.....	Mod. Alc.	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	Alcoholic.	.....
...tic.	.....	.....	.....	.....	3 Alcoholic.	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	2 Alcoholic.	.....

GENERAL PARESIS.

.....	.....	.....	.....	Paralysis.	.....	.....
.....	.....	.....	.....	.....	Ins. Dep.	.....
.....	.....	.....	Sen. Dem.	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	Insane.	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	Alcoholic.	.....

EPILEPSY.

.....	.....	.....	.....	.....	D. P.	.....
...t.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
...leg.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
.....	Alcoholic.	Alcoholic.	Alcoholic.	Alcoholic.	Alcoholic.	.....
.....	.....	.....	.....	.....	.....	.....
...lic.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	Arr. Dev.

NARCOTIC INEBRIETY.

.....	Alcoholic.	Ins. Recov.	.....	.....	.....	M. D.
.....	.....	.....	.....	Insane.	.....	.....
...is.	.....	.....	Suicide.	.....	Par. Morph.	Nervous.
...is.	Apoplexy.	.....	.....	.....	Opium.	.....
.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	Al. Morph.

IMBECILITY.

.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....
...tic.	.....	.....	.....	.....	Deaf Mute.	Neurotic.
...olic.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....

OTHER PSYCHOSES.

.....	.....	.....	.....	.....	Same.	.....
.....	Peculiar.	.....	Insane.	.....	.....	.....
.....	.....	.....	.....	Ins. Recov.	.....	.....
.....	.....	.....	.....	.....	2 D. Pr. I.	F. Mnd.
.....	.....	.....	.....	.....	.....	Re. Ins.
.....	.....	.....	.....	.....	Insane.	Ins. Recov.
...e.	Insane.	.....	.....	.....	.....	Insane.
.....	.....	.....	.....	.....	.....	Insane.
.....	.....	.....	.....	.....	.....	.....
...ecov.	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	Apoplexy.

The attention has already been directed to the much lower rate found, especially in manic depressive and dementia præcox. A certain proportion of the discrepancy can doubtless be accounted for by the failure to discover the existing hereditary taint. The difference is so great, however, as to make one think that perhaps too much stress has been put upon heredity.

Besides manic depressive and dementia præcox, several other groups showed considerable hereditary influence. In alcoholic insanity the large percentage of alcoholic family history is the striking feature.

General paresis apparently showed a large percentage, but the influence of heredity is probably not as great as the figures might imply.

Epilepsy gave a heredity of both psychoses and alcoholism.

Psychoses, peculiarities and habits among relatives were common in narcotic inebriety.

Imbecility likewise showed considerable hereditary influence.

The frequency of alcoholic family history in certain psychoses is quite marked. As might be expected, the largest percentage of alcoholic heredity was shown in alcoholic insanity. In the manic depressive group and dementia præcox also, alcoholism in the relatives was far from being unusual.

While it may not be possible from the present evidence to conclude with absolute certainty as to the kind of psychosis in the relatives of manic depressive and dementia præcox cases, yet a few general statements are possible.

The prevalence of psychoses in the manic depressive group as compared with the percentage of the peculiar or eccentric type in dementia præcox is noticeable. In the manic depressive cases, although there is frequently doubt as to the character of the psychosis, the evidence seems strong as to the existence of some kind of a psychosis. On the other hand, in dementia præcox the relative is often described as queer, eccentric, or by some similar term.

The evidence seems to be against the theory as an absolute rule that cases of manic depressive and dementia præcox do not occur in the same family. At least one well-marked manic depressive woman was shown to have an undoubted dementia præcox brother and there were several other possibly similar cases, the diagnosis, however, not being so certain.

On the other hand, there are a number of instances of the same psychosis in the relatives both in dementia præcox and manic depressive.

HYSTERICAL INSANITY, WITH REPORT OF CASES.

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Hysteria is a mental disease, one of the so-called functional disorders. It has no ascertained pathology. People rarely die from hysteria alone, and, if they do, nothing in a pathological sense can be found to account for the conditions present in life. Yet it presents many serious symptoms, definite physical signs, and symptom complexes which very much simulate definite organic conditions—conditions which show more or less constant pathological changes in certain organs as, for instance, hemorrhage and softening in hemiplegia, sclerosis in tabes, spastic paraplegia, etc. Post-mortem examination confirms, in a positive way, organic disease, and only in a negative and unsatisfactory way, hysterical or functional conditions.

These severe symptoms, anæsthesia, paralysis, contractures, blindness, and the various somatic disturbances are, however, present and real, even if no histologic change can be found to account for them. They are not simulated. They differ from organic lesions in that they can be cured. They are often very suddenly cured, but not by drugs, diet, proper hygiene, etc., but by some mental influence, some sudden emotional shock, by suggestion, hypnotism, an anæsthetic, or by some means that makes a profound impression upon the mind of the patient.

Hysteria is very frequently seen by the general practitioner, but often is not given the consideration it deserves. The neurologist sees much of it, and gives much time and attention to it, and considers it a very important subject. The alienist, on the other hand, to whom the disease really belongs, has paid but little attention to it. He has had frequent opportunities to see it and to study it. He has control of his patient and can keep him or her under constant and close observation, yet some textbooks on mental diseases do not mention the subject, others refer to it occasionally as occurring with or as a complication of some of the well-known psychoses, and a few give it the importance of

a separate heading and devote a few pages or a chapter to its consideration.

The subject of hysterical insanity and hysteria as occurring in other psychoses has not been given the attention it deserves in publications of this kind. Neither is there a clear and definite idea of its symptom complex as a distinct form of insanity.

Very few will deny entirely that hysterical insanity does not exist, but in many hospital reports it is not mentioned as a separate disease. Hysterical manifestations are sometimes mentioned in reports of cases of other psychoses, as in dementia præcox, manic-depressive insanity, and in regard to epilepsy. That there is a certain close connection between dementia præcox and hysteria has been shown. In one of the cases reported in this paper the case at first was thought to be dementia præcox. Hysteria occurs in certain types of individuals. Dementia præcox occurs in certain types; this also may be said in regard to other psychoses. Different persons, under the same circumstances, react in different ways. What may cause a psychosis in one type of an individual has no such an effect upon others. A study of the type of individual is, therefore, very useful and is really a necessary part of the history of the case, and must be given great consideration in making a diagnosis.

Psychological studies, therefore, should be given great attention by alienists, and comparisons made between normal persons, the eccentric, the semi-insane, defectives, and the insane. Hysteria has been studied in this way extensively, so that persons of a certain type and with certain characteristics are spoken of as hysterical, and these characteristics as the common stigmata.

Psychogenic factors are now being taken into consideration as etiological factors in the causation of mental diseases, and by means of psycho-analysis and comparative studies facts are being discovered which are of the utmost value, and which will give some valuable indications in regard to prophylaxis and treatment.

Hysterical insanity is admitted by most authorities, but the conception of it seems to differ much with individuals. No English books that I have seen give a very clear idea of the different forms of the disorder. Some speak of hysterical mania, hysterical melancholia, hysterical stupor, hysterical paranoia, etc. Others deny the existence of such conditions and classify these

conditions as mania, melancholia, paranoia, etc., with hysterical complications. Woodman, after studying a large number of case histories, reports twenty-four cases, which he classifies into seven divisions. Raecke makes three forms:

1. A form, with excitement and stupor, in which there may be delirium and somnambulism.

2. A form, with depression, which includes attacks of distress, frightened delirium, stupor, mental clouding, with occasional paranoid episodes and ideas of persecution on a permanent basis of melancholia or hypochondria.

3. A paranoic type of compound hysterical insanity which is built up mainly out of accumulated delirium, imagined episodes, somnambulistic "twilight" conditions, and eventually the development of a dual personality.

Janet regards hysteria as a mental disease and defines it as a form of mental depression characterized by the retraction of the field of personal consciousness and a tendency to the disassociation and emancipation of the systems of ideas and functions that constitute personality. Its etiology is found in the stigmata, that is, hysteria occurs in certain types of individuals who, when examined, present certain peculiarities which are designated as the stigmata. Upon this basis following some emotional shock (which acts as the direct cause), as a trauma, an intoxication, an illness, a death, a love affair, a fire, or other things that may cause pain, regret, worry, grief, anxiety, overwork, disappointment, and other emotional conditions, we have suddenly or gradually some manifestation of a hysterical condition, such as a paralysis, a contracture, a convulsion, or some sensory, visceral or special sense disturbance, or some distinct mental upset; the person becomes insane. He may be excited, delirious, maniacal, or depressed; inactive, dull, stuporous, unconscious; or confused with clouding of consciousness, or he may develop ideas of persecution (paranoic delusions). There may be a complete change in his personality, he becomes like another person; then, after a shorter or longer period of time (suddenly or gradually), there is recovery, and with this, no or imperfect remembrance of the past condition—a more or less complete amnesic period.

The stigmata are really the main or the most constant symptoms. To some or all of these stigmata are added many other symptoms,

often apparently widely different, but in reality all due to the same cause, "a depression or exhaustion of the higher mental functions, with retraction of the field of personal consciousness and disassociation of ideas and functions." Such a hemiplegia would not show a brain, cord, nerve, or muscle change; an anæsthesia, no nerve disease; blindness, deafness, aphasia, etc., no organic lesions. Also various hysterical visceral conditions, as aphonia, vomiting, hiccough, polyuria, uterine and ovarian conditions, etc., which closely resemble organic diseases would show no pathological changes. This comparison does not apply as positively with regard to hysterical psychic disorders that resemble mental diseases, because so little is known as regards pathological changes in the brain in regard to most mental diseases.

When all these widely separated symptoms are considered they can be seen to be related, and can be explained by the definition "mental depression with retraction of the field of personal consciousness and disassociation and emancipation of the system of ideas and functions that constitute personality."

The principal stigmata are divided by Janet into two classes: 1st. Proper stigmata which belong exclusively to hysteria. 2d, The common stigmata which may also occur in other neuropathic conditions. Under proper stigmata, which he considers the essential stigmata, are suggestions and conditions with similar properties and closely allied to suggestion, as absent-mindedness, subconsciousness, equivalence, and transfers.

The common stigmata consist of a peculiar mental make up (a neuropathic constitution), persons with deficient will power, loss of self-control, heightened self-consciousness, a tendency to exaggeration, with morbid craving for sympathy; persons who are selfish, self-absorbed, often unhappy, discontented, fault-finding, complaining; who are entirely wrapped up in themselves; who are unable to long concentrate their attention upon things outside of themselves; who have periods of reverie, and consequently show imperfect memory for things not directly connected with themselves.

The proper stigmata will be considered with the psychic symptoms. The symptoms of the disease are very numerous and comprise a large number of widely different conditions. They are classified as visceral disturbances, sensory and motor disorders,

and psychic disorders. All are really psychic disorders. We desire to consider only the psychic disorders and one of the motor disturbances, convulsions.

Among the essential stigmata, all of which Janet summarizes "as a retraction of the field of consciousness," are

Suggestibility, where, unconsciously, the patient takes up ideas and develops these ideas to the fullest extent, associating the different parts subconsciously and acting upon them.

Absent-mindedness. Their attention is limited. They are able to think of and do only one thing at a time, therefore, many things occurring about them are not noticed or remembered, although they have apparently seen, heard, or otherwise noticed them.

Transfers are changes from one part to a corresponding part of a similar condition.

Equivalence is the replacement of one condition by a different one.

Hypnosis is closely related to suggestion, and only those who show the essential features of suggestibility can be hypnotized. Hypnosis, then, can only be induced in a certain number of persons, and those persons have been or are liable, at some time, to show hysterical symptoms, if some exciting cause presents itself (trauma, emotional shock, etc.). Hypnotism, therefore, only occurs in hysteria, and hypnotism is only an artificially induced somnambulism.

Somnambulism is one of the most characteristic symptoms of hysteria and occurs only in hysteria, according to Janet. Somnambulisms are states occurring in hysterical persons and lasting a variable length of time, in which there is a sudden or gradual change from the conscious state to that of sleep, or a dream-like state, in which the patient may assume many peculiar attitudes and perform numerous simple or complicated acts in which all the senses may be brought into play, or may lie dormant. He acts out in reality ideas and scenes which exist at the time in his mind. He moves, talks, looks, listens, and does things in a certain regular order. During this time they are oblivious to everything outside of their dreams, and all they know or feel are things connected only with their dream. They are, in reality, another personality. After a time the other or normal personality sud-

denly or gradually comes to the front again; they become conscious and resume their life where it was broken off at the beginning of the somnambulism. For the period of the somnambulism there is a complete loss of memory for all things that have happened—a complete amnesia.

A somnambulism is then a complete disassociation of consciousness, with an exaggerated and independent development of an emancipated idea or ideas, and associated with an amnesia. Somnambulisms are simple or complex, monoideic or polyideic—monoideic when one idea is disassociated, polyideic when a system of ideas is disassociated.

Fuges are somnambulistic states in which a predominant idea is present, but the mind also grasps other things, so that these persons may start out with a definite purpose in their mind; they are able to travel, to take long journeys, which may last for days, during which time they meet people, ride on trains, work, secure food, etc. During this time the person has other characteristics from his former self. He is really another person for the time being in everything, except that he has the same body.

Double or multiple personalities are more protracted and complicated somnambulisms, in which the same person, at different times, leads two or more dissimilar lives, independent of each other. In complete double existence, where two periods alternate during a lifetime and do not know each other at all, they are called, by Janet, reciprocal somnambulisms. These cases are very rare. In incomplete existence, when one personality gradually overshadows and dominates the other personality, he calls it a dominating somnambulism. Then there are cases which combine the reciprocal and dominating somnambulism and have more than two personalities; these are multiple personalities.

The constant and characteristic features of all somnambulisms are amnesias. These may cover the time of the somnambulism or may extend back and take away all previous memories. They may last for a few minutes or for days, months, or years; they may be complete or incomplete.

The object of this paper is to report several cases showing amnesia. Some have been diagnosed as hysterical insanity, others as other conditions, and while we all may not agree upon certain

cases, it is believed that hysteria has played a definite and prominent part in all these cases.

These cases are taken from the regular male admissions to the New Jersey State Hospital from November, 1907, to June, 1909.

Of 105 cases (of all kinds) personally received and examined (representing most of the time every other male admission, part of the time every third male admission), ten are abstracted and reported here; two are cases of Drs. Sandy and Watson.

Case No. I.—I. C., a West Indian, age 27, hat-rack man in hotel.

Family History.—Parents living, father neurotic, mother neurotic, an invalid since coming to the United States twenty-five years ago. Both maternal grandparents died of tuberculosis. Paternal grandparents were French Jews and healthy. A maternal uncle of patient in an insane hospital for many years. He is said "to have fits, followed by violent headaches; following which he would take knives and forks and wander to the sea." An uncle of patient's mother was insane, but not in a hospital. Two brothers and three sisters living; eight children dead, "all died before one year of age, one of croup, one of convulsions, twins at birth, one of teething, a twin sister of patient at birth, one premature at six months." An older brother is nervous and irritable, and has a child who has been in a children's hospital for "nervousness." Others are well.

Personal History.—Pregnancy and birth normal; child was delicate until two years of age. It was stated that he had convulsions until two years of age. His mother later denied that he ever had convulsions. Breast-raised, dentition normal. After the age of two he became healthy and not different in any way from other children. He was light hearted, friendly, cheerful, fond of music, had no bad habits, began school at six years of age, made good progress. When eleven years of age had some scalp disease; "his head was a mass of sores and his hair came out," and was out of school some time on account of this; returned and continued in school until fourteen or fifteen. Got along well in school and with others. After leaving school worked in a brick yard for three years; considered a good, reliable, efficient worker. Then in a grocery store for two or three years as a general utility man, then as an hotel waiter, and later as a bartender from October, 1903, to August, 1904. Was married in August, 1904; marriage considered very satisfactory, lived happily with wife, had one child, born October, 1905, now living and well. Following marriage worked in a hotel one month, then in a grocery store from October, 1904, to February, 1905. From February, 1905, until January 8, 1907, worked as a hat-rack man in a hotel; had a good position, was considered an efficient worker, kept house, and was living happily until June, 1907. Patient admits occasionally drinking when in company. Never a constant drinker; says that he is easily affected by alcohol.

Etiology and Onset.—In June, 1907, his wife became sick. He worked hard all summer, and with his hard work, worry and care of his wife he became tired out, run down and in poor health. In August he made the remark that he thought his mind was going to give way. In September took a trip for his wife's health. He returned worse than he was before. He was dull, depressed, and melancholy instead of being happy and cheerful as he used to be. His wife was benefited by the trip, but a few days after their return she again became sick. He returned to his work, although not feeling well. He became more depressed when his wife again became sick. He continued worried and depressed until about the middle of November, when he attempted suicide by gas. He closed up his room, attached a rubber hose to the gas and put the other end in his mouth. He was discovered nearly dead, but was revived. Before this a revolver and a razor were taken from him. He was acting in a suspicious manner, but made no attempt at suicide with these instruments. About this time he made the remark that "he thought the world was against him." His wife said that before this attempt at suicide he would get out of bed at night, go to the radiator, listen and look down it; he would call and awake her and say: "Look at them, Hatty, don't you see them; don't you see them? They are coming after me." He was taken to his father's house in Philadelphia. He recovered from the effects of gas, and improved otherwise to some extent, but was still depressed and despondent. He told his father that he would make a man of himself and not attempt suicide again. Returned to his own home alone on Thanksgiving night. Work was dull and he was idle two weeks, then returned to work; here he acted very strangely. He told the people at the hotel and at his home that money had been stolen from the hotel, that people talked about him and accused him, and that detectives followed him. He was constantly apprehensive and afraid of arrest. He told that they gave him $50 to buy stamps with, to see if he was honest. He was suspicious of people about the hotel, and thought that they were trying to catch him in some dishonest act. He told of a man dying after he had taken him a glass of milk, and thought that he would be accused of causing his death. He continued at work until January 8, 1908, but was apprehensive and suspicious. He had false sight and hearing when home at night. He made the remark that if he saw the patrol coming after him he would drop dead—and talked of it being better to be dead than to be crazy. On January 8, 1908, returned from work about 2.30 p. m. He came in the house and asked the person there for a piece of paper to use for shaving purposes. He then left and went to shave—the next known of was hearing a scuffle. Later, people broke in and found the wife dead with her throat cut, and the patient with his throat cut leaning against the wall. One-half of his face was lathered and the other half shaved. The baby was lying on the floor covered with blood from the mother; apparently no attempt to injure the baby had been made. He was taken to a hospital.

Dr. W. Blair Stewart kindly furnishes the following: On admission

I found the whole throat laid open and the larynx exposed. He was highly excited and very weak, but surgical measures revived him and ultimately resulted in the parts healing. He had to be kept in a straight-jacket all of the time, as he endeavored to tear his throat open again, and on one occasion threatened violence to his female nurse. His case at that time was one of acute melancholia, with a tendency to dementia. He left the hospital February 7, 1908. His sister states "that while in the hospital he did not realize or talk about what had taken place. He thought that his wife was living and asked to see her and the child. He mistook a nurse for his wife. He tried to strangle a nurse several times and assaulted the physician with a chair. He talked while in the hospital." From the hospital he was taken to jail—the sheriff gives the following account of him while there (February 7, 1908, to March 31, 1908): "He made several attempts to pull the wound apart, tried to drown himself in the bathtub; he would pile up all of the chairs in the place; at times he was irritable and violent, threw chairs at attendants; since being in jail has not spoken a word. He is continually on the move, wandering around in an aimless manner—only once in awhile sitting down. He frequently moves his hands about, works his lips and murmurs, sometimes as though trying to talk, but no word comes from him. Sleep is not good. Has not appeared to be afraid or apprehensive. Indifferent to his surroundings and to others. Does not laugh or cry; not untidy." His sister states "that since being in jail he has apparently not known any of his relatives. He has not spoken to them or even noticed them." Was brought here March 31, 1908. Came without any trouble.

Upon Admission.—Wandered aimlessly around the room, did not look at physicians or other people, did not notice anything going on about him, finally sat down and began to move his hands about. Seemed to comprehend; was asked questions, but gave no answers. Was led to ward. On the ward was quiet, obedient; gradually learned to follow ward routine. Would not talk for several days—makes a peculiar noise in his throat and with his mouth. Pushes food, both solid and liquid, down his throat with his fingers. He laughs, smiles, and makes faces. Wanders around the ward in an aimless manner, sometimes touching and feeling different objects or persons as he comes to them. Keeps his head down, does not look about. Shows many mannerisms.

Physical Examination.—April 10, 1909. In this he does not co-operate, but makes no resistance; he is very playful, imitates physician, is good natured, seems to understand, and does most things that he is told. Will not talk.

Abstract of Physical Examination: Fairly well built; height, 5 feet 5 inches; weight, 135 pounds. Face, oval; head and face symmetric. Palate, high and narrow (no body defects). Fairly well nourished, skin and mucous membranes healthy, numerous scars—two scars of neck, two scars of left elbow, one on right elbow (suicidal attempts). Temperature, normal.

Smell and Taste: Gives no answers. Plays with bottles. Makes faces in a playful way in regard to taste.

Ears: Pays no attention to watch tick; hears ordinary talking.

Eyes: Expression bright, playfulness, pleasure; nothing abnormal about use or control of eyes and lids; pupils react to light and other tests (no perimeter test at this time).

Cutaneous Sensibility: (No answers.) Apparently feels when touched.

Pain Sense: Anæsthesia—pin pricks all over body paid no attention to. No pain reaction to pin pricks, cold, or heat. Does not draw away or show pain from a burning match.

Sense of Position: Stands and sits when told. No tenderness of nerve trunks. Analgesia of ulnar nerves, anæsthesia of eyeballs.

Vasmotor and trophic disturbances, salivation. Dermatographia, localized perspiration.

Reflexes: Deep, all present and normal.

Superficial: Plantar, gluteal, abdominal, epigastric, react. Conjunctival and scapular absent.

Motor Functions: Good motion of all facial muscles, face expressive, and he makes many grimaces. Muscles of neck that were cut interfering with swallowing, and to a less extent with respiration. Unable to protrude tongue beyond teeth. Has to push food down his throat. All other muscles normal.

Gait: Peculiar. He goes around with his head bent down and his shoulders bent forward, shuffling. Inco-ordination not shown by tests. Balancing power good.

Grip: Weak; he makes but little effort. No fibrillary twitching. Slight tremor of fingers.

Reading, Writing, Speech Test: No co-operation. Organic reflexes normal, no convulsions, sleeps well. When asked if he dreams he laughs, but gives no information. Respiratory, circulatory, and digestive organs negative. Appetite good. Urinary and genital organs negative, except faint trace of albumin in urine.

Mental Examination.—Demeanor: Always quiet, orderly, and obedient, follows ward routine. Shows many mannerisms, makes grimaces, smiles, laughs, and appears to be happy. Not seclusive, wanders around the ward, going from place to place, doing many odd, foolish and amusing things. Decorates his person with paper, rags, broom splints, etc. Shows hallucinatory attitude at times (sight and hearing). Shows echopraxia, imitates movements of physician and others in a playful manner. For a few days after admission he would not talk, but made a peculiar noise in his throat. Later began to talk, and could talk quite distinctly; would not answer questions in a relevant manner or give any account of himself. Made foolish remarks at times. Face very expressive, expression changeable, sometimes that of fear, sometimes that of happiness, pleasure, playfulness, clownishness. Is not untidy, cares for himself.

Stream of Thought.—Sometimes will talk spontaneously or will answer

some questions. At other times will not talk. To-day he appears to be afraid, shows hallucinatory attitude, has a look of fear and horror on his face. What are you afraid of? "Those things on horses, they are after me." How long have they been after you? "Fifty million years." Do you see them? (He points to dark corner of room.) "Look, you can see them." Do they talk to you? "Yes." He fixes his gaze in that direction, and an expression of great fear comes over his face, he makes motions with his hands as though to push them away and says: "Let them alone; go back, go on." Suddenly his facial expression changes, he laughs and smiles, he looks out of the door and says: "See my horse out there; take your hand off that horse, Boswell" (attendant). It is regretted that more and better samples of his talk were not written down, but this was neglected at the time. In answer to questions absolutely nothing can be elicited from him in regard to any events of his past life. When questioned says that he has no wife, no child, no sister, no relatives, "all I have is Boswell and you."

Delusions, Hallucinations, Illusions.—No delusions or illusions can be elicited. Hallucinations of sight and hearing are present, with hallucinatory attitudes. Somatic sense deceptions are present—frequently puts his hand to his throat and makes efforts as though he wanted to pull his throat apart. He sometimes acts as though he had peculiar feelings of some kind in his head. He taps it, beats it, and makes motions indicating that he feels some peculiar sensation in his skull. He will not, or is unable to, explain the sensations.

Delusional Developments (non-paranoid): He may possibly have some delusions in regard to contamination. He frequently brushes his clothes and picks small particles of dirt from his person, but at the same time he does not avoid dirt. He will lie on the floor or crawl under the beds and benches.

Hysterical Complex: There is probably an amnesic period, at least he pretends not to remember anything about his crime, wife, or child. He does not recognize or notice his sister when she visits him; acts toward her as he does to other people. Says he has no baby, wife, or family.

Mental Organization: Orientation and grasp of surroundings. He will give his name. (At first he would not or could not give his name. His name has been told him by attendants.) He knows the name of one of the attendants and the ward doctor. He will not tell where he is, the date, time, the nature of the institution, or other things connected with his stay here.

Memory: Retention, school knowledge, past life, etc., nothing can be elicited. Will not read, write, or repeat speech tests. His speech is peculiar, low, mumbling, and indistinct, as a rule, and hard to understand, but sometimes more clear and distinct, and can be understood. Other notes between April 10 and June 1, 1908, show no change in his condition; mannerisms, playfulness, grimaces, foolish actions, hallucinations, and hallucinatory attitudes continuing; as a rule, happy and contented, but

apathetic in regard to his environment; sometimes talking, at other times refusing to talk; not knowing or refusing to recognize relatives when they visit him, and continuing so until June 5, 1908. Up to this time he was regarded as a case of dementia præcox. Prior to June 5 had been visited by his sister, brother, father, and mother; he acted toward them as he did to strangers. On this date was visited by mother, sister, and for the first time by his baby. The sister gives the following: "He came in the room with the attendant as usual, not noticing anyone. When he was spoken to and the baby mentioned, it produced no effect. He was told by the attendant to look at them; he did so but paid no attention to them. The baby was then held up in front of him and he was asked to remember her. Suddenly there seemed to be some change come over his eyes; he looked intently at the baby; his eyes lit up as though he recognized some one he knew. He took her, embraced and remembered her, and he just shook all over and was very nervous. He then recognized his mother and sister, and then asked where his wife was. (He was told by the attendant that she was sick.) Then he looked about and said: 'Mother, this is not my room.' Noticing the attendant, he asked who he was and what he was doing there. (The attendant said he was a friend of the family.) He then wanted to know where he was. He became excited. The attendant told him he was in a hospital, and had been very sick, and tried to calm him. He acted toward the attendant as he would toward a perfect stranger. Twice during the interview he had to be taken from the room because of his excitement and emotion." When seen by the physician (who did not know of the visit and its results), while making rounds on the ward two hours later, he appeared to be like another person. He came up to the physician, looking and acting entirely different, and asked if he was in charge. Patient stated whom he had seen, and what he had been told by his relatives and the attendant (who told him as little as possible, and nothing about his crime, etc.). Said he could not understand why he was in here, and could not account for being here. He claimed to have no knowledge of anything from January 8 until to-day, when he recognized his baby, mother, and sister.

From the time he saw his baby he has talked and acted in an entirely different manner. He is polite, attentive, takes interest in others and his surroundings; is sociable, agreeable, mingles with others, shows no mannerisms, talks spontaneously, gives relevant answers to questions, talks freely and frankly about his past life up to January 8 and after June 5. He also wrote an account of part of his life, and has written a letter to his wife, whom he thinks is at home sick.

Stream of Thought: "About the end of August I began to feel unwell. I felt haggard, tired, and dreary. My back and shoulders hurt, and I had pains all over me. I worked from 7.30 a. m. until 11.00 p. m. My work is not so hard, but I have much to remember and was on my feet all of the time. When I went home at night I was always very tired and went right to bed. In October I went on a vacation and returned to work

on the 16th. I did not feel better after my vacation, and was tired and had a haggard feeling, and worrying because my wife had not improved on the trip. The trip was really taken for my wife's health. I returned to work and worked up until some time in November. They say that I tried to kill myself with gas, but I do not remember. All I do remember is going to get the gas tube. I do not remember whether I got the tube from the cellar or in the pantry. When I came to myself, they say I talked of money and prayed for something to eat, and whistled. When I woke up in the morning I did not see my wife and baby. I was later taken to my mother's home in Philadelphia. I did not feel natural during this time. I remember returning to Atlantic City alone on Thanksgiving Day. I was around the house until December 26, when I began to work. Others told me that I talked and acted funny." (Denies all recollection of saying and doing queer things, or seeing or hearing voices, or being suspicious or taking poison of any kind, or thoughts of suicide, or the reason for getting the gas tube.) "I remember working from then until January 8, and of leaving the hotel for lunch on that date. I remember leaving the hat rack, going out in the usual way. I am not sure whether I rung on the time clock or not. I am not sure whether some one walked home with me or not; but that is the last I remember until June 5, 1908, when I saw a gentleman by the name of Boswell, an attendant here; also my baby, mother, and sister." In a postscript, he says: "While in Philadelphia, after the time they said I tried to kill myself, one day my mother went to the store at the corner of the street, and I was sitting in the kitchen of my mother's house and was reading the morning paper, and I found myself in the bath room, and I could not tell how I came to get in the same. I did not tell my mother because I knew it would worry her. I was told by my wife that I bounded out of bed, and that I talked of funny things and ran to the window. This I have no recollection of, and as far as I can remember, I felt all right. What I mean to say, I felt all right after I came back from my vacation; in fact, from the summer of 1907. I began to feel my strength leave me, and I can say to-day I feel like myself once more. I know for a fact that I feel better this day than I did last year in August." No delusions, hallucinations, or insane ideas of any kind can now be elicited. Complains only of his throat, says that he has a metallic taste in his mouth; thinks he has a tube in his throat.

Amnesic Period.—January 8 to June 5, 1908. Mental organization is very good, well oriented, good grasp of his surroundings, as far as he has been told. Data of personal identification and history of past life very fully and correctly given. Memory and retention good. Reads and writes correctly. Has good insight and good judgment.

June 23, 1908. Was told to-day that he cut his own throat. This produced no effect upon him as he had seen and felt the scars, and its cause had been intimated to him. Up until now he believed his wife sick and at home. He has written and asked about her, and been impatient because

he has not seen or heard from her. Was told to-day that she was dead. This was a great emotional shock to him. He cried bitterly, showed much real sorrow, and was much depressed and upset by the news. Continued depressed for a week, but gradually became more active again, talking, taking interest in things, etc.

July 18, 1908. Has complained of pain in his head and vertigo for the past two days. No anæsthetic areas present.

July 23, 1908. Was told to-day that he killed his wife—showed real sorrow and self-condemnation. Became again inactive, thoughtful, depressed.

August 1, 1908. Not as bright and cheerful as formerly. He complains of not feeling well at times. He will talk about his crime, but claims he has no knowledge of it, and that he is innocent of any intentions of wrong doing, and that if he did it he was insane and did not know what he was doing. Protests against being called a murderer by other patients.

September 1, 1908. Makes physician see him and talk to him each time he passes through the ward. Complains at times of headaches and vertigo, which is relieved by bromid or migraine tablets.

December 1, 1908. Still solicitous about his health; complains that he is nervous, cannot sleep, of indefinite aches and pains, of muscular twitching, and of certain sensations in his throat. Still half believes that he has a tube in his throat; says certain muscles twitch, offers to show them, but as yet has not been able to do so. He wants each symptom he has explained, and a reason given for it. If he is given medicine and assured it will relieve him, he is satisfied for a time; but if at all neglected he again complains. He is always looking for attention and constantly desiring new privileges. Enjoys the dances, chapel services, entertainments, and diversions of any kind.

January 1, 1909. Transferred to another hall, because of his numerous complaints of being annoyed.

February 1, 1909. After being transferred was thankful for the change, contented for awhile, and more happy.

March 1, 1909. Good physical health. Mentally, there is considerable emotional variation. He at times becomes depressed, discontented, and fault finding. He claims attendants do not treat him right, that patients call him names, etc. Does not think he is treated as he should be. At these times he worries, cries, is very unhappy, sends for physician; later says if he had not had medical assistance it would have been all over with him (meaning suicide). He is suspicious and open to suggestion. He says that he heard attendants say, in speaking of him, that the doctors have him under the influence of dope all the time. Several times he has mentioned this to the physician, and has been assured that it was not so, but he seems unable to get the idea out of his head, as he constantly refers to it. He complains of somatic disturbances, his eyes being blurred, of nervousness, twitching, insomnia, etc., and asks for medicine. Puts himself in the way of the physician and makes him stop and talk each time he passes through the hall.

March 9, 1909. Transferred to another hall because of not being able to get along there, makes constant complaints.

April 16, 1909. Complains of various somatic sensations, some paresthesia in limbs; no areas of anæsthesia, contracted visual fields are present. Left eye red under 35, blue under 55, white under 55. Right eye red and blue, extending as far as 60 in the widest place; white within 45.

Mentally, he remains clear, well orientated, not demented, without delusions, hallucinations, etc., and with good insight and judgment.

Case No. II.—This case has not been as yet officially diagnosed. I offer it, however, as showing the Ganser symptom complex. The question of simulation has been seriously considered by the committing physicians, and also here. Personally, I consider it a case of hysterical insanity.

J. H., born in New Jersey, age 45, married, sanitary presser. Admitted December 14, 1908.

Anamnesis.—F. H., father, eccentric. A cousin (S. G. B.) insane and a patient here. Old records are very incomplete, but state "First admission March 7, 1895, age 45, common school education, milliner, single, temperate. First attack: Has been deranged six months or longer, not marked until the past three months. Etiology: Worry over an adopted niece, who had an illegitimate child. No heredity, parents temperate, but are second cousins. Appetite fair. Sleeps only under a hypnotic, menses only once in three months. Delusions: Fancies that familiar objects are not really what they are, all things are white, hears strange noises. The depression is not profound but sufficient to make her very unhappy. She is not social and prefers to be alone. General health deranged, indigestion, insomnia. Does not worry about her detention. Discharged, improved, June 1, 1895."

Patient is said to have been intelligent, and to have received a good education. Disposition, melancholy and reserved. A great smoker of cigarettes, a hard drinker at times, and always very nervous. Four years ago he disappeared for six weeks.

Physician's Certificate.—The onset of the present attack was gradual. Patient's physical health impaired. Has Potter's asthma; cleanly. On August 25 he shot and killed his neighbor, Edward Ford. He had frequently threatened suicide before that time, and had made an assault on his wife because he believed she was unfaithful. Supposed cause of insanity: The predisposing factors were an eccentric father and a mother who died of tuberculosis. The exciting cause was a stroke four years ago and the excessive use of alcohol. A maternal cousin (S. G. B.) was insane and was an inmate of the New Jersey State Hospital at Trenton. Has used alcohol to excess for the past four years until his arrest last August. Has also been an inveterate cigarette smoker. The patient said he was an inventor of a patent seat attachment which was worth millions of dollars, and that "they" were trying to get his secret away from him. "They" had sneaks watching him, "they" had put poison in his meat, and there was a stench in the water so that he could not drink it. He

heard them whispering about him, and saw them making signs. He knew they were watching him because he had dropped pieces of paper, which they would pick up and examine very closely, expecting to find a plan of his invention. They had also taken pieces of paper out of his pocket and were working day and night to get possession of his secret; he would give me no names, but said that they were very prominent and influential people. The expression of his face was that of a man who was under great tension; his eyes were usually fixed on one spot, and he seemed to be waiting and watching for something to happen. He had the appearance and manner of an insane person. A prominent symptom was his indifference to his coming trial for murder. Has vivid auditory hallucinations and delusions of persecution, loss of memory of earlier life, and the chronological order of events, could not recall the names of his children, the place where he lived, nor his wife's maiden name. His wife says: "He has changed greatly in his disposition and mental condition; that he would get cranky spells, would be very irritable, and that there was hardly any living with him. He was very suspicious of her and watched her closely. He talked of suicide. During July, 1904, he went away and was gone six weeks, all but two days; when he returned he was thin and sick, and looked worse than a tramp; he looked as though he had been through a spell of sickness and could not work for two or three months; complained of severe pains in his head, could not sleep nor eat, sat up night after night, and was near crazy. He had no recollection of where he had been or what had happened to him." On the morning of August 25, 1908, patient shot and fatally wounded E. F., a resident of B. On several occasions prior to this he had maltreated his wife under the unfair assumption that she had been too intimately connected with said neighbor. The exciting cause of insanity was a sun stroke occurring four years ago, and the too free use of alcohol. When interviewed by the physicians it was difficult to obtain any definite answers to the questions put to him. His memory appeared so defective that it was impossible for him to correctly recall any of the events in which of late years he was an active participant. He states "that yesterday or the day before a man brought a woman here and said she was my wife, when I never was married." "Marked defects were noted in orientation. While the patient did not seem much depressed he had a strained expression to his countenance." Upon admission, was quiet, pleasant; paid no attention to things going on, talked in answer to questions, and some spontaneously. At one time became suspicious of physician; answered questions, but unsatisfactorily; gave no information about his early and recent life, said or pretended that he did not know, assumed hallucinatory attitude. Had to ask Mr. Gaskill everything. (Mr. Gaskill was his jailor.) What is your name? "Joseph H——." How old? "I don't know." About how old? "Ninety or ninety-five." Where were you born? "I don't know, sir, Mr. Gaskill, he knows." Ask Mr. Gaskill? He looks away, assumes a listening attitude, quickly turns and says, "Bordentown." He again looks away, listens. What are you listening to? "Oh, just to whisperings of the

conspirators. Mr. Gaskill, he keeps them away from me though." Who? "Everyone—they tried to poison me on the boat. Mr. Gaskill has stopped them. He says it is a deep-laid plot that he cannot fathom," there are many in it, etc.; they are trying to secure his patent, etc. How long has the plot been going on? "Ever since I can remember."

Physical Examination.—December 17, 1908. A well-built, well-nourished, healthy man. When asked, says he feels good; is open to suggestion. When asked if he has headache or other pains, he complains of a dull headache and a dead feeling and of pain in his arms and legs. Gives no, or evasive, answers to tests of smell, hearing, taste, and sight. Expression at times peculiar; he frowns and looks away intently, as though trying to recall an answer. Some paresthesia. He tells when and where touched very slowly, makes mistakes. Pain sense diminished, shows no evidences of pain upon the legs, resists when abdomen is pricked, other areas are diminished, some tenderness of nerve trunks in arms, none in legs, otherwise negative. Mentally, quiet, orderly; follows ward routine, keeps away from other patients, at times is afraid, will cry and ask to be sent back to Mr. Gaskill, but ordinarily seems contented. He will talk in answer to questions, also spontaneously, but gives no information, refers things to Mr. Gaskill. He is not oriented for time, person, or place. He says that the last (or the first) thing he remembers is that he was along the sea shore and that he was pushed over board by the conspirators; that after a long time Mr. Gaskill came along and picked him up and took him to the ship. Mr. Gaskill has protected him since then, and kept others from stealing his patent. He was sent here by Mr. Gaskill from the ship because there seemed to be something a little wrong with him—and to get the pain out of his head. Says there is a plot, that he is watched, annoyed, and they are constantly trying to steal his patent. He claims not to know or denies everything, in regard to his past early life, work, marriage, children, home, Ford, murder, jail, etc., and dates everything from being picked up at sea. He will fix no date for this, nothing more definite than that it was a long time ago.

December 25, 1908. Acted and talked as though he had never heard of Christmas. He gives the same answer to questions each time, although questions are changed, and attempts made to break into his past life. He is inactive, sits or lies about the ward, does not associate or talk to others, unless he is spoken to; acts as though he was afraid, keeps by himself, and is suspicious. When questioned he has a perplexed look upon his face as though he was trying hard to recall something; at other times has a distant, dreamy, far-away look. Does not take much interest in his surroundings, frequently asks for medicine for his bowels; he thinks the conspirators sometimes steal it off the tray. Dr. Cort, one of the examining physicians, visited him recently; patient acted and claimed that he had never seen him before. There is a small spot of granulation tissue on the top of his head—he constantly picks at this. This is caused, he says, by a plank hitting his head while he was in the sea.

January 6, 1909. He says, spontaneously, to-day to the physician that he has been trying hard to remember the questions I have asked him, and continuing, says: "It seems as though it wants to get in. Do you think there is a break there (he points to his head)? It won't stay long enough to hold it, and the whispering." What is your age? "Age, age, I don't know." What is your name? "J. H." Where born? "I don't know—on the boat, wasn't it—I don't know. I don't belong here, do I? They are too rough. I am not out of my mind, my mind is out of me; I don't seem able to recall anything. I was sitting on the bench this morning and some one struck me right in the middle of the back." Who? "I did not see anybody, they (conspirators) were whispering around me; I listen a great deal to try to get a word here and there—to get something—if I could only make it stay—yesterday I eat my dinner and then vomited it up. (Idea of poison put in food by conspirators.) Doctor, can I have a little tobacco? Duke's smoking tobacco, that is the kind—I believe my mind is in that—sometimes there is so much noise that I can't work on my patent—I want to get back on the boat as soon as I can. Don't you think they will come for me soon?"

January 11, 1909. An officer from his home, whom patient knew well, visited him to-day, and talked to him of past events. Patient did not know him; talked and acted toward him the same as toward others.

January 20, 1909. Suspicious, somatic complaints, constantly annoyed by conspirators. Life is a constant struggle against them.

January 25-29, 1909. Chill, fever, follicular tonsilitis, etc. Produced no mental change. Contracted visual fields are present. In left eye all colors within the circle of 35, red largest, the blue about the same as white. Right, red and white within 40, blue within 30.

Case No. III.—N. G., colored, age 17, single, student.

Family History.—Parents normal. One paternal cousin alcoholic, another cousin had "spasms," with recovery. Maternal grandmother had "spasms and sinking spells." Scrofula in three other members of mother's family.

Personal History.—Nothing abnormal until onset of present trouble. Disposition reserved. Happy when all went well; if not, he would grieve, brood, and cry. Made good school progress. Entered Howard University in October, 1907. Took two years' work in one year. He went to Atlantic City during the summer of 1908 to earn money to return to school.

Etiology.—Financial troubles, worry about work, home sickness, and, finally, some physical sickness.

Onset.—During the latter part of July, 1908, he became worried and depressed, finally sick ("septic sore throat"). His thoughts became retrospective. He became emotional—would have crying and laughing spells. In August he joined the Methodist Church. This made a great impression upon him. "In September he began to have attacks when he would stretch out his arms, his eyes would glare, he would get stiff, he would sink to the floor, would seem unconscious, and then go into a spell which would last an hour or more. During some of these spells he

was highly excited—would just rave, cry out, kick, bite, jump up and down, assume posing attitudes, imagine that people were trees, that he was playing ball, talk and call to people he knew, preach, sing, pray, and call to his mother. At these times his attention could not be obtained; he would not answer if spoken to, did not seem to know those about him, or where he was; would take off his clothes and throw them at the wall and be indecent. Had false sight and hearing, would imagine people were present and call them imps and devils. Would carry on in this way until he became exhausted, and then be quiet and sleep for a time. Had to be strapped down. After coming out of one he would ask for his mother, would talk better and say that everything seemed dark to him. Had several such spells at home and also while in jail, where he was taken so that he could be controlled until he could be sent here."

Admitted.—September 9, 1908. Upon admission he seemed confused and dazed, was suspicious, would not talk, did not know where he was. Was quiet, but would not stay in bed for the next two days. Gave irrelevant answers to questions. Was not oriented. Suddenly he cleared up, talked about himself, could not understand his situation, said: "It all seems strange to me."

Physical Examination.—September 14, 1908 (after he had cleared up). Showed defects of smell, anæsthesia of eyeballs, a mitral murmur, and sprained ankle.

Mental Status.—September 17, 1908. He was then perfectly normal. Gave a good account of himself, except for certain periods. He denies doing and saying many things. "If I did so, I do not remember it." But remembers things up to a certain time. Says he was constantly worrying and thinking of home and school, and that he would go to sleep and then dream about being at home, in the wood, etc. Says his limbs would feel as though they were asleep, and that afterward he would have a very stupid feeling, a swimming feeling in the head, and sometimes a feeling in his throat, due to indigestion. He was normal from September 12 until taken to his home in Illinois, September 25, 1908.

Comments.—A young colored boy, away from home, overeducated, and overworked during the school year. During vacation out of work, financially embarrassed, and much worried. Finally sick. Became religious and joined the church, then had several grand hysterical attacks with amnesic periods. Sent to insane hospital, where he was in a dazed condition, with clouding of consciousness for a few days, then rapidly recovered and remained normal until discharged about two weeks later.

Case No. IV.—J. I., age 40 years. Occupation, potter. Born in England.

Family History.—Father a drunkard, a paternal uncle drank. Mother used alcohol moderately, and was abused by her husband; she left him when patient was quite young. She died of gastric cancer about one and a half years ago. On the maternal side an aunt had nervous prostration, an uncle kidney trouble, the grandfather used alcohol and died of Bright's

disease. An aunt of patient's mother died of cancer. A brother of patient has been an alcoholic since he was twenty-two years of age; goes on periodic sprees, and is gone for many months—wanders all over the country. Has now been missing for several months. His whereabout is unknown. Has been a patient in several hospitals for delirium tremens and alcoholism.

Personal History.—Early life normal, made good school progress. Began work when ten years old. Became a sanitary potter, always industrious and an efficient worker until the past few years, since when drink has interfered with his working time, but not his work. Disposition: Reserved, goes around by himself, "melancholy," his only hobby and recreation being gardening and walking. Marriage: Satisfactory, four children, lived happy with and cared for his wife and children. Habits: Began to drink when twenty-three years of age, drinking occasionally with friends. Since then he has gone on sprees from time to time for a day, or a few days; but has not lost time from work, or had amnesic periods until about fourteen months ago.

Onset.—Fourteen months ago his mother died a slow death from carcinoma. He watched by her and nursed her in an oil-stove-heated room. Says he worried much about her, and also some insurance he held in England. A few days before she died he started to drink a little. He remembers buying a half pint of whiskey, "leaving the saloon and walking a short distance down the street, and then nothing until I come to on the road to Langhorn." There was in this instance an amnesic period of a day and a night.

He has taken five or six similar trips since then, the last and longest one being two months ago, when he was gone over a week and found himself in Jersey City.

Some Parts of His Stream of Thought.—How long have you drank? "Seventeen years, but not heavily until this last year, when my mother died, then I seemed to go all to pieces, and have drank heavily ever since. I get despondent and get to drinking. I drink so much that I don't know what I am doing. I go right off then; I just feel that I got to go. I lose my head and start off." Do you know where you are going? "I don't know, I have no idea; it seems as though I were asleep like and then wake up; maybe I will be standing or walking at the time. It comes just like you were waking up, then I look around and think what place is this; I wonder where I am; then my mind goes back and I remember I have started off on that drunk." Tell me about your last walk. "I had been drinking about two weeks; my last remembrance was standing on the bridge at Mulberry Street talking to my brother. I had a bottle of whiskey; I gave him a drink and watched him go away. I took another drink and remember walking from the bridge and taking two or three steps (Sunday night), and then nothing more until Thursday (ten days later), when I was sitting down with my back against a barrel on some old wharf. I got up and looked around, saw a policeman

and asked him what place it was; he said Jersey City. I asked him what time it was and he said about 6.30 (a. m.), so I started to walk home. When I woke up I found my hands all sore, as though I had been working, and I had $5.20 in my pocket and a pair of overalls, a pair of laborer's shoes, two shirts and two undershirts, all done up in a shoe box. When I started out I had no money." He states that he has never gone over the same route twice, and knows nothing about what he does or says during his absence. "The last few times it seems as if I knew and did not want to get away. I would keep inside the house and walk around the room. The last two times I made up my mind that I would stay at home." His wife states that between intervals of drinking he is perfectly normal. As soon as he begins to drink he acts queer, looks wild like, is restless, does not talk to people at home, except to say a few words; does not stay in saloons, wanders from one to another; does not associate with people, but knows where he is and those about him. Does not eat or sleep, walks all the time, drinks night and day, finally disappears and is gone for days; then comes back and is unable to recall events of the days he was gone. During his last spell, before admission, he remained at home. Following a spell he is depressed, cries much and desires to be put out of the way, so that she has to hide his razor and knives, as she is afraid he will do himself harm.

The last drinking spell ended by a fit. Wife did not see him in this fit. His account of this is: "I had drank for a week, then I had had nothing to drink for two days; on the second day I had the fit. My wife had gone out to see the doctor. I just sat in the chair talking to a neighbor; I was just talking to her, that is all I know about it. When I came to it was just like as I had been asleep. I saw a lot of people there and wondered how they got there." Says he knew those he saw and where he was. He came to the hospital as a voluntary patient to see if he could be cured.

Physician's Certificate States: "Patient said he felt that he must go away, get away from something. Feels he should take his life sometimes, felt that it was not safe for his family to be with him. Walked to and fro across the room. Very nervous."

Physical examination negative, except increased deep reflexes, slight tremor, a mitral murmur, vasomotor disturbances, and alcoholic gastritis. (Last drink three days ago.) Visual fields but slightly contracted.

Comments.—Epilepsy, hysteria, alcoholic amnesia are three conditions to be considered. Accepting Janet's views on hysteria I believe this to be a case of hysterical insanity, and consider his convulsion as a hysterical convulsion. There is a positive history of periodic alcoholic excesses; but prior to his mother's sickness and death there was never any loss of consciousness, fuge or amnesia. Following this emotional condition I think hysteria has been added to the alcoholism, and has assumed the most important position, and that the fuges and amnesia are hysterical conditions.

Epilepsy and Hysteria—Hystero-Epilepsy.

Do the two conditions occur together? I believe they do in some cases. I think epilepsy is sometimes diagnosed when it is not present, and the condition is one of hysteria.

Following are four cases reported. Three of them are admitted with the history of epilepsy. They are supposed to have had epilepsy for some years, with quite frequent convulsions, yet in the hospital only one of the four ever had a convulsion.

This man has attacks but shows no psychic symptoms. In all the disease has begun in adult life. We see many cases of epilepsy here, but the character and disposition of these cases seem different than in the ordinary case of idiopathic epilepsy.

The cause of the disease in Case V is given as a head injury many years before. Attacks are brought on by emotional disturbances. The man is easily affected by alcohol.

In Case VI injury and sun stroke were present years previous to the onset of the disease. Overwork and close application in a hot, noisy room were given as the cause.

In Case VII epilepsy is not proven. There is the history of an episode with indecent exposure and suicidal attempt following lack of work, worry, and a family quarrel.

In Case VIII the onset and etiology date from purely emotional causes.

All are foreigners. The immediate cause of admission to an insane hospital in all cases were episodes, periods of excitement or violence, conditions that had not occurred before. Some of these patients have had convulsions at quite frequent intervals, but without psychic symptoms. In all there was clouding of consciousness and amnesia. Were not these somnambulisms or fuges hysterical manifestations in cases of epilepsy? In only one case am I convinced that the diagnosis of epilepsy is fully established. Emotional causes were prominent factors in causing the episodes. All were arrested for a criminal offense during the episode. Here a medico-legal consideration presents itself.

Case No. V.—C. W., a German, age 44 years, married. Occupation, stone mason. Admitted July 12, 1908.

Family History.—Maternal cousin insane, father tubercular.

Personal History.—Negative until twenty-three years of age, then, while in the German army, he fell twenty feet, striking the back of his

head; was unconscious and delirious three days. There was no paralysis, no convulsions, no headache. Made a good recovery in four weeks and was well until eleven years ago (age 33), when he had some kind of a spell while at work; these spells continued about every three or four months until three years ago. Spells are described by himself and wife as follows: "Spells come on when I get mad; I feel bad in my stomach, and she can hear something run up and down from my mouth to my stomach, and out of my mouth comes some sour water, and then my head feels so heavy and like a drunk feel; and then I sleep and don't know nothing until the next morning, when my wife tells me what I do. That I talk about what I do (work, etc.), and about being here twenty years and not getting my papers." Wife states that he laughs, cries, talks, while in a spell, and that the minister has great influence over him in stopping them. For the past three years he has had what she describes as big spells. "His eyes go around; he sometimes bites his tongue, froths at the mouth, falls down and is unconscious, sometimes for an hour. After one he is confused, and does his work all over again; sometimes he laughs, sometimes cries after a spell. These big spells occur now every four or five weeks. He has no little spells at this time. Is easily affected by alcohol."

The reason of his admission here was an episode of excitement—a fuge—after spending Sunday in the country with some friends and drinking some beer he returned home. His children quarreled that evening over a lead pencil; he became mad and went to bed. Had seven or eight "big spells" that night, and severe headache the next morning, stayed home and slept Monday. On Tuesday was better and worked all day; came home that night. Had a quarrel that day with a bartender—was all upset; talked to his three-year-old child as he would to a man. Was irritable, later left the house and returned at midnight with his brother. Went to bed, but soon after became excited, talked loudly, rapidly, and incoherently; finally quieted down at 6.00 a. m. and slept until 3.00 p. m. the next day. Was normal from then until Friday night; worked Thursday and Friday, quarreled with another workman and returned from work earlier than usual Friday night. Appeared to be out of his mind, excited; some household remedies and the minister quieted him down, and he finally went to bed and slept for awhile. Woke up, called his wife, talked rapidly, became excited and noisy; said he must phone to the Kaiser to ask pardon for not informing his regiment that he would not return. He talked about a letter he should have written to this effect, but which he had neglected to do; was anxious about this and afraid of punishment, so wanted to telephone to the Kaiser for pardon. He demanded money and threatened his wife. He seemed afraid to go out, appeared to think some one would catch him. Finally, his face became very white; he pushed his wife aside and ran out and down the street. Later, it was learned, that he went from place to place trying to get in to use a telephone; finally got into a saloon and

tried to call up the Kaiser; could not get him, so pulled the telephone from the wall and ran out. Early in the morning tried to get into a hospital to telephone; ran away from there and wandered into a cemetery and lay down under some bushes, where he was discovered by an officer, who woke him. He fought and resisted the officer, but was finally overpowered and taken to the jail about 8 a. m. Saturday morning. Was examined.

Physician's Certificate Says: "He was excited and his talk was rambling and disconnected. He seemed in a dream-like state. He also seemed to have delusions in regard to being an important officer in the German army." Was brought here on Sunday, was quiet, talked about himself in a rambling way, half English, half German. He knew the day, where he was, and the police officer. When examined he showed no psychosis, but there was a partial amnesic period for his peculiar actions, and he had a very imperfect knowledge of his admission and the next two days. The diagnosis of epileptic insanity with hysterical attacks, or hystero-epilepsy, was made. He did well, had no attacks of any kind while here; was discharged August 28, 1908.

Case No. VI.—W. S. C., age 46 years, English, widower. Occupation, file cutter. Admitted June 5, 1908.

Family History.—Negative.

Personal History.—Childhood environment not good. Began work very early, enlisted in the army when seventeen years of age. Saw service in South Africa, was shot in the head, suffered hardships of war in Africa and India. In India had a sun stroke. Epilepsy began eight years ago. At first petit-mal, later grand-mal attacks occurred. Petit-mal attacks are more frequent. Admitted here because of a hysterical episode, a fuge. "His wife died in February, 1907, and that worried him much; since then he has been afraid someone would wrong his daughter. Two nights before admission he had several spells; early in the morning he got up and said to his daughter: "A., you know we are married." He grabbed her and tried to assault her. She knocked him down and escaped. He went to work that morning, worked about five minutes, left his work without a word to anyone and walked seven miles to another town, stopping at various farm houses on the way and telling the farmers that King Edward had placed upon him a great responsibility, and that he was now ruler and owned these farms. He ordered the farmers out as he went from place to place. He was finally arrested and brought to the jail. There he was excited and talked in a rambling manner upon religion and the saving of Great Britain, and, if it was the will of God, America.

Upon admission, June 5, 1908, he was well orientated but slightly excited, talked freely about his spells. He remembered some things he did during this episode; says, "God's voice told me, in the name of King Edward, to order the people out and take possession." In the hospital showed no psychosis; there was a partial amnesia. He has since had numerous petit-mal attacks, but no excitement or psychic equivalents.

Case No. VII.—C. E. H., Englishman, age 43 years, married. Occupation, iron molder. Admitted March 14, 1908. A man out of work, worried, unhappy, quarreled with his wife, attempted to assault his daughter, exposed himself indecently, was arrested and put in jail; there attempted suicide, was sent here. He denies the indecent exposure and attempt at assault. Has no remembrance of it. He describes his attacks as: "I don't know what come over me, only I get awful nervous; the least thing puts me out of the way. I get wild, it seems as though my whole insides were working. I get talking to myself or at random. It goes dark, like a shadow, or a scale comes over my eyes; then I have headache and thoughts come to me to put myself out of the way because no one wants me."

While in jail, after he had made several attempts at suicide, he says the following scene occurred while he was awake: "I fancied that I had been away a long time and had returned; all the streets were lined with people; I was preaching to them and hundreds were converted. I saw a light from heaven shine on my head like a ring you see in pictures." He relates other visions that have occurred at other times.

Both he and his wife deny that he ever had convulsions. Wife states that sometimes he is uneasy and restless, moans and kicks while asleep. He sometimes dreams of being paralyzed, unable to move, and complains of a feeling in his hands as though they were dead, which lasts for three weeks sometimes. Sleep not good. Anæsthesia of eyeballs.

Patient upon admission was orientated, but unhappy and slightly depressed for a few days. He talked freely and acted in a rational manner. Demeanor was normal a few days later, and continued so until his discharge, December 14, 1908. The only thing shown here was some unhappiness, slight depression for a few days, and regret that he attempted suicide. There was no retardation, no self-accusation, and not enough depression to make a diagnosis of manic-depressive insanity. A positive history of convulsions could not be established. The man used alcohol; but alcohol could not be connected with this attack. A diagnosis of a psychic epileptic equivalent was made.

Case No. VIII.—A. G., Hebrew, age 60 years, married. Occupation, shoemaker. Admitted November 29, 1907. First fit occurred seven years ago. He was arrested and sentenced to pay $5 or spend two days in jail. He became frightened and had a fit in court. Another occurred four months later, and others at more frequent intervals until 1907. For a few months before admission he was very nervous, worried about money that was due. On November 25 said it was his last day, and had a fit. Fell asleep, woke up later crying and laughing; became excited, noisy, destructive; had to be tied down; was sent here.

He was much excited for a few days, disorientated, confused, suspicious, but gradually cleared up. Was then perplexed and unable to understand how he got into this place. An amnesic period was present. Had no convulsions while here; was discharged January 8, 1908.

Was well for a year, then the spells returned, following a severe cold. Daughter states: "They occurred at night, he is unconscious, breathing is labored, bites tongue, foams at the mouth, but there is no twitching anywhere. He lies absolutely quiet, his eyes closed, and is unconscious all night and for hours the next day. When he comes to he is very weak, and has no remembrance of being sick." She states that since his first admission to this hospital, he always loses his mind two days after the spell, and continues in this condition for three or four days, during which time he becomes very much excited, laughs, talks, sings, etc., but afterward can recall everything that happens during this excitement.

On March 4 had a light spell at night. Felt uneasy, was suspicious, and thought people walked about outside of the house. Got up and looked out, was apprehensive, walked up and down, talked and became excited, quieted down and went to bed at 6.00 a. m.; slept until 9.00 a. m.; came downstairs and seemed to be all right. Had another spell on the fifth, assaulted his son, became excited and had to be tied down. Remained quiet the rest of that day and all that night until March 6. Had no fit on March 6; went to church, there got mad over something and started to hit several people; started for home, was hit with a snowball; "this made me excited and I had a big fight"; when the officer arrived he lay down, kicked, bit, and spat at, and gave them much trouble to take him to the station. He was examined.

Physician's Certificate States: "Patient said he was Jesus Christ, loaned money, was rich, was hand cuffed in cell, was excited in talk and manner. Talked incessantly and incoherently. Thinks he is another person, imagines he is a bank president, and thought I was President of the United States. Spat at everyone around him, was on his knees all the time, talking and shaking his fist."

Was brought here with considerable trouble, March 6, 1909. Upon admission, was excited, talked rapidly, was orientated; he quieted down, told about his trouble, was bathed and put to bed without trouble. Slept part of the night, but early in the morning he became excited, noisy, violent, hard to control, fought desperately anyone who came near him. Was finally put in a continuous bath. All day he was noisy, shouted loudly, talked incoherently, sang, showed great psychic and motor excitement, rhyming, flights of ideas. Happy when let alone, but very ugly and resistive when approached. Refused all food. The next day the excitement was less marked. Violently resisted tube feeding on the 9th. Continued much excited, refused all food and attention; was kept in continuous bath much of the time until March 12, when he took food, became quiet, would talk, accepted attention, etc. Assumed his normal demeanor and continued so until his discharge, April 26, 1909. Never had a fit of any kind while in the hospital. Later he remembered some of the incidents of this period and imperfectly about his trip and admission here. The man never used alcohol.

Hysteria and Dementia Præcox.

Three cases are reported. All were doubtful cases. If they are dementia præcox they are atypical cases. All presented prominent manic-depressive features at some time during their course. None of them showed mental deterioration. All had some insight. All improved, were discharged (one eloped), and although out of the hospital but a short time are reported to be doing well. None have been returned. Hysteria is certainly a prominent element in all these cases. Impulsive acts were present in all the cases; visions, hallucinations of sight and somatic complaints were common features. Anxiety, fear, and apprehension were present in all three cases. Anæsthesia and sensory disturbances were present in all cases.

Case No. IX.—G. G. H., age 23, married, United States, electrician. Admitted April 8, 1908; discharged August 30, 1908. First change noticed was three years ago following an injury to his head. One year ago shot himself, after having a few drinks and quarreling with his wife. On April 6 became apprehensive; was afraid he was going to be blown up by dynamite and sulphur, and was afraid of being poisoned. Was sent to a hospital. Tried to jump out of window (suicide); was uncontrollable at home and taken to jail; refused to leave his room to-day, became stiff and rigid, was mute, had to be carried to the train. On train he acted in a boisterous way, sang, laughed, cursed, struggled, attempted to escape, was unsuccessful, so became rigid and mute, had to be carried to carriage and lifted out, then walked in hospital. Sat in a praying attitude with hands together, slid to floor, went through a hysterical convulsion (opisthotonos), which lasted about five minutes. Then showed catatonic symptoms. Held hands in air (cerea flexibilitas-mutism) but obeyed commands, answered questions when commanded. Talked while being bathed. When put to bed he pushed his hands through a window glass near the bed; gave no reason for this.

For five weeks he continued cataleptic—mutism, refusal of food, negativism, hallucinatory attitudes, posing, hallucinations, somatic sense deceptions. Later he showed a depressed condition—depression, retardation, apprehension, anxiety, unsystematized delusions of persecution, illusions, somatic sense deceptions and delusions, some insight.

In August he was much improved but very changeable in disposition and mood; sometimes bright, cheerful, happy, almost exhilarated; at other times unhappy, worried, discontented; expressed no delusions, denied hallucinations. Had quite good insight, explained some of his actions, showed good judgment.

He was regarded as a case of dementia præcox with improvement or a remission, although the case was not entirely clear. He differed from

other cases of dementia præcox. The case at times resembled a manic-depressive attack. He improved much and is still outside the hospital, and said to be at work and doing well.

Case No. X.—C. F. J., United States, age 23, single. No occupation. Admitted April 10, 1908; discharged July 24, 1908.

Family History.—Mother neurotic, hysterical. Father an alcoholic, and insane.

Patient irritable as a child, made school progress, worked a short time in two places, did not think he received enough pay, so resigned. Since the age of twenty he has had no occupation, but has looked after some property for his mother; traveled and amused himself the rest of the time.

In 1905 was neurasthenic. Spent some months in California, but did not improve. Returned home and took up physical culture treatment—improved some. In 1906 went to Florida; there he became depressed, afraid, seclusive; on one or two occasions got up at night and went to a neighbor's; improved in a few days and was brought home; was well until July, 1907, when he had a similar attack lasting a few days. In March, 1908, he was neurasthenoid, became restless, did several peculiar things, was depressed, anxious about his health, disappeared from home on two occasions, and acted in an irrational manner while away. In April got out of bed, came downstairs, broke a glass door, walked out in the street in his night clothes, where he was found by his brother. He was confused, did not know where he was, called his brother other names, said, "Is this you, Mr. A——, who is this?" The next day he was quiet and remained at home. The following day resisted his brother and escaped from the house. Did several impulsive and foolish things. Was finally arrested, examined in jail.

Physician's Certificate States: "The patient said he heard voices in his ear that threatened him; that spells came over him sometimes, and he did not know what he was doing. He was restless and excited, wandered about the house, was stealthy in his movements and irrational in conversation." Upon admission was oriented, told of many things, boasted of what he had done, fabricated, but when closely questioned became confused and unable to explain former statements. Made numerous subjective complaints, was open to and easily influenced by suggestion. Mental examination showed apathy, mannerisms, silliness, impulsive acts and queer thoughts, which he could not satisfactorily explain; hallucinations of hearing, sight, dream and pseudo hallucinations, illusions, and some ideas in regard to another personality. He says at times he has periods of loss of memory. When he hears names he associates these names with himself in his past existence. He thinks he has lived in other lands in ages gone by. He says you might live and die, but the vital spark is transferred to some other sphere; it does not die but is transferred to another body in some other place, and in this way we have lived through different ages in Egypt, Rome, France, and other countries up to the present time. His orientation was good; he showed no mental

deterioration. Memory and retention good. Had some insight. Judgment was poor. He was discharged, improved, July 24, 1908, and still remains outside. He has always been neurotic, eccentric, unstable, has had numerous hobbies. Smoked to excess. No alcohol.

Case No. XI.—Dr. Watson's case. E. T., U. S., age 19, single. A mason's helper. Admitted December 31, 1908; eloped May 30, 1909. An incorrigible boy, sent to reformatory, and from there here. Here he has at different times shown apathy, negativism, mutism, catatonia; at other times manic symptoms. Before admission was said to be depressed and made an attempt at suicide. For a time opinion was divided as regards manic-depressive insanity or dementia præcox.

Nearly every night, and always following any excitement (dance), he is noisy, violent, has hallucinations of sight and hearing of an unpleasant nature, and thinks dogs and men are coming after him; he tries to escape, becomes impulsive, fights, struggles, finally quiets down and goes to sleep. The next day remembers nothing about it. He has frequent grand hysterical attacks, convulsions, etc., and all the stages given by Charcot.

Case No. XII.—Dr. Sandy's case. J. T., colored, United States, age 35, married, laborer. Admitted October 19, 1909. Normal until three years ago, then is said to have had something like a "stroke," followed by unconsciousness and partial paralysis. Since then his disposition has changed. He has been ill natured, quarreled with family, has not worked. The family state that he thought he had been in a railroad accident and lost both legs. One month ago he had another "stroke" and was carried home.

Physician's Certificate States: "When I saw him immediately after the attack he seemed dazed. No questions would be answered, incoherent mumbling, inco-ordination marked. Delusions of marital infidelity. Says he has lost money, a decline in mental power." When examined mentally he was at first dull and apathetic, then gradually improved and became brighter as the examination proceeded, answered more promptly; but at times returned to his dull, dazed condition. Expressed a number of expansive ideas; at the end of the examination he denied these, and said he never stated them. Orientation was imperfect; at times he acted as if he was entirely oblivious to everything about him, and as if he did not hear the questions. Sometimes has a rather dazed expression. He is very susceptible to suggestion. Has some insight.

Physically, he presents a flaccid paralysis of the right arm. Reflexes are all present in both arms, and about equal and normal. He claims both legs were paralyzed—not now, only the left leg is. Gait is shuffling, he drags the left leg slightly. Reflexes in left leg are increased. They are normal in the right. The leg paralysis is flaccid. No ankle clonus. He shows contracted visual field, red larger than blue, in left eye; at the widest points white at 70, red 45, blue 30, right eye, white 70, red 60,

blue 55. Although his arm and leg are supposed to be paralyzed and helpless, upon suggestion he can be made to run, jump, lift, and hold out heavy objects, and to otherwise use the parts in a way that requires considerable strength.

Conclusions.

From personal experience hysteria seems to be connected with insanity in about 10 per cent of male admissions. If hysteria is much more common in females, it would seem that among the female insane it should be a very prominent and important factor. It is claimed by some that nearly all criminals are defective in some way. Several of these cases are criminals, others have committed criminal acts and have been arrested before being committed as insane. The question of responsibility comes up here. Practically all of these cases recover. Should they be held for the criminal acts committed? If, after commitment in a hospital, they recover should they be allowed their liberty or be indefinitely confined in an insane hospital? It would seem that they should not be held responsible for a crime committed while insane. If it can be definitely proven that they were sane when the crime was committed, and that the hysterical symptoms are the result of arrest, trial, and imprisonment, upon their recovery they should be tried and made to serve out their sentence. The old question of simulation and hysteria here presents itself again. It is necessary to be very careful upon the part of committing physicians to settle all questions in regard to simulation before they advise the court that the prisoner is insane, or was insane when he committed the criminal act.

The prognosis in hysteria is good. Cases of hysterical insanity do not deteriorate mentally.

In conclusion I wish to express thanks to Drs. H. A. Cotton, W. C. Sandy, F. S. Hammond, F. S. Watson for assistance, and to Dr. G. H. Kirby for valuable suggestions.

Papers and books by Janet, A. Meyer, A. Hoch, Jung, Woodman, Diller and Wright, Raecke, Prince, Coriat, and numerous English text-books, abstracts, and papers by various authorities on this subject, have been freely consulted.

THE ETIOLOGY AND GENERAL BACTERIOLOGY OF TYPHOID FEVER.*

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In a study of the etiology of typhoid fever it is not the mere enumeration of the predisposing factors common to infectious diseases in general, or even a detailed study of those which seem to assume an important role in this connection, which should receive the first attention.

In the continuance and spread of typhoid fever are concerned the primary underlying principles of the clinical history of the disease, and the life history of its specific organism, both within the human body and during its saprophytic existence. From being considered as a comparatively frank and simple disease with certain well marked and distinguishing features, typhoid fever in a broad sense, under modern methods of investigation, has been found to be an extremely broad and complicated subject, requiring for its solution the best efforts of clinical medicine and biological science.

Typhoid fever is not simply an infection; it is in all cases a true *septicemia,* and its specific organism not only is present in the intestinal tract and discharges therefrom, but the circulating blood, and from this may reach and colonize in any organ of the body from prodromal stage to convalescence. The rose spots of the skin, the gall bladder, the urinary bladder, the middle ear, the testicle, the bronchi, the spleen and lymphnodes, and the various bones of the body all form suitable locations for its growth and multiplication.

It has been repeatedly found in the circulating blood as early as the fourth day of the disease, and Kayser found it in 100 per cent of the cases he examined during the first week. Pratt, of Boston, in a single autopsy, isolated typhoid bacilli from the heart's blood, the spleen, the liver, the kidney, a mesenteric lymphnode, the gall bladder, the urinary bladder, the right middle ear and the bone marrow. By the same worker it was isolated from the gall bladder twenty-one times out of thirty examinations. Fox found localization of typhoid bacilli in the

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testicle of 46 per cent of cases examined. It was isolated from the urine in 25 per cent of all cases examined by Jacobi and Munch. Gwynn estimated that 500,000,000 typhoid bacilli per cc. were present in a case he reported. It is frequently found in the sputum when bronchitis is associated, and Deudonne recovered typhoid bacilli from the sputum seven weeks after fever had disappeared.

While the intestinal discharges are the principal means by which typhoid bacilli leave the body, the intestinal changes in typhoid fever are regarded by many as merely co-ordinate with the general infection, and Baumgarten stated the belief that intestinal lesions should be regarded merely as metastases. Undoubted cases of typhoid fever without intestinal lesions occur, and conversely, severe typhoid ulceration of the intestines has been observed without any disturbance of health. Typhoid fever then is a general infection in which local changes can occur.

Not only is it a true septicemia, but it is one manifesting itself in such manifold phases, and with such varying degrees of severity that if characteristic symptoms only are sought for, its presence must frequently be undetected, and what is of far more importance, the infectious and contagious nature of the condition will remain unrecognized, and it is to this feature of typhoid infections that the persistence and prevalence of the disease is largely due.

The introduction of improved methods of diagnosis has resulted in treating as cases of typhoid infection in a sanitary sense, a great portion of febrile diseases in which previously no precautions were taken. It is of interest to note that while formerly in many cities the number of recorded deaths due to all continued fevers not considered typhoid, and those from typhoid fever reported as such, were about equal, during the past eight years there has been a gradual but steady decrease in the former, and a corresponding increase in the latter. For example, in St. Louis previous to 1900 the number of deaths from all fevers, not typhoid, were in excess of those due to that disease. In 1900 at the time when the Widal reaction was coming into general use, a special circular was sent by the health board of that city to general practitioners requesting that all cases in any way resembling typhoid be carefully investigated. The results were striking. In 1899 the deaths from typhoid were one hundred and thirty-one, and from other fevers one hundred and forty-eight; in 1901 the typhoid figures rose to one

hundred and ninety-eight, and the others decreased to eighty: in 1902 the rate was two hundred and twenty-two to one hundred and two, and in 1903 two hundred and eighty-eight to ninety-one. The difference in the previous and subsequent figures represents exactly the decrease in the opportunities for typhoid dissemination in that city.

At present, however, while it is not the cases sufficiently severe to cause death in which errors in diagnosis and consequent opportunity for spread of infection are so likely to occur, the same opportunity frequently does occur in that great number of atypical conditions accompanied by transient fever, and vague general and local complaints that clinically are regarded as "touches of malaria," intestinal toxemia, etc., and which are in reality different manifestations of typhoid infection and septicemia.

Since the discovery of individuals, apparently normal, who have never manifested a single symptom of ill health and who yet harbor the bacilli in enormous numbers, it is manifest that the symptoms of typhoid infection may range from those of classical type down through all the vague complaints to which the body is subject, to nothing. The typhoid bacillus, while always ready to infect, frequently does not cause typhoid symptoms.

From a standpoint of etiology and prophylaxis the term *typhoid fever* is a misnomer, and the condition is better described as *typhoid infection*. For the diagnosis of this in all its forms no single symptom or train of symptoms will suffice, and it is to be made only with the aid of the best bacteriological and laboratory methods.

Bates, of the Panama Service, in analizing two hundred consecutive cases treated in the Ancon Hospital, in which a diagnosis of typhoid fever was ultimately confirmed, found that 32 per cent were decidedly atypical, many manifesting only slight fever and malaise for a few days, and others with total absence of abdominal signs, and it is to these and one other type of typhoid condition that the actual continuance of the disease is largely due. They do not resemble typhoid fever, they are not recognized as typhoid fever, and are not reported as such; prophylaxis and sanitation are consequently not carried out, and there is but one possible result—contact infection and general dissemination.

While the frequency and importance of contact infection, both direct and indirect, can no longer be doubted, and is receiving constantly more attention, it is not sufficiently appreciated. That an individual

suffering from typhoid infection in any form, with symptoms or without, at any stage, as well as any article with which he has the slightest contact is a virulent focus of infection and a real and eminent danger to every person directly or indirectly associated with him, is a factor which cannot be underestimated, and which should be considered as the underlying principle in the general etiology of the disease. For whatever the mode of entrance is, and no matter what the carrier may be—water, milk, food, flies, or contact—every case of typhoid fever either directly or indirectly results from a previous infection in which adequate prophylaxis was not instituted, and this occurs not only in unrecognized cases, but far too frequently after a correct diagnosis has been made. In the investigation of typhoid fever in Washington in 1906 the United States Public Health and Marine Hospital Service in the official report, states, in regard to prophylaxis: "Of the four hundred and ninety-two cases treated at private residences the treatment of stools and urine with disinfectants was efficient in one hundred and forty-five cases, inefficient for 286, and of doubtful efficiency for fifty-one. Of the two hundred and eighty-six patients whose stools and urine were inefficiently treated, the lack of efficiency was due to the small quantity of disinfectants used for one hundred and ninety-seven, and to shortness of time of exposure for eighty-nine. In the fifty-one cases of doubtful efficiency this was because the material used was some patented preparation, the value of which as a disinfectant is doubtful. In eighty-nine cases no attempt whatever at disinfection of excreta was made." All of these cases at private residences were under the care of reputable physicians and one hundred and nineteen were attended by professional nurses, and yet in almost 75 per cent the most common and important prophylactic measure was either totally neglected or inadequate, and while not supported by actual investigation, it is probably not incorrect to presume that in this respect Washington is fairly representative of at least a large number of other cities, while in rural districts neglect is fully as great, if not greater than in cities, as the epidemics of Lowell, Ithaca and Butler can testify.

Not only at the height of the disease is a case of typhoid fever a source of infection, but during the early days as well. According to Conradi, who based his conclusions on an extensive study of contact infections, not only is the infection transmitted most often during the earliest stages of the disease—before its true nature has been recog-

nized—but it frequently takes place during the incubation period. That the bacilli may remain long after convalescence is now well known.

In addition to the clinical types of the disease, however, both frank and obscure, there is yet another source of initial spread of infection, which from being infinitely more difficult to detect may remain for years a constant menace without an indication of its nature. The fact that persons in average health might harbor the cholera spirillum in their intestinal tracts or the diphtheria bacillus in their throat has been known and its importance in prophylaxis appreciated for some years; but it is only recently since the suspicion that a similar relationship might exist in the case of man and the typhoid bacillus has actually been confirmed. It has been found that persons apparently well may discharge typhoid bacilli in the urine and feces months and even years after passing through an attack of the disease, and that persons who have never shown a symptom of illness, but who have been associated with cases of typhoid fever, may become carriers of the bacillus in a similar manner.

One of the earlier instances of chronic carriers, reported in 1899, was that of a patient who five years previously had been treated for typhoid fever in the Johns Hopkins Hospital, returned suffering from a cystitis, which on investigation was found to be due to the typhoid bacillus in almost pure culture. Since then many similar cases of chronic typhoid bacilluria have been noted. It is, however, in the feces that the so-called carriers most frequently discharge the bacilli. In 1906 Leibetrau reported an instance in which frequent cases of typhoid occurred in new comers at a mill at different times since 1896. In 1905, because of several deaths, an investigation was made in which it was discovered that one of the permanent residents at the mill was discharging typhoid bacilli in his urine and feces in almost pure culture. Kayser reports three instances of bacillus carriers investigated by him; two resulted in milk epidemics which were traced to the presence of persons at the dairies who were discharging the bacilli in their feces after unrecognized attacks of the disease. The third case was that of a woman, forty years of age, who at the age of ten had had typhoid fever. In 1904, thirty years after the attack, fecal examination showed the presence of large numbers of typhoid bacilli. Lentz mentions a case in which the bacilli persisted for even a longer period of time—forty-two years.

It is not only in those who have had the disease that the typhoid bacillus has been found to persist, but persons who have never been ill may carry it for years in a similar manner. In 1902 Drigalski and Conradi isolated the typhoid bacillus from the stools of four persons who had showed no symptoms of any kind, but who had been in close contact with cases of typhoid fever. Liebtrau, in 1906, reported the case of a woman, an attendant in a prison, who was found discharging typhoid bacilli in the feces two years after having nursed two cases of the disease. She was well and had never been sick. The occurrence of typhoid in inmates who had been there so long that they could not have acquired their infection outside led to her discovery and isolation, after which no more cases appeared.

While the source of bacilli in the feces of carriers has been the subject of considerable discussion, the results of a number of recent investigations tend to show that it is not as formerly supposed, the intestine from which they principally originate, but the gall bladder. This organ offers a favorable location for the persistence and multiplication of the organism both in chronic carriers and the usual clinical type of the disease. Not only is the bacillus found in the bile at autopsy, but it has been proven that after injecting typhoid bacilli into the circulation of a rabbit they may be recovered from the gall bladder in so short a time as eight hours. In the gall bladder the typhoid bacilli may give rise to no symptoms, or, as frequently occurs, be the cause of cholecystitis and gall stones. Neiter and Leifman, in 1906, found at autopsy the gall bladder of a chronic carrier filled with calculi and the seat of a growth of typhoid bacilli in pure culture. In an instance reported by Leibetrau, the carrier, a woman, had suffered with attacks of jaundice and gall stone colic ever since having typhoid fever.

While the frequency with which bacillus carriers occur is not definitely known, it has been variously estimated by different observers. At the typhoid observation station at Idar, Lentz found that 4 per cent of all cases became carriers, and the average results of Lentz, Klinger and Drigalski in investigations of one thousand seven hundred and eighty-two cases gives a total of fifty-three cases, or a frequency of about 3 per cent. If this estimate is approximately correct, then in the United States, where about 300,000 cases of typhoid fever occur each year, there will be in that time between 8,000 and 9,000 additional bacillus carriers at large, and when it is recollected that many of these individ-

uals may be daily in close association with any of the common food supplies, it is obvious that opportunities for epidemics as well as isolated cases from this source are not lacking. In themselves then, the initial sources of typhoid dissemination are not obscure.

Typhoid fever as a disease results from a lack of prophylaxis in cases of typhoid infection. This occurs in three ways:

First, from non-recognition of certain mild or atypical forms of the disease; second, from failure to properly isolate and disinfect after the diagnosis is made; third, bacillus carriers.

But, while the manifestations and history of the typhoid bacillus in the body and the manner in which it is discharged therefrom are of the first importance, the means of its dissemination are hardly less so. Although the typhoid bacillus belongs strictly to the parasitic class, it is nevertheless capable of a more or less prolonged saprophytic existence in any article commonly used by man, and on this period of viability depend the possibilities of time, distance and circumstances under which typhoid infection will occur.

The viability of the typhoid bacillus under almost every conceivable condition, in every medium from distilled water in the laboratory to growing crops in the field has been a subject of study for bacteriologists and sanitarians ever since its discovery in 1880, and while the results have been of the greatest interest and importance, for practical purposes much of this problem remains as yet unsolved.

Of all the natural media studied in this connection, drinking water, from which as a carrier of infection by far the greatest number of all typhoid epidemics arise, has naturally received the greatest amount of attention, and various observers have sought by isolation from natural waters, direct bacteriological experiments and epidemiological studies to demonstrate the presence and determine the longevity of the bacillus in this medium under conditions as naturally occur in various types of water supplies.

The typhoid bacillus, from the relatively small numbers in which it occurs in any limited amount and its almost constant association with large numbers of intestinal bacteria which mask its presence on laboratory media, is an extremely difficult organism to isolate from natural waters, and the instances where the presence of typhoid bacilli in water supplies has actually been demonstrated are extremely few. Wilson, in 1905, after investigating the literature, was able to collect but six

authentic reports in which isolation, and complete proof of identity, were obtained. All the instances occurred in Europe; four isolations were from shallow wells, and two from public supplies. In no less than three the contamination was supposedly from urine, for which reason isolation was obviously less difficult. For the purpose of deciding the frequency of water borne typhoid infection however, epidemiological evidence is entirely adequate, and it is estimated that about two-thirds of all typhoid epidemics result from infected water.

The fact that the typhoid bacillus is a parasitic organism, requiring for its growth and multiplication, organic matter in a comparatively concentrated form, and that many of the bacteria present in natural waters exert a distinct inhibitory and deleterious effect upon it, would naturally lead to the conclusion that in general the period of life of the typhoid bacillus in drinking water would not be great, and while a great majority of laboratory experiments performed under highly artificial conditions are valueless from a practical standpoint, those reported by Jordan, Russell and Zeit, in 1904 and 1906, are more rational and seem not only to confirm this belief, but to indicate that the period of longevity is inversely proportional to the organic and bacterial content of the particular water.

The observers mentioned in seven series of experiments placed typhoid bacilli in permeable sacs, such as to allow free ingress of surrounding fluids and at the same time prevent escape of the organisms contained in them. The sacs were suspended in various natural waters and the contents examined at intervals for typhoid bacilli. In the sacs suspended in the comparatively pure tap water from Lake Michigan the bacilli were found alive after seven days, but not later. In a similar lake water they lived ten days. In the heavily polluted water of the Chicago and Illinois rivers they were not found after three or four days, and in the Chicago drainage canal, practically an open sewer, none lived longer than two days. These experiments while apparently closely fulfilling natural conditions in water under which typhoid bacilli rapidly disappear, are in themselves not entirely exempt from criticism, and the results of investigations in many instances of water borne infection are equally convincing that under other natural conditions to which drinking water is subject the typhoid bacillus may remain alive and virulent for a considerable period of time.

An instance of its persistence in well water was reported by Kubler

and Neufeld, who in 1898 isolated B. typhosus from a well which had been contaminated by washings from a chamber used by a typhoid patient. Four weeks later they again isolated an identically similar organism and as fresh infection in the interval was excluded they conclude that in the often occurring combination of soil and water the bacillus may remain viable for at least four weeks. Tavel cites a case where apparently the water of a public supply became infected in the pipes from negative pressure and remained infective for several months.

In a single house supplied by a private pipe arising twenty inches from the end of the main, typhoid cases recurred long after an epidemic which had visited the town had subsided. This continued from October to April, seven cases in all occurring. At this time the blind end was exposed and found filled with slimy water, a sample of which was sent to the laboratory, where B. typhosus was found and identified. In this instance typhoid bacilli had apparently persisted and remained virulent in a public supply for five months.

The fate of typhoid bacilli in public water supplies is naturally a question of great importance, not only from a scientific standpoint, but economically as well, for on this is based, partially at least, the principles of water purification in which the problems of time, distance and natural purification of streams largely enter.

According to Sedgwick the longest well established distance which typhoid germs are known to have traveled to cause infection of water supplies is fifty-seven miles—in the case of the Detroit epidemic of 1892. The greatest assumed journey—one hundred and thirteen miles—from Oil City to Pittsburg. The same authority states, however, that distance is a secondary consideration and no limit can be placed on this if the rate of travel is fast enough. In other words, it is a question of time alone, and examples of the influence of this factor are seen in numerous epidemics. In Lawrence, Mass., a water borne epidemic occurred after the water had been subjected to the purifying influence of a storage reservoir for one week. In 1892 an epidemic at Detroit resulted from the dredging of old sewage deposits from the bottom of the Black River at a distance above the city requiring ten days for passage. A water borne epidemic of over 1,000 cases in Grand Forks, Minn., was caused by the removal of accumulated sewage several months old from the pipes of a city sixty miles above. At Covington, Ky., the water of the Ohio River, more or less polluted, is kept in

storage basins at times as long as thirty days, and yet the city suffers severely from typhoid fever, due apparently to infected water.

These and numerous other instances point quite plainly to the fact that while bacteriological experiments may indicate that the majority of typhoid organisms quickly perish in water, it is impossible by any means yet devised to predict with certainty at what time an infected natural water will become safe for human consumption under the innumerable combinations of circumstances and conditions to which such water is prone. And it is obvious that whether the longevity of the typhoid bacillus be small or great, so long as the streams from which raw drinking water is obtained continue to be the common carriers of accumulated wastes of the communities along their course, which are acting merely as relay stations to myriad generations of typhoid bacilli in their progress from source to outlet, typhoid fever will continue to be a water borne disease.

The remedy for the condition, however, lies not so much in the prevention of all contamination of water supplies—an obvious impossibility, but in the purification of the water prior to use. Investigation has shown that a large number of the water borne epidemics would have occurred even if the streams in question had been protected from the controllable gross contamination of city sewers. The epidemics of Plymouth, Ithaca, Lowell and Butler, in each of which over 1,000 cases resulted from a single case in an isolated house, above the intake of the city supplies, are typical examples of this. Moreover, while the result of concentrated infection borne over a short distance is well understood, very little is known about the effect on a community of a small amount of infection carried for greater distances. In other words, a town or city having an untreated water supply from which all proximate infection has been excluded may still suffer from typhoid fever due to a far distant and much diluted infection in such a manner that the infective agent will remain undetected.

It is not known how many typhoid bacilli are necessary to produce the disease, and as advanced by Rosneau, while a much diluted and attenuated infection may not have the power of directly causing the disease, occasional typhoid bacilli taken in water may for a time remain latent, and give rise only to apparently sporadic cases of the disease, when the infected individuals are subjected to some depressing influence. In other words, this is a possible cause of bacillus carriers.

While it is not the purpose of this paper to discuss the different methods of water purification, the efficiency and results obtained in the use of combined storage and sand filtration plainly indicate that at least as far as infection conveyed by public water supplies is concerned, typhoid fever is indeed a preventable disease.

From water itself as an infective agent, a consideration of its natural combinations naturally leads, under many of our public sanitary systems, to a study of the persistence of typhoid bacilli in sewage, feces, dirt, mud, dust, ice, oysters and cadavers, any or all of which may have a more or less intimate association with certain types of public supplies. The frequent failure to cultivate B. typhosus from the feces in undoubted cases of typhoid fever has led a number of observers to believe that not only were the intestinal lesions not the chief source of the bacilli, but that they occurred in the feces in large numbers much less frequently than commonly supposed.

Lentz and Tietz in the examination of two hundred and five typhoid stools were able to isolate the bacillus in but 15 per cent, while others have found it as low as 2 per cent. But, while undoubtedly there are instances in which the bacilli may be absent or in very small numbers only, the many difficulties in isolation would suggest that negative results be received with caution and typhoid stools be regarded as practically always infective.

In feces and sewage the typhoid bacillus does not find a favorable environment, and in general the close association with enormous numbers of intestinal bacteria and their products cause its rapid disappearance. Park states that it is unusual to isolate typhoid bacilli from feces if more than six hours have elapsed before examination. MacConkey (1902), investigating the longevity of the typhoid bacillus in sewage, found that in the raw unfiltered product it did not live after thirteen days, and in one series of experiments it could not be found on the sixth day or later. On the other hand, the coating of mucus or albuminous material received from the intestinal contents may act as a protecting envelope in an environment, such as water.

An interesting instance was reported by Levy and Kayser in 1903. The stools of a typhoid patient were placed in a cemented vault between September 8th and 13th, 1901; as the patient was then removed to another locality for treatment it is presumed that no further infection of the vault occurred. The contents of the vault were removed

and placed on garden earth as manure on February 6, 1902. When this became known the local physicians took specimens of the soil in which the feces had lain and sent them to the laboratory for examination, where B. typhosus was recovered from them. In this instance the organism had persisted in feces, or feces and soil together for at least five months, with a temperature ranging from below 0 to 11° C.

The results of practically all experiments performed with soil indicate that in this most frequent receptacle of infection typhoid bacilli are capable of prolonged existence.

Firth and Horrocks, in 1902, reported a number of elaborate experiments in which natural conditions were closely followed. Inoculating the soil with an emulsion of typhoid bacilli and keeping it moist with rain water they were able to recover the bacillus up to the sixty-seventh day, and up to the fifty-fifth day even when the ground had been frozen a part of the time. Using the soil from around a drain and moistening it with raw sewage, the organism was recovered after sixty-five days, although the ground had been frozen for several days. In dried soil the bacillus did not persist as long as in moist, but lived twenty-five days after the completion of the drying to such a consistency as to be blown about as dust. Harrison and Harrison, in India, showed that in even absolutely dry dust the bacillus lived over four and one-half days, and for three days when exposed to sunlight.

The viability of the organism in soil and dust is closely related to water borne infection. Typhoid excreta deposited on the banks or in the vicinity of streams, may so infect the soil that it remains infective until such time when by rain or thaw the infection is washed into a water course from which a public supply is obtained, as occurred in the well known epidemic of Plymouth.

Investigating the longevity of typhoid bacilli in cadavers, Loesner working with the bodies of pigs, placed the spleen of a typhoid patient in the cadaver, which was wrapped in cloth, enclosed in a wooden box and buried to a depth of five feet. In this instance he found the bacillus after ninety-six days, but noted no tendency to infect the surrounding soil.

As is well known, typhoid bacilli are resistant to freezing, and the part played by ice in the causation of disease is naturally of both interest and importance. But, while there are a number of isolated instances of seemingly authentic ice infection, of which that of the St.

Lawrence State Hospital is an example, these are comparatively few, and Sedgwick and Winslow after reviewing the literature, express the opinion that no epidemic of typhoid fever has ever been satisfactorily traced to such a source. These observers further state that, as a result of their own series of quantitative experiments, they consider the outlook on this subject decidedly reassuring, and that under the general condition of collecting, handling, storing and consuming both natural and artificial ice, typhoid infection from this source can but infrequently occur. They found that not only was there a reduction of 99 per cent of the typhoid bacilli during artificial freezing, but state that under natural conditions the mere physical phenomenon of that process causes a casting out of 90 per cent of all the organisms originally present in the water. And for the reason that the pathogenic germs in the most highly polluted stream are comparatively few, the probability of any remaining in the ice is small. The long period of time, moreover, usually elapsing between collection and consumption, is a strong factor in the disappearance of contained organisms. Park found that at the end of four weeks the percentage of reduction of typhoid bacilli in ice was 99.996, and reached completion in six weeks. The chief danger from this mode of infection undoubtedly lies in the early use of a highly infected product, such as might be due to extreme carelessness in the manufacture of artificial ice or the harvesting of natural ice from a grossly polluted water.

In addition to ice as an indirect mode of water borne infection there arises the subject of shell fish, among which of chief importance are oysters. It has been estimated that a yearly crop of these along the Atlantic and Gulf coasts amounts to over 25,000,000 bushels, and with the degree of sewage pollution to which their natural environment is subjected the frequency of typhoid infection from this source is readily appreciated. If by some happy chance the oysters escape contamination in their home waters this oversight is quickly remedied by the highly interesting manner in which they are fattened for market. Apparently the most efficacious being to plant them in water in proximity to a sewage outlet. In the words of the dealer: "The dirtier the water, the fatter the oyster." That sewage contamination of this variety of food is common and frequent was positively demonstrated by a series of experiments performed in the bacteriological laboratory of the Boston Board of Health in 1906. In clams obtained directly from the beds in

the vicinity of Boston Harbor, or bought in the open market, sewage organisms were found in from 60 to 100 per cent in the different lots examined. Not only must typhoid bacilli frequently be injested by oysters and claims, but they are capable of surviving therein for considerable periods of time. Foote found that in oysters inoculated and kept at 50 and 60° F., typhoid organisms lived for twenty-eight days in the shell juice and eight days in the stomach.

Complete sterilization of shell fish is supposedly accomplished by the various processes of cooking, but that such is not always the case was conclusively shown by the cooking experiments of the Boston Board of Health in 1906. In these, oysters, clams and lobsters known to be contaminated were subjected to a number of methods of preparation, and the reduction in sewage organisms noted when the articles were subjected to varying degrees of heat for different intervals. It was found that particularly in steamed clams and roasted oysters complete destruction of sewage organisms was by no means accomplished within the time and with the degree of heat required in these processes, and that a number may even survive the time and heat frequently employed in restaurants for the preparation of oysters and clams in the form of stews, and while sewage organisms are slightly more resistant to heat than typhoid bacilli, these experiments indicate the possibility of infection from this food after cooking as well as when raw.

It is in connection with indirect contact infection that the viability of typhoid bacilli on various fabrics demands attention, and that this may be the means of dissemination is shown by the case cited by Parkes in 1903. In this instance some blankets last used in military services in South Africa were sold under emergency without being cleaned, a number going to a training ship. An outbreak of typhoid fever occurring soon after on the ship, a number of the blankets were sent for examination to Klein, who found B. typhosus present on them. The period of time between the previous use of the blankets and the finding the bacillus was about six months.

Firth and Horrocks found the organisms to survive seventy-four days on khaki and eighty-seven days on blue serge, when these were inoculated with emulsions of bacilli; when inoculated with typhoid stools the bacilli lived seventeen days. It is not, however, in the long survival of the bacillus that the chief danger from this source arises. But rather in immediate contamination of the hands and clothing of

those handling the bedding or similar articles in contact with typhoid patients. This is undoubtedly a frequent means of infection, not only to those in immediate contact, but in turn to those with whom they associate.

That various insects, the chief offender among which is the house fly, should find food and human excreta equally desirable as feeding places is not only a regrettable fact from an esthetic standpoint, but a serious one in the spread of disease in general, and typhoid fever in particular. From excreta to flies and from flies to food is a cycle in the life of the bacillus from which typhoid fever richly deserves its title of a filth disease. In fact, it is only under conditions in which the most ordinary sanitary precautions are for some reason neglected that any considerable opportunity for fly infection occurs; as, for example, the surface leakage from defective sewers and exposure of excreta from typhoid patients. In this manner military camps most frequently offer the conditions necessary for this form of infection. In his report on typhoid fever in camps during the Spanish-American War, Dr. V. C. Vaughn says: "Flies swarmed over infected fecal matter in the pits, and then visited and fed upon the food prepared for the soldiers in the mess tents. In some instances where lime had recently been sprinkled over the contents of the pits, flies with their feet whitened with lime were seen walking over the food." Direct evidence of this means of infection is given by Hamilton, who demonstrated the presence of typhoid bacilli on the bodies of flies who had visited a sewer in an infected neighborhood. Ficker found the bacillus capable of living for at least twenty-three days on the bodies of flies artificially infected.

Prophylaxis against fly infection, however, is certainly neither complicated or obscure; for while food is a first necessity, the typhoid dejecta must be handled, and flies we will always have, still a union of the three must only result from a total lack of the most ordinary precautions, in other words, common cleanliness.

As an example of typhoid infection through other parasites, the helminthitic theory, originating recently in France, deserves brief attention. This theory, the principle supporter of which is Guiart, ascribes the role of inoculating agent in typhoid fever, cholera and other intestinal diseases, to intestinal worms, chief of which in typhoid fever is the whip worm (trichuris trichiuria). The theory is based on the high percentage of whip worms found in typhoid cases by some inves-

tigators, and upon the fact that intestinal worms may wound the mucosa. It is assumed that the uninjured mucosa forms an impassible barrier to the bacteria which, however, may pass through these wounds. The theory claims that typhoid bacilli in the intestines are harmless unless parasitic worms are present as wounding agents. While some evidence appears to favor the supposition that intestinal worms may act as described, very little has been adduced to show that this is of any serious import in the etiology of typhoid fever.

Stiles, who examined the stools of two hundred typhoid patients in Washington, D. C., in 1906, found that 92.5 per cent of these showed no infection with intestinal worms, and but 7 per cent showed whip worm infection, an increase of but 1.32 per cent over the general frequency of whip worm infection. These findings fail in every way to support the theory, and much direct evidence is needed in order that it be generally accepted as having any decided bearing on the subject.

The last, but far from least important problem in the etiology of typhoid fever and over which control is gradually being assured against almost insurmountable difficulties, is the milk question. It is unnecessary to here emphasize the obvious suitability of milk as a culture medium; but that this most widely used article, which is in every way best adapted to bacterial growth and multiplication, should be liable to typhoid infection from almost every recognized source, in every known way in which such infection is transferable, is a circumstance which places milk second only to water as a means by which the disease is spread.

While it is impossible to arrive at a precise conclusion as to the total percentage of all typhoid infections due to milk, various epidemiological statistics place it as the second most frequent cause. Schuder, who collected the reports of six hundred and fifty epidemics, found that four hundred and sixty-two were spread by water, one hundred and ten by milk and seventy-eight by all other means. Raudnitz, of Prague, states that one-fourth of the epidemics of typhoid fever in Austria are due to contaminated milk. Crae, after an inquiry into the causation of six hundred and thirty-eight epidemics, found that in 17 per cent the infection was conveyed by milk. In Washington, D. C., during 1906, the United States Public Health and Marine Hospital Service, after an investigation of eight hundred and sixty-six cases of typhoid, reported that 10 per cent of all cases, or one-third of those in

which a cause could be definitely assigned, originated in various milk supplies.

The frequency of this mode of infection is necessarily great, both from the nature of the product and the manner in which it is handled and consumed. From the time of leaving the cow till it reaches the consumer, milk is liable to contamination with any and all forms of dirt; from the air, from flies and insects, the hands and clothing of farmers, dairymen, middlemen, dealers and drivers: from the vessels in which it is contained, from other milk with which it is mixed and the water with which it is diluted. Not only is every means thus offered for the entrance of bacteria into market milk, but the conditions necessary to their enormous multiplication before consumption are at hand. It is rare in cities that at least forty-eight hours and frequently seventy-two hours do not elapse between collection and delivery, and all too common that the temperature at which the milk is kept in the interval offers no impediment to rapid germ development. This is well attested by various city health laboratory reports on the bacterial contents of market milk. In St. Petersburg examinations of samples of milk as delivered at houses showed the presence of from 10,000,000 to 82,000,000 bacteria per cc. Samples of market milk in New York City have shown counts as high as 35,000,000 and London milk 32,000,000. In 1906 the average counts of samples in Washington was 22,000,000 and the maximum 307,000,000 per cc. In Boston previous to the adoption of a standard of 500,000 bacteria per cc. and a temperature of 50° F., conditions were similar

While the presence of any kind of bacteria in large numbers is unnecessary and not desirable in milk on general principles, it has not been definitely proven that the ordinary saprophytes which constitute the greater number of those present are in themselves harmful. Their number, however, is a most reliable guide to the possible chances of specific infection to which the milk has been subjected, and the condition under which it has been handled and kept. The presence in milk of enormous numbers of bacteria of any variety indicate that the sample is either dirty, old, improperly cooled, or all three. If dirty the possibilities of infection are obvious, if old or warm any infection that may have gained access has multiplied itself a thousand fold. For, unlike water, in which a few typhoid bacilli may rapidly die out, in milk a single bacillus, under favorable conditions, may multiply to such a

degree as to not only heavily infect the particular sample, but in addition any quantity of other milk with which it is mixed.

Although the comparatively short time elapsing between collection and consumption renders the question of viability of typhoid bacilli in milk of less importance, it is of interest to note a few of the bacteriological findings in this and other dairy products. As in water, isolation of the organism from market milk is extremely difficult, and Reynolds, then commissioner of health, in 1902 stated that although special search had frequently been made for the typhoid bacillus in Chicago milk during the last eight years, it had been found only three times. In 1905, Conradi found the bacillus in milk from a bakery which had supplied persons who had acquired the disease. Eyre demonstrated the ability of typhoid bacilli to multiply in milk freshly drawn from the cow under aseptic precautions. In one instance with a small amount of initial infection (seventy-eight typhoid bacilli per cc.), the numbers reached 60,000 per cc. in twenty-four hours, and 10,000,000 per cc. at the end of forty-eight hours. Bruck, in 1903, found the bacillus alive in the cream separated from artificially infected market milk after ten days, and in butter made from the cream twenty-four days.

But, while the behavior of typhoid organisms in milk after entrance therein may be of secondary interest, the various ways in which they may enter is of the first importance. While somewhat general, the statement is nevertheless true that every time milk is touched, handled, contained in or exposed to any agent, animate or inanimate, not aseptically clean in the ordinary sense, it is subjected to a possible typhoid infection. The multiplicity of ways in which milk may receive typhoid infection is best illustrated by the summary of milk epidemics prepared by Busey and Kober. In all there were one hundred and thirty-eight typhoid epidemics directly traceable to infected milk. "In one hundred and nine instances there was evidence of the disease having prevailed at the farm or dairy. In fifty-four epidemics the poison reached the milk by soakage of germs into the well water with which the utensils were washed, and in thirteen of these instances the intentional dilution with the polluted water was admitted. In six cases the infection is attributed to the cows drinking or wading in sewage polluted water. In three instances the infection was spread in ice cream prepared in infected premises. In twenty-one instances the dairy employers also

acted as nurses. In six cases the patients while suffering from a mild attack of enteric fever, or during the first week or ten days of their illness, continued at work. In one instance the milk tins were washed with the same dish cloth used among the fever patients. In one instance the disease was attributed to an abscess of the udder. In two others to a teat eruption and to a febrile disorder in the cows. Four originated in creameries, and in one the milk had been kept in the sick room." By this summary it appears that by far the most frequent manner of infection lies in the direct and indirect contacts from those suffering with some form of the disease, and it is here that the disease in the early prodromal stages and the various unrecognized, undiagnosed and consequently untreated forms of typhoid infection assume a significance that cannot possibly be overestimated. And this does not cease to operate when only those handling milk are themselves infected; the same hands which care for the sick, at the farm, dairy and store, frequently collect, handle and dispense the milk or clean the vessels in which it is contained.

In the light of what is now known about bacillus carriers and the vague, unrecognizable nature of many typhoid infections, it is obvious that any person, ill or in health, may be regarded as a possible source of typhoid organisms, and for the same reason it is equally plain that the fewer individuals there are coming in contact with milk supplies, the smaller the opportunities for typhoid infection by this means become. It is estimated that in the United States during each year one person out of every three hundred has typhoid fever. Lumsden states that the city of Washington is supplied with milk from about 1,000 dairy farms at each of which the average population is seven persons; on this basis about twenty-five cases of typhoid fever a year may be expected to occur in those associated directly with Washington's milk supply, and a number of proportionate to size with that of other cities.

In addition to the infection of milk occurring through direct or indirect contact of those suffering with the disease, the other common means of typhoid dissemination operate through this medium. As in other foods, milk may be infected by flies, insects, dust, dirt and water, and it is in the poorly situated and unhygienic distributing dairies and city milk depots that this is most likely to occur.

In general, then, the opportunities for typhoid infection of milk are so many and complex, that it is only when every step in its collection

and distribution, and every individual engaged therein are under sanitary control and medical supervision, that this source of infection will cease to be the second most common in the etiology of the disease.

SUMMARY.

1. The initial source of typhoid infection is the typhoid patient in the broadest sense, and for a thorough understanding of the etiology and an ability to prevent dissemination, full knowledge of the manifestations of the disease in all its forms and the behavior of the specific organism in the human body are necessary.

2. Typhoid fever is a true septicemia, and the bacillus may be present in any part of the body and discharges therefrom from the prodromal stage until after convalescence.

3. The manifestations of the disease may be none, hardly perceptible, mild, severe, typical, and atypical. Persons in usual health may carry and discharge the bacilli for years.

4. The initial spread of infection results from: 1st, failure to recognize many of the mild and atypical forms of the disease: 2nd, failure to carry out efficient prophylaxis after the diagnosis is made; 3rd, bacillus carriers.

5. The most frequent means of dissemination is by water, the second by milk. In these and other articles in daily use the typhoid bacillus is viable for considerable but uncertain periods of time, and no limit can safely be placed on the duration of the infective power of any infected article under natural conditions.

6. In so far as the specific cause of the disease is definitely known and its means of dissemination understood, typhoid fever is a preventable disease, the only rational prophylaxis being not only the safeguarding of common food and water supplies, but the early recognition and isolation of infective individuals and the immediate destruction of the specific organism as it leaves the body.

TYPHOID FEVER IN STATE HOSPITALS AS ILLUSTRATED AT THE NEW JERSEY STATE HOSPITAL AT TRENTON.

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The manifestations of typhoid fever as a disease naturally appear in a similar manner wherever it exists. It is equally true, however, that the prominence of certain features in distribution, rapidity of spread and mode of dissemination are largely influenced by the surroundings encountered and circumstances under which it occurs; and the nature of these influences will to a degree determine the procedures necessary for its control.

An epidemic outbreak and a number of sporadic cases of typhoid fever at the New Jersey State Hospital at Trenton have pointed out certain features of the disease as it occurs in institutions, and have emphasized certain points of particular application as to what efficient methods of control under these circumstances should include.

Outlined in brief the features of an illustrative epidemic at the Trenton State Hospital are as follows: With the appearance of a case of typhoid fever in April, 1907, this being supposedly the first in the history of the institution, the principal interest at once aroused was in regard to the possible source of the infection, and, when a week later the Widal reaction had definitely proven the presence of four more cases, wonder over the origin of infection still further increased. Sanitary authorities were consulted and the seemingly inevitable water analysis, always conspicuous on such occasions, was diligently performed. It was also advised that an open spring located between a laundry on one hand and a public highway on the other from which a part of the institution's water supply was taken be covered over in order that "dust" might be excluded.

In the meantime cases had continued to occur. It was generally agreed that the whole affair was most mysterious; "Nothing much could be done because the source of infection could not be located."

At this time every effort was made in order that the individual cases be correctly diagnosed, no one was considered typhoid until satisfactorily proven so by a Widal, in which event nursing in a separate room on the same ward was instituted.

During the third month, there being 12 cases in all, and no abatement in view, a general consultation of various sanitary representatives was held, additional water analyses conducted and inspections made.

Conspicuous among the valuable results of these activities a cow-yard was found to be "dirty" and a number of outlying privies were located.

The source of infection, however, was as obscure as before. Among the various opinions expressed it was shown that "it was possibly the water, that the milk was suspicious, fly season was beginning so flies might have something to do with it"; "driven well water was surely above reproach"; "it couldn't be the spring water for even if it did contain colon bacilli, did not the chemical analysis show that it was all right?" "Perhaps some of the cases were only 'paratyphoid' after all."

Cow-yards, stables and privies were very diligently cleaned; water and milk carefully scrutinized and scientifically handled and examined from every standpoint and clinical diagnoses established beyond a shadow of a doubt. But—the water continued to be used, the raw milk was still served and the patients yet remained on the wards. The affair was so difficult to manage because the source of the trouble was so perplexing.

To still further add to this already over-vexed problem, about this time (during the third month) a public sewer running within 100 feet of the before mentioned spring demonstrated a stoppage in the pipe by overflowing through a manhole onto the street.

At this hint the spring was finally cut off, and it, together with the sewer, at once became the center of renewed vigorous investigations conducted in force by two separate sanitary bodies.

Here there appeared to be some scientific rivalry, for after some very exhaustive tests and collection of much data exactly opposite conclusions were reached.

By one it was demonstrated that the spring water was contaminated by sewage from the blocked and leaking sewer; the other held that there was no connection between this and the epidemic. High dispute over the troublesome and elusive source of infection continued, and masterly arguments on all points of the question were presented; but in spite of this highly animated and instructive discussion the number of typhoid cases steadily increased.

Finally, having received no real assistance or advice from any one where it might reasonably have been expected, in the middle of the fourth month with over 50 patients on hand, what appeared to be desperate measures were taken.

Every typhoid patient was removed to a floor of a wing specially set aside for the purpose, where he and his belongings were treated as dangerous and contagious.

Every "suspected" typhoid case was treated as a real typhoid case from the first symptoms and the fashion of waiting for Widals was abandoned. Patients were screened, kitchens were screened and typhoid excreta really destroyed; no article of food, milk or water was allowed which had not first been thoroughly boiled, fried, stewed or otherwise sufficiently *heated;* copious amounts of antiseptic solutions were placed wherever food was prepared and kitchen help were made to really clean their hands and keep them so. In fact every effort was made to simultaneously discourage the usual and everywhere prevalent indiscriminate mixing of feces, fingers, flies, foods and mouths.

Under this enforced regime, promptly within the incubation period, the epidemic after causing over 100 cases and 20 deaths subsided.

At last the much sought for source of infection had been found! The infection had evidently been in something which the affected individuals had taken into their mouths!

The conclusions to be drawn from such an occurrence are almost too obvious to warrant comment. But not only have instances similar in every essential feature always occurred in the past, but at present there is every indication that they will continue to occur with the same refreshing frequency in the future.

If instead of screening springs, testing sewers, examining water, analyzing milk, condemning cow manure and arguing *ad*

nauseum over the nice points of the source of infection, some steps are first taken to *stop* all these sources of infection, any or all of which are possibly concerned, no more of this infection can gain entrance; and if instead of regarding typhoid as a medical curiosity to be scientifically proved before being credited, the first suspicious symptoms of the first case and of all subsequent cases be regarded as dangerous calamities, the infection which is already present will not be further spread by contact.

An eminent public health official has likened a typhoid outbreak to a surgical hemorrhage. With the patient rapidly bleeding to death no one would dream of deciding on what vessels were concerned before applying the tourniquet.

No more in an institution with a typhoid epidemic on hand should time be wasted in a futile search for some obscure source before attempting to check it. It may be the water, but we are not sure; it may be the milk, but this cannot be proved; it is possibly flies, but we cannot demonstrate this. We do not know the exact source, it may never be found and what is more, at present we do not care what it is.

We do know that typhoid fever results from taking typhoid excreta into the mouth and can occur in no other way; if all the carriers of excreta (in every instance food, flies and fingers) be efficiently dealt with simultaneously and at once there will be no further epidemic, no matter which particular carrier is concerned and so far as the immediate emergency is concerned that is all is necessary.

The endemic and sporadic form of typhoid in institutions, however, differ essentially from the epidemic type in more particulars than the mere number of cases concerned, and in certain points of prophylaxis must be considered from a different standpoint. For in these forms the exact nature of the source of infection may be a point of very essential importance in preventative measures.

In addition to the obvious necessity of preventing contact infection from a case already observed, the occasional occurrence of typhoid cases, especially if repeated, raises the question of whether they are the isolated results of an infection accidentally carried in from without, or whether the source of infection (as pre-

eminently illustrated by bacillus carriers) is located in the institution itself.

If the latter, not only are further cases sure to occur, but the undiscovered focus may at any time give rise to an epidemic, and it must either be located or its presence excluded.

In the hospital at Trenton, subsequent to the described epidemic, there have been two instances of sporadic typhoid, neither in themselves of particular interest, but illustrating certain points in the occurrence of the disease in this form.

In May of 1909, a demented female inmate died after being confined to bed four days with an illness not clinically determined.

Fortunately, from the standpoint of subsequent prophylaxis, an autopsy was obtained and this illness was found to be typhoid fever at about the third week; a discovery a trifle late, but still helpful.

Since because the possibility of typhoid fever had not been considered clinically, no precautions during the illness of this patient had been taken and the preeminent characteristic of typhoid fever in institutions promptly demonstrated itself by the appearance of another case in a patient, who, it was subsequently learned, had assisted with the nursing of the undiagnosed first case and had varied these duties by distributing the ward trays and assisting at feeding operations.

This combination of circumstances is no exceptional instance, but one that without fear of contradiction can be said to occur not occasionally, but frequently, in any institution in existence. It is merely rendered unpleasantly conspicuous because instead of carrying the usually mild and harmless fecal matter, in this instance the ward tender dealt in excreta which happened to contain typhoid bacilli.

What the possible consequences of this state of affairs would have been if unrecognized is unpleasant to surmise, and are best referred to as "the epidemic that might have been." For since the possibilities were realized, after removing the already infected individual to a separate building, the other necessary prophylactive indications were fulfilled and an outbreak averted.

The first step was to recognize early any other cases that might occur on the ward and to prevent spread of infection from the original ward to other wards.

This was accomplished by twice daily regarding, with grave suspicion (and a clinical thermometer), every individual on the hall and by so isolating the entire ward with its 35 inmates and attendants, that it, and all its specially provided utensils became practically for two entire months a painfully antiseptic and much shunned separate building.

The second, no less urgent, indication was to detect or eliminate as a factor a possible primary source of infection in the neighborhood of the first case.

This possibility was investigated by serum reactions and fecal examinations of each of the 38 individuals, repeated at least five times during the two months' isolation period; and, although the results of all this was negative so far as detecting a focus of infection in the hospital was concerned, the equally satisfactory conclusion was reached that it was not there to be found, and the efforts further repaid by the detection of two individuals who from the previous attentions of the infected ward-helper had become acute bacillus carriers without contracting the disease.

In this instance, because adequate precautions were immediately taken and really enforced, no epidemic or further secondary cases followed; but had not autopsy determined the nature of the first case, the activities of the second individual been promptly checked and the other precautions taken before further damage was done, it is obvious that the factors for another epidemic would have been amply sufficient.

The second instance of sporadic typhoid observed at the Trenton Hospital, essentially similar to the first, serves as an additional illustration of the two essential features in the occurrence of typhoid fever in institutions; the necessity for early diagnosis and danger of contact infection.

This was the case of a male patient who after a suspicious illness of some days showed on the first trial a high serum reaction and shortly afterward had intestinal hemorrhages.

Here the condition was diagnosed, but for institutional purposes it had not been diagnosed in time; for again, promptly within the incubation period an attendant who had cared for the patient, developed typhoid fever. No further cases followed because the same methods of isolation and quarantine adopted in the previous instance were again rigidly enforced.

Even in such instances as those given, where cases arise at long intervals and in entirely separate parts of the hospital, the occurrence of two or more sporadic typhoid cases in an institution at once suggests the possibility of bacillus carriers.

It is needless to comment at length on the great relative frequency with which these individuals are generally found; said by the German investigators to be three per cent of all recovered typhoid patients and by Park to be one in every 500 of all persons; but in institutions the subject is one which is particularly applicable.

It may be said, in passing, that following the epidemic in the Trenton Hospital, 50 recovered patients furnished two chronic bacillus carriers (a frequency of four per cent). But since these individuals were discovered and properly kept in isolation until death two years later no results of their activities were observed and an illustrative instance of bacillus carriers in insane aslyums may be quoted from the investigations of Nieter and Liefman in an asylum of Germany[1] where the most extensive systematic studies of the subject have been made.

In this institution, previous to the investigation, typhoid fever had been endemic over an extended period. In spite of all sanitary regulation of the water and food supplies, prompt isolation of all clinically recognized cases and thorough methods of disinfection, the disease continued to occur from 1901 to 1905. Sixty-three cases in all, and a final epidemic of 35 cases occurred; the condition finally necessitating a systematic investigation.

This was conducted by means of repeated bacteriologic fecal examinations of each of the 900 inmates, and lead to the discovery that among the 250 women patients of a certain wing in which the disease had been most prevalent, seven of these individuals were chronic typhoid bacillus carriers. This was an astonishing ratio of one carrier to every 35 individuals, but some months later further examinations demonstrated the presence of four more similar cases among the female inmates. It was thought that with the isolation of these 11 carriers, typhoid in the institution would cease. Contrary to expectations, however, shortly after, the disease again appeared and repetition of the whole series of exami-

[1] Nieter and Liefman, Munch. Med. Woch., Vol. 53, No. 33, p. 1611. Same, Vol. 54, No. 33, p. 1622.

nations resulted in the detection of still further carrier cases in two more female inmates, giving in all 13 positively demonstrated chronic carriers among the total 900 inmates. A source of infection, needless to say, beyond detection save by laboratory methods.

Although this instance is doubtless extreme in the number of carriers discovered, it is still but one of very many essentially similar instances demonstrated in institutions.

Indeed, it is noteworthy that most of the original investigations of the subject were made necessary by continued endemic typhoid in asylums. Although not as yet demonstrated in this country, the universal frequency with which carriers have been found in the German institutions, indicates in no uncertain manner that in any institution where typhoid occurs with any frequency these individuals may be expected and must be searched for.

What to do with chronic carriers in institutions after they are detected also seems to have been more nearly solved in Germany than elsewhere. As a substitute for the inefficient treatment by medication and the irksome and uncertain method of continued isolation, Dehler[2] was the first to suggest and carry out cholecystostomy as a remedy for the condition.

In Dehler's cases the operation was performed on two women carriers who previously had caused repeated outbreaks in an asylum, and who because of untidy habits were unmanageable in isolation. Following incision and drainage of the gall bladder, typhoid bacilli which previously had been constantly present in the feces, completely disappeared after the fourth and ninth day, respectively; the operation resulting in permanent cure in both instances.

The exceptional opportunities for carrying out this procedure in institutions are obvious and it must appear as not only the most rational method of treatment, but one which under the circumstances is perfectly justifiable.

But, aside from the phases of typhoid fever in State hospitals which present each it's own particular problem to be met in it's own particular way; the checking of epidemics regardless of source; the searching for and eliminating of a particular source of

[2] Dehler, Munch. Med. Woch., Vol. 54, No. 16, p. 779. Same, p. 2134.

infection in endemic and sporadic forms; and the special consideration of bacillus carriers; what are the most essentially important factors generally applicable to the whole question?

In prevention of infection in institutions, as nowhere else is demonstrated the absolute necessity for early diagnosis on the one hand and the possibilities of contact infection if this is not done on the other; and to each of these factors of early diagnosis and contact infection under hospital conditions a special meaning must be given.

In State hospitals early diagnosis of typhoid fever does not mean as elsewhere, recognition of more or less suggestive symptoms and an early demonstration of some specific scientific test.

If prevention is to be worthy of the name, early diagnosis here means the recognition and clinical application of the fact that any and every illness, regardless of symptoms and manner of occurrence, not otherwise adequately and fully explained, is a possible case of typhoid fever and must be clinically regarded and handled as a *real* case of typhoid fever until proven otherwise.

Laboratory methods are valuable and necessary, but under such circumstances their proper function is not to make the first decision. They assume their proper relationship to the clinical diagnosis of typhoid fever in institutions only when used to confirm or disprove the nature of a suspected case *after,* and not before, prophylactive measures are taken.

For among all the possible means by which typhoid infection is conveyed in general, there is in institutions always one, which if not prevented, will at once operate in every instance no matter by what means the original infection gains entrance, or through what other agents it continues to operate.

This mode of dissemination among a large number of closely associated and uncleanly individuals is contact infection with a special significance.

Every case of typhoid fever occurring in an institution subsequent to a given primary case, where the common food and water supplies are once rendered innocuous as they first reach the institution, is due to preventable contact infection and can occur in no other way. For it matters not, so far as the credit of the sanitary management and ultimate results are concerned, whether the infection of a given resident individual results from his direct

bodily association with a primarily infected person; or whether the latter's infected discharges are conveyed to him in a round-about manner through the intervention of a second individual; or are carried by flies or otherwise indirectly conveyed either to him or to the once safe-guarded food and drink which he receives.

It is in each instance an infection resulting from failure of prophylaxis within the hospital itself; a hospital contact infection occurring under official medical supervision possessing full executive power.

The prevention of entrance of an initial infection into an institution is frequently impossible, the difficulties of the entire subject are great and the criticisms many. Whether justly or injustly deserved the possibilities of credit to the administration are small and the probability of censure great.

But whatever the circumstances may be, and no matter for what other conditions the management is held accountable; by early diagnosis and prevention of contact infection in every typhoid case that occurs, it is within the power of the administration to take such steps that will once and for all decide that no matter how disastrous subsequent events may be, or to what particular cause they may be due, they will be shown on investigation not to have arisen from preventable causes within the institution itself.

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(From the Pathological Laboratory and Wards of the New Jersey State Hospital at Trenton, New Jersey, U. S. A. Dr. Henry A. Cotton, Medical Director.)

Some peculiar nucleolar and cell alterations in the ganglion cells of the cerebral cortex.[1])

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With 3 plates.

The presentation of subjects by means of single isolated observations, while as a rule objectionable, is nevertheless justifiable when the purpose is to record a certain combination of clinical features and anatomical findings not previously observed; and this the more so in the field of psychiatry where as yet correlation of clinical and anatomical data is limited.

It is believed that certain of the histologic features here described have not been before specifically mentioned in connection with a psychosis; nor so far as ascertained are references to these changes in any connection in the literature other than limited.

The subject must therefore be largely presented as a history of a psychosis, description of the histologic alterations and such conclusions as seem warranted from the manner of pathologenesis in the few recorded instances, other than psychoses, in which similar alterations have been observed.

Before describing the present case and its findings it is in order to call attention briefly to the structures in which the unusual pathological changes are in this instance displayed, to note the infrequency of recorded similar alterations in them and to comment on such changes as have already been described.

It is a noteworthy fact that with few exceptions, even in the descriptions of systematic and classical histo-pathological researches on the nerve cells of the cortex, not limited in scope to a purely psycho-pathological connection, as well as in the numerous reports of cell studies from isolated instances of a great variety of conditions, the subject of nucleolar changes of a definite nature are scarcely, if ever, mentioned.

That such changes are indeed rare, if not unknown, among the conditions most frequently producing organic alterations in the cortical nerve elements in association with phyic disturbances must be conceded from their total absence of description among such studies as those of Alzheimer, and those from the laboratory

[1]) Read at the Annual meeting of the American Medico-Psychological Association, Atlantic City, N. J., June 1—4, 1909.

of Nissl on such conditions as general paralysis, arteriosclerosis, senile brain atrophies and scleroses and epilepsy.

From this and from their comparative immunity even in the more severe forms of various experimental lesions it would seem that the nucleoli have an inherent power of resisting to a marked degree the numerous delaterious effects to which the cells may be subjected.

It is a fact of common observation that in many of both acute and chronic degenerative and destructive changes of various types which so greatly alter the structure of nerve cell body and nucleus, the nucleolus retains not only a relative degree of its normal contour and staining reaction, but frequently in so conspicuous a manner that it may represent the sole remaining structure recognizable in the end stages of cellular disintegration.

While as before indicated, references to previous observations on the subject of specific nucleolar alteration are meager, two types of such changes, both designating a double or multiple quality of the nucleolar body, but fundamentally different in origin and having no reference to psychoses, are recorded: One type is mentioned by Marinesco and Levi in studies of embryonic phenominia; the other s noted by Marinesco, Achucarro and others in certain toxic disturbances of nerve cell structure.

The former variety of alteration includes certain nucleolar types found in various cellular species of central nerve organs free from diseased conditions, which while not abnormal in a strictly pathological sense, must in certain of the cell species at least, be regarded as instances of departures from the usual forms.

Such types having to do chiefly with the processes of cellular developement their significance is seen in the manner in which the embryonic cell structure is transformed into that of adult type.

In these changes the cellular species to which any given cell or cells belong must be considered, for that which is normal when present in one type does not hold with elements of others differing in function and anatomical distribution at a similiar period of developement.

In this connection Marinesco[1]) in his studies of fetal nerve cells states as a general principle that in proportion as the nerve cells develope the nucleoli diminish in number and the number of nucleoli in adult cells of various cellular species is inversely proportional to the degree of specialization of function.

In this manner while the small poorly differentiated cells of the sympathetic and spinal ganglia may and do retain their fetal multiplicity of nucleoli even after complete developement, the more highly specialized cells of the anterior horns of the cord, cells of Purkinje and the pyramidal cells of the cortex, which in the embrymic state also contain multiple nucleoli, at a certain period of developement loose this characteristic and end by having but a single nucleolus or rarely two.

From such facts it may be argued that when examples of a highly differentiated cell type, such as the larger cortical pyramids of the adult, are found to present phenomina of developemental processes such as double or multiple nucleoli they may be regarded as elements which have retained characteristic of the embryonic stage, and in fact represent types of cellular anomalies.

[1]) Marinesco, Journal für Psychologie und Neurologie. Vol. V, 1905.

Another explanation of such forms among the cells of higher types is given by Levi[1]) in his classification of cells based on the chromatin arrangement in the nuclei.

In this the nucleoli, consisting of almost pure chromatin, play an important role and indicate more or less distinctly into which group of the classification different cells are placed.

The first group is distinguished by a reticulated chromatin, as in such elements as the granule cells of the cerebellum.

The second includes the cells containing nuclear condensations of chromatin in the form of granules, and two, three, or four nucleoli, one being larger than the others, such as are found in the cells of the fascia dentata, substance of Rolando and even in the small pyramids.

In the third and most highly specialized group, in which are placed the larger pyramids, the motor cells, and cells of Purkinje, the chromatin is concentrated into the form of a single homogeneous spherical more or less central nucleolus, and forms in fact the familar nuclear and nucleolar picture seen in Nissl preparations of the cortex.

Levi, however, includes in the last group certain cells of similar type which may possess a double nucleolus, one sphere usually being larger than the other, and he regards this double quality of the nucleolus, especially when seen in the larger cells, as a transitional type between this and the second group of the lower order. In other words, cells belonging to a higher type, but which possess, or have retained, certain of the characteristics of cells of a lower degree of developement.

It will be seen that the theories of both Levi and Marinesco as applied to unusual nucleoli thus far considered are based on similar principles and that these have to do primarily with the developemental processes taking place in the nerve elements with resulting anomalies, and are not concerned with extrensic conditions affecting the cells after their complete formation is attained.

But, while as previously mentioned, destructive nucleolar alterations due to such causes are not common, a limited number of essentially pathological processes capable of producing them are on record. These conditions while of rather widely varying natures, have one important and fundamental principle in common. They are all essentially toxic in character, and the changes by which they are characterized depend directly upon the poisons of whatever nature with which they are associated, and while here as well as in the cellular anomalies of Levi and Marinesco multiple nuclear encloseures are characteristic, certain additional features definitely differentiate them from those of the developemental group.

The best known and most widely studied condition in which such nucleolar changes are found is rabies, and Siciliano, Cajal, Golgi, Marinesco and in greater detail Aschücarro[2]), have each described nucleolar pictures of similar nature.

These are characterized by hypertrophy and swelling of the nucleolus, fragmentation resulting in double nucleoli, multiple nucleolar corpuscles and dust-like

[1]) Levi, Rivista di Patologia Nervosa e Mentale. Vol. I, 1896.

[2]) Achücarro, Works of the Biological Laboratory of Madrid Part 3, Vol. VI, August 1908. Achucarro-Nissls Arbeiten, Vol. III, Part. I.

nuclear granules, accompanied by loss of the nuclear membrane, induration and other degenerative phenomina in the cell bodies finally ending in destruction of the cell.

In such changes are seen the evidences of the direct effects of an active specific virus, and the nucleolar alterations form a part of general cell intoxication, which, however, as shown by the studies mentioned, exerts a selective tendency on the cells of Ammon's Horn.

As examples of similar, but still more specific toxic action in the production of nucleolar changes are the experimental intoxications of newly born animals with strychnine described by Marinesco[1]). The changes described by him as occurring in the cells of the anterior horn show plainly the direct effect of the poison on the motor elements of the cord. In these are produced striking pictures of the over stimulated nucleolar structures leading to a process of budding, in which the nucleolus divides into a primary and secondary nucleolus or smaller multiple nucleolar corpuscles and granules, and in which secondary nucleoli are seen sprouting from, and attached to, the original nucleolus as well as free in the nuclear contents (Fig. 1, Plate III). These changes are ascribed by Marinesco to an emergetic nutritive stimulation of the nucleolus by the poison.

Bacterial toxins under certain circumstances have also given rise to marked nucleolar alterations in a manner preseumably similar to that of strychnine intoxication. By producing an experimental supurative meningitis by the injection of pus beneath the spinal dura mater of dogs Marinesco[2]) has observed in the spinal ganglia directly envolved in the inflammatory process cells with nucleoli showing similar distortion, budding, and fragmentation, (Fig. 3, Plate III).

In a similar process Sano noted in the spinal ganglia cells containing not only multiple nucleoli, but double nuclei as well, and in his opinion the same cause, namely the bacterial toxin which undoubtedly caused a proliferation of the connective tissue cells of the capsule, was capable of inducing the nuclear division in the nerve cells.

From the foregoing brief mention of distinctive nucleolar variations and alterations as described by the observers referred to, it may be seen that the conditions in which such types may be encountered, as applied to the pyramidal cells of the cortex, are of two general orders; the one concerned with the presistance in the adult of elements retaining characteristics of their embryonic existance, in other words cellular anomalies; the second resulting from the energetic action of various toxins on the fully developed cell and its structual constituents.

It is the purpose of the paper to record an instance of occurrance of such changes in connection with a psychosis and to assign the role of causative factor for the changes observed to one or the other of these conditions.

History of the Psychosis[3]). The patient, (E. S.) was a white man, age 47 years, single, a railroad brakeman and switchman by occupation. Admitted to the New Jersey State Hospital at Trenton February 23, 1908.

The family history: shows a strong tendency to alcoholism in nearly all the male relatives. The father drank to excess and was killed on the railroad while intoxicated.

[1]) Ibid.

[2]) Ibid.

[3]) By Dr. W. A. Taylor, State Hospital, Trenton, N. J.

A brother was an alcoholic and died of cirrhosis of the liver. The paternal grandmother, and grandfather, mother and one brother all died of tuberculosis. No history of mental disturbance in immediate or remote relatives.

Personal History: The patient was born in the United States, went to school and received a fairly good education, learned well and showed good ordinary mental capacity.

After leaving school he became a mill-worker. He held his positions well and was an efficient workman. Other than alcoholic excesses which began at an early age, there was nothing in the developement and early life of the patient to indicate that he was in any way abnormal or below the average in intelligence and ability.

He began to use alcohol while a yong man. While previously a steady drinker, the first excess occurred at the age of twenty-seven. Since that time he used alcohol constantly, and in large quantities. He drank daily, principally whiskey, and frequently became intoxicated. He wandered through different parts of the country working on railroads, but could not hold his positions. From facts subsequently learned he probably suffered on one or more occasions from delerium tremens or alcoholic hallucinosis. About two weeks before admission he went on a spree, wandered about, lounged around saloons, became troublesome and abusive, was arrested on a charge of drunkeness and sent to the county jail where it was noted that he was under the influence of liquor when admitted.

The onset of the psychosis begins at, or shortly before this time.

In the jail he was sleepless and restless, paced his cell, destroyed his clothing, and was generally untidy and filthy. He would not eat and was apprehensive and suspicious. He gave evasive answers to questions and probably had hallucinations or illusions of sight, all of an unpleasant nature.

At times he was expansive and talked of controlling railroads etc.

On admission to the hospital he was nervous and restless, but was well oriented, he stated that his troubles came from drinking, and that he wished to be treated for this condition.

The physical examination made at the time showed a man with poor general nutrition. Evidences of chronic alcoholism were indicated by a well marked tremor of the hands and tongue and gastric disturbance. There was also a slight transient paresthesia of the legs. Otherwise, however, as concerned motion, sensation, reflexes, special senses, gait, station and sterognosis there was no disturbance. The palpable arteries were not sclerotic. Veneral disease was denied and there was no detectable evidence of this. The heart and lungs were apparently normal.

The physical examination so far as any essential organic or neurological conditions were concerned was negative and nothing beyond the effects of alcoholism and lowered nutrition was evident.

Mental Status: During the first week after admission the demeanor was variable and the patient showed changes in his behavior during a single day, and from day to day.

At times he would stay quietly in bed, obey orders and requests, eat and sleep regularly, talk and answer questions well.

At others his actions would change entirely, and he would become restless, disorderly, threatening and abusive. At such times he could not be kept in bed, and constantly wandered about getting into trouble if not watched. He would destroy his clothing and bedding, at times constantly fumbling and arranging the bed clothes showing considerable anxiety and agitation. At such times he was filthy in his habits.

He had peculiar ideas and delusions of the Devil, thought the Devil was in his body and would try to expel him by spitting, coughing and violently rubbing his eyes and nose.

He was not disoriented and showed no clouding of consciousness. He recognized his surroundings and those about him perfectly.

Occasionally he would not talk except to answer questions; while again he would become loquacious and exhilarated, would talk freely of himself and boast of his ability to cure disease by reason of the Devil in him.

When not agitated or disturbed he could give an accurate and fairly connected story of his past life with dates and places, but showed distractability in response to his delusional ideas. His spontaneous conversation showed moderate expansiveness, and a tendency to disconnected flights of ideas.

„My name is E. J. S., Nicetown, Pa. I was master of ceremonies when I was fifteen yahrs old. Keep your mouth closed, God enters when the Devils goes out. It is a queer thing to say, but this hospital will not have an insane person in it when I go out. They are cured now, all will get well by the power of God alone. He has chosen me as a vessel to do his will and helps me banish the Devil from the world. I am glad you came in, the Devil just went out. The Devil enters in at the mouth, and you have to expel him either by your mouth, nose, eyes or ears. I saw him in the cell. If anyone sees him they fall over dead."

As shown in his conversation the patient at the time was mildly exhilerated, in answer to questions he said, „I never felt better in my life. I am not worried or afraid, I am my own self again, free and easy and full of life and happy."

Irritability was well marked and he would abuse and spit at those about him when compelled to obey commands.

Paranoid ideas — were not conspicuous, and did not form an essential feature of the psychosis.

Hallucinations — of both sight and hearing were present, although not continually. At times he would wander about his room or on the hall looking into corners and staring at the ceiling. He imagined he could see the Devil and hear him talk. He thought that he could find the Devil in the bed clothes, and then would constantly fumble and rearrange them. He also occasionally mistook persons and called the physicians by fictituous names.

At this time there were no evidences of deterioration or clouding of consciousness. Orientation was unimpaired, he recognized perfectly his surroundings, gave dates correctly, knew the names of his attendants and appreciated the nature of the institution. He recited the occurrences of his past life without essential errors, told of his various occupations, places of residence and spoke freely about his drinking. Memory of events subsequent to his admission was also unimpaired.

When quiet and undisturbed he showed cosiderable insight into his condition. He realized that he had hallucinations and flase ideas, and blamed drinking for all his trouble. He said that he was not insane, but „flighty" because of drink.

The essential points of the above examination were apparently the sudden onset, motor restlessness, irritability, occasional agitation, exhilaration, tendency to limited flights of ideas, hallucinations and somatic deceptions with good orientation, some insight and absence of evidences of deterioration or physical signs of importance. On these grounds the evidence was in favor of a manic-depressive psychosis colored by alcohol, and the diagnosis was so made.

During the three months subsequent to his admission, his condition did not improve. His behavior in general was somewhat similar to that already described, but it was noted that he showed less inclination to talk in a relatively clear manner, even occasionally.

There was no marked distractability, but his attention could not be held, and he would rarely answer questions relevantly.

He became more resistive and purposelessly abusive. He could not be kept clothed, and was almost constantly very dirty and untidy.

He was not productive, except in reaction to hallucinations, delusions and illusions which became more marked.

He imagined that he saw various animals, and would spit at them and try to kill them with anything in reach. If not watched he would attack any person about him. At times he would go through imaginary scenes of his past life, flagging trains, giving signals, shouting commands, etc. He would also assume religious poses and attitudes of defense.

He was not exhilerated during this period, and there were no flights of ideas. His conversation consisted chiefly in obscenities and profanity. He would swear loudly and violently at imaginary persons. He could not be induced to converse in any manner.

The condition in fact was characteristic of a continued delerium and at the fourth month after admission he had become disoriented, had lost grasp on surroundings, time, and passing events. He was entirely occupied with his own hallucinations and delusions, and showed no insight. His physical condition was poor and he lost weight.

Shortly after, five months after admission, it was noted that his physical health had become still more impaired. He developed a cough with muco-purulent expectoration and the lungs showed signs of beginning consolidation. The delusions and hallucinations continued, but were seldom expressed. At times they were of an expansive type, imagining that he was the Pope, Napoleon, etc. On the whole he became more quiet, although still abusive and resistive at times.

He refused to talk with his relatives when visited, would not answer questions relevantly, and sometimes not at all. He continued disoriented, took no interest in his person and paid no attention whatever to anything that occurred about him. He was not depressed, and there was no retardation. Physically he continued to fail progressivelly, night sweats and fever developed, and the pulmonary signs were much exaggerated. He lost weight rapidly and bedsores appeared.

He died October 9th, seven and a half months after admission.

The symptoms and signs of his last illness were approximately three months in duration; but from the type of the psychosis which doubtless marked the condition to a considerable extent, the disease probably extended over a somewhat longer period, and the time of the onset of the disease corresponded more or less closely with the change in demeanor and mental status noted at about the fourth month of the psychosis.

Summary: — A man aged forty-seven with a strong family history of alcoholism and tuberculosis developed normally and showed good ordinary ability and efficiency as a young man. Became early addicted to the use of alcohol, drank constatly and frequently to excess and suffered socially and physically from this cause.

Finally, after excessive drinking he suddenly developed a psychosis, at first resembling a manic-depressive type modified by alcohol, but without clouding of consciousness or delerium. A few months later physical impairment and signs of pulmonary tuberculosis appeared. At approximately the same time the picture of the mental condition became altered and marked hallucinations and clouding of consciousness with disorientation, complete disregard for person and events, and other indications of a continued profound delerium became the most conspicuous features. Death from pulmonary tuberculosis seven and a half months after onset of psychosis.

While it cannot be denied that various physical diseases are capable of sometimes influencing to a marked degree the symptoms and course of mental disturbances, it is not the purpose at this point to definitely assign the incidence of tuberculosis in the case as a specific causative factor for the change which undoubtedly did occur during the course of the psychosis.

It is desired merely to call attention to the fact that the patient was already suffering from the effects of one form of intoxication, namely alcoholism, and that coincidentally with the addition of another, and specific form the toxemia the mental symptoms were altered and assumed the form of a toxic delerium.

Whether or not it is justifiable to connect the organic changes observed with the intoxications as a cause and the mental condition as an effect must be judged largely on the character of the anatomical findings.

Autopsy: one hour after death.

Summary of the gross and microscopic findings of the organs of the trunk.

Extensive bilateral obliterative pleurisy.

External adhesive pericarditis.

Slight peritoneal effusion.

Moderate chronic aortic and mitral endocarditis.

Marked brown atrophy and fatty degeneration of the entire heart muscle.

Moderate aortic atheroma.

Advanced diffuse nephritis chiefly effecting the parenchymatous elements.

Chronic interstitial hepatitis with marked fatty degeneration and granular atrophy of the liver cells.

Complete tubercular consolidation of both lungs with one smal cavity at the right apex.

Marked wasting of all soft tissues of the body.

No tubercles found except in the lungs.

Cultures from the cerebro-spinal fluid negative.

Head: Scalp dry and anaemic, adherent to bone. Calvaria not unusual. Dura shows a preceptable degree of thickening over the vertex and has lost to some degree the normal semitransparency over the frontal poles; rather loosely adherent along the longitudinal fissure, and for a short distance on either side but can be detached without essential difficulty. Middle ears and accessary sinuses clear.

Pia slightly hazy over the vertex and flanks; most noticeable along the sulcal vessels. Over the cisterna is moderately thickened, but no exudate, and pia strips readily from the cortex without tearing. Fluid slightly increased in amount. The basal vessels show a slight general opacity of the walls, more particularly in the larger primary trunks. At the points of bifurcation the walls of the primary divisions show a mild degree of thickening, but no areas of atheroma or other gross changes. Tubercles not found either in the pia or on the walls of the vessels.

Brain of good size; weight 1490 gms. Configuration of the major convolutions and sulci shows no departure from the normal. The convolutions of the frontal and central regions of the convexities and flanks, show a readily perceptible, but not severe grade atrophy. They are narrowed and the adjoining sulci correspondingly widened and moderately distended with fluid. This is more noticeable from the fact that the remaining portions of the brain are quite free from these changes and present an almost normal surface appearance.

General consistency of the brain a trifle increased; to the touch feels flabby and inelastic; no localized areas of essential difference perceptible.

Section of the cortex a little paler than normal; white matter smooth and glistening. The floor of the fourth ventricle shows a small number of very minute reddish points over the left trigonum vagi, otherwise ependyma of both fourth and lateral ventricles clear; no granulations.

Pons, medulla and cerebellum negative. No focal lesions found in the fresh specimen or on dissection after hardening in formalin.

The findings of the autopsy as described were in themselves neither unusual or of particular interest. The two essential features being a fairly well marked brain atrophy in the frontal and central regions and an extensive pulmonary tubercular infection which had produced well marked evidences of a sevee general intoxication with a fatal result before any marked indications of necrosis at the primary seat of the process or secondary dissemination of infection had opportunity to develope.

Technique of microscopic examination of the Brain: Blocks of tissue were removed from the usual areas including the frontal, central, calcarine, hipprocampal and temporal convolutions and cerebellar hemispheres and fixed in alcohol, formalin and Zenker's fluid.

The Zenker blocks were embedded in paraffin and sections were stained with hematoxylin and eosin, eosin and methylene-blue and by Mallory's phosphotungstic acid

hematoxylin method for neuroglia. The formalin material was used for Marchi and Sharlach R. fat stains and Pal's Method.

The alcohol blocks were cut unembedded and stained by the original Nissl Method with methylene-blue soap solution.

The latter method gave by far the best results for the pictures encountered, and numerous sections were prepared with varying periods of fixation and cut at different thicknesses for purposes of comparison and elimination of artifacts.

The description of cell pictures and general cortical fields are made chiefly from these preparations cut at a thickness of 10 microns. The drawings were made from similar preparations with the aid of the camera lucide.

Histologic Findings: The histologic features of chief importance were confined almost entirely to minute changes in the individual elements and but little of note was observed in reference to the general structure. In the pia a moderate degree of chronic thickening of fibrous type was noted, but no indications of cellular infiltrations or characteristic lesions were observed. The larger vessels were likewise not noteworthy beyond a slight general thickening of their walls. The architecture and layering of the cortex was of usual type, and there were no essential departures from the normal in general arrangement.

In the detailed examination of the different areas it was at once noticed that considerable differences in the intensity of all the cell changes existed in different regions.

In the Purkings cells of the cerebellum and in both large and small cells of the calcarine areas the special nucleolar alterations were hardly perceptible, and the pyramids of the cornu Amonis showed them but slightly. In the temporal cortex the changes were moderately severe, while the cells of the first frontal convolutions and para-central lobules presented all grades of cellular change with a frequency and intensity that was in notable contrast to the other areas.

For this reason the description of both general and special cell alterations are taken chiefly from these areas as presenting them in their most characteristic form.

That the underlying process producing these changes was essentially degenerative and destructive as well as selective in its effects upon the nervous elements was shown by the marked character of the nerve cell changes and the disproportionately slight alteration in those structures, namely, vascular and interstitial, which are commonly found to accompany or account for lesions of the parenchymatous elements. For while there did occur a readily distinguishable cellular glia reaction, in which regressive forms were prominent, such as constantly accompanies organic changes of the central nervous system in general; and the endothelial elements of the smaller cortical vessels showed a moderate though suggestive tendency to increase in size and number, there was a total absence of severe gliosis, perivascular cell infiltration, essential arteriosclerosis, focal lesions or other alterations of like nature.

Among the cell changes in general were a great variety of types and these presented a complete range from elements but comparatively slightly effected to those in the end stages of distintegration, and which included all the various intermediate and transitional forms between the two extremes. For purpose of description, however, it is convenient to devide the alterations into two principal groups; one representing elements which had preserved to a certain degree their structural integrity, and the other as including various types of advanced degeneration and cellular death.

In all forms the nucleolar changes were noted with varying degrees of frequency and intensity, and it is to this feature and the enormous relative frequency with which the entire set of cellular alterations were observed that the interest of the findings is largely due.

The earliest and least destructive stage of the process, which eventually however, ended in unmistakable disintegration, was seen in alterations which are best described as indurations and shrinkage of the cells such as have been noted in certain phases of various experimental intoxications such as ricin, though naturally to a somewhat less

degree. The cells thus effected were always more or less distorted, both cytoplasm and nucleus were intensely and diffusely stained and the chromatin granules of the larger elements hardly distinguishable. The processes quite constantly were deeply colored, sometimes broken, frequently tortuous or irregularly swollen. The nucleus was commonly excentrically placed and the limits of the nuclear membrane and cytoplasm were almost, or completely obscured. Occasionally in addition to the general marked intensity of staining of the cytoplasm there were situated in the cell bodies a few irregular clump like masses of chromatin which showed an even darker staining reaction than the remaining portions of the cell and gave to it a deeply blotched or mottled appearance.

Not only were such-changes in the individual cells of a striking nature, but the notable selective tendency of the alterations for certain varieties of cells and the frequency with which it was observed among these elements constituted an additional feature of the picture. While observed to some degree in the cells of the outer layers, the elements chiefly affected were found far more numerously among the medium sized pyramids of the deeper areas. In this zone of the cortex scarcely a field was noted which did not contain one or more cells of this type, and it was by no means infrequent to find a large number of successive fields in which not a single pyramidal element had escaped. In this manner with high magnification the picture was that of a number of dark irregular nerve elements standing out conspicously from the surrounding ground substance.

It was in such cells that the nucleolar alterations were seen in by far the most characteristic manner and the frequency with wich these occurred in any given field appeared to be directly proportionate both numerically and in individual intensity to the alterations in the cells as a whole.

The nucleolar changes themselves as seen in such cells consisted in a condition by which the original single nucleolar body had given place to multiple nuclear encloseures, and from the evident manner of their formation these must be regarded as having their origin from the primary nucleolus by a true process of budding or fragmentation.

When seen in a passive rather than an active stage of the transformation, the cell, in addition to the general shrinkage and induration, presented a picture characterized merely by the presence within the nucleus of one or more small bodies possessing an identical staining reaction with that of the nucleolus, and in this stage apparently bearing no direct relationship to the original body. In number the secondary corpuscles varied, as did they also in size. Occasionally but one extremely minute granule could be detected. More frequently there would be two or three enclosures plainly visible, though always smaller than the primary nucleolus, and not infrequently the number would reach as high as four, five or even six distinct corpuscles of varying size (**Fig. 3, Plate I**). In such pictures, although the general condition of the cell and the appearance of the nuclear enclosures themselves suggested a possible fragmentation of the original nucleolus, there was no direct evidence that they had originated in this manner.

In other cells, however, showing the same general changes this could be verified and the different phenomina of the process followed through the various forms of transition from the earliest indication of nucleolar alteration to the terminal condition of apparent nucleolar multiplicity.

The stage of first inception of these changes, which because of the advanced stage in which the cells were usually seen was relatively infrequent, consisted in a simple hypertrophy of the nucleolus by which it became disproportionately large and presented a swollen appearance without alteration of contour. In a more advanced stage the form of the nucleous appeared changed and its regular round or oval outline gave place to a slightly irregular form which showed a slight but noticeable prominence or bulging at one point in the circumference. Such projections still later became more pronounced and took the appearance of small oval buds attached to the nucleolus by continuity of substance, either broad and distinct or delicate and attenuated, according to the varying stage of separation. In cells thus affected were frequently seen two or more of the secondary fragments extending outward in a linear beadlike formation from the original

nucleolus to which one of the corpuscles was still attached, while others were scattered through different portions of the nucleus.

It is in all such budding and fragmenting nucleolar forms that the resemblance to the nucleolar pictures described by Marinesco in his studies of experimental strychmic intoxication and suppurative meningitis, and by Achicarro in the cells of Ammon's horn in rabies is seen (**Compare Fig. 3, Plate I** with **Fig. 4, Plate III**).

Even aside from the nucleolus the alterations of the entire nerve cell are strikingly similar to those resulting from strychnine intoxication. In both is seen the induration and irregular shrinkage of cell body and nucleus, the deeply stained cell processes and the fragmented and budding nucleoli (**Fig. 2, Plate I** and **Fig. 1, Plate III**). Although the latter and the accompanying nuclear distortion is noticeably more conspicuous in the experimental conditions, there is still a marked general similarity in the processes of swelling, hypertrophy and division of the nucleolus, and the differences in intensity are no greater than might be expected between the results of a severe and acute intoxication with a poison such as strychnine and the more gradual and less intense type of intoxication as occurred in the present case.

In addition, however, to the pyramidal cells which presented both general and special indications of a toxic alteration, other types of cells were observed, which while also possessing more than one nucleolus showed but slight if any other apparent departure from the normal.

In contra-distinction to the selective tendency of the degenerative cell types to appear among the pyramidal cells, the second, and at first sight apparently non-degenerative forms in which special nucleolar qualities were observed, were confined with few exceptions to the deepest layer of the cortex among the polymorphous and fusiform elements.

While not so frequent in occurrance as among the frankly altered cells of larger size, the number of small deeply placed cells showing multiple nuclear enclosures was by no means small and because their presence alone in the absence of more suggestive changes would place them among the cellular anomalies of Levi, rather than among those altered by toxins, they warrant separate consideration.

Among the deep lying elements although rather infrequent examples were found which presented in a very incipient stage the indications of induration which had so markedly affected the larger elements, the marjority showed such slight and negligable changes that it is necessary to regard them as being nearly or entirely normal aside from the intra-nuclear condition (**Figs. 11, 12, 13, 14** and **15, Plate II**). As in the larger elements this was characterized by the presence within the nucleus of one, two or more secondary nucleolar corpuscleswhich corresponded indentically in staining reaction and general appearance to those observed in the other variety of cells containing them, and only differed in that while in the larger degenerated cells the actual process of fragmentation was frequently observed, in the smaller and otherwise normally appearing cells, pictures of this condition were seen with extreme infrequency and could be found only with considerable difficulty after prolonged search.

Cells of this type possessing multiple nucleoli and showing practically no indication of degenerative phenomina are comparable to the fetal nerve cells of the cellular anomalies of Marinesco and Levi. For aside from the general accompanying condition there is little to definitely differentiate them from such cells except a slight difference in the placing of the secondary corpuscles cells (**Compare Fig. 2, Plate III** and **Fig. 13, Plate II**).

This variation while not particularly striking is nevertheless suggestive of the dissimilarity of the two conditions. For while in the embryomic cell types the secondary nuclear enclosures lie distributed irregularly throughout all portions of the nucleus without definite relation to the principal nucleolus, the similar multiple nucleolar bodies in the cells of the present case were always situated to one side of the original nucleolus which was slightly displaced in the opposite direction; such an appearance suggesting that the secondary bodies were the result of a process of budding or division of the

primary nucleous similar to that occurring so characteristically in the large indurated cell types.

In speaking of the cell degenerations in general it was mentioned that these were divisible into two types. One of these has already been described as the various forms of induration and shrinkage, the second, a later stage of the first, indicates even more distinctly the severity of the alterations to which the cells had been subjected and offers additional evidence that the process to which the nucleolar changes are ascribed was of a selective and highly destructive nature.

Such cells, while found to some extent in various localities, still unmistakably followed the distribution of the degenerated pyramids of the frontal and paracentral regions and the two types of changes were most frequently observed side by side.

Indeed, transition forms between the two were readily distinguishable in elements which had retained the general indurated appearance of the earlier stage, but which had lost to a large degree their affinity for the stain. Such cells appeared as inconspicuous shadows with intensely irregularly swollen processes showing an identical staining reaction with the distorted cell body in which but the faintest indication of intracellular detail was visible. When any such detail could be detected however, the same fragmented or double quality of the still persisting nucleolus was plainly evident (**Fig. 1, Plate II**).

Other cells of advanced degenerative type were characterized by a markedly vacuolated condition of the cytoplasm. In some the vacuoles were small and numerous, giving a finely reticulated appearance to the cell body (**Fig. 6, Plate I**); in others the vacuoles were intensely conspicuous and frequently as large as the nucleus which was displaced or even absent, causing such forms to be hardly recognizable as nerve elements (**Fig. 3, Plate II**). In some which showed great displacement of the nucleus and disintegration of the cytoplasmic chromatin a resemblance to the axonal reaction could be detected (**Fig. 10, Plate II**). Among other forms showing terminal conditions were those in which the nucleus was extremely shrunken, intensely stained and surrounded by either a faintly stained protoplasmic body with a peri-nuclear halo or merely by a hardly discernible zone of almost unstainable dust like particles (**Figs. 5, 7 and 8, Plate II**).

Not only in such markedly destructive varieties of changes to which the last types belong, but in the entire picture of the microscopic findings there is evident the result of a process which from the first brought about a parenchymatous degeneration and destruction of a markedly severe grade and exerted a selective tendency to affect the pyramidal cells of the frontal and central regions.

These changes while in some respects slightly resembling those ascribed to chronic alcoholism are such both in character and intensity, that this cause alone is inadequate to explain their occurrance even aside from the more unusual features of the nucleolar alterations. The latter so far as ascertained have not heretofore been noted in connection with any psychosis and but rarely in other conditions, even experimental in nature (certain of which they most closely resemble) and when observed have always been with good reason ascribed to the direct action of the toxins with which the process was concerned.

In the present case there is equal evidence of two active toxemias which in themselves though of a different nature constantly produce wide spread organic changes.

From this and the similarity of the special changes observed in the nerve cells to those in similar elements of other toxic conditions foreign to psychical disturbances it is deemed justifiable to conclude that in the instance cited, the two factors, alcoholic and tubercular intoxication, were the agencies in the production of the special changes observed with an accompanying clinical picture of a prolonged delirium psychosis in a manner not as yet described.

Explanation of the plates.

Plate I[1]) Figs. 1, 2, 3 and 4. Betz cell and medium sized pyramids from the para-central lobule showing ultiplem nucleoli. The Betz cell (fig. 1), shows the early effects of induration and two irregular nuclear enclosures. In Figs. 2 and 4 the cells are much indurated, and the process of budding of the nucleolus is seen. In Fig. 3, fragmentation of the nucleolus has resulted in multiple small granules. The satellite glia in Fig. 2 is of regressive type.

Figs. 5, 6, 7, 8, 9 and 10. Small cells from the deeper zones of the frontal and para-central cortex showing the condition of the nucleoli and minor effects of degeneration.

One of the cells in Fig. 5 contains a cytoplasmic vacuole. The nucleus in Fig. 6 is greatly displaced, and the nucleolus shows swelling and irregularity. The protoplasm is finely vacuolated. Figs. 7, 8 and 10 show early forms of induration. Fig. 9 is an early stage of shadow cell type.

Fig. 11. Moderately indurated Betz cell with three secondary nucleoli.

Plate II. Fig. 1. Shadow form of indurated pyramid from the para-central lobule showing eccentric palely staining fragmented nucleolus and greatly irregular swollen processes.

Figs. 2, 3 and 4. Forms of vacuolated cells from the deep layers of the frontal and temporal convolutions.

Fig. 3. From the first temporal shows marked swelling and irregularity of the processes and two well marked vacuoles about which are condensations of stainable substance. The nucleus and nucleolus are not visible.

Figs. 5, 6, 7, 8, 9 and 10. Showing advanced forms of degeneration in the layer of the small pyramids.

In Figs. 5 and 7 the cell body is much swollen and faintly stained. In Fig. 5 (B) the nucleus is shrunken and greatly out of proportion to the nucleolus which is slightly enlarged. In the cytoplasm a few deeply stained granules remain.

In Fig. 6, the nucleus shows an abnormally rounded form and contains one secondary nucleolus.

Figs. 8, 9 and 10, show end stages of cells functionally dead. In Figs. 8 and 9, the nuclei appear as the most resistive part of the cell, but are greatly shrunken, indurated, and darkly stained in contrast to Fig. 7. In Fig. 8, the nucleus has become partially pyknotic.

Fig. 10. Cell showing marked displacement of the nucleus with disintegration of the cell body, somewhat resemebling the axonal reaction. There is a suggestion of vacuole formation.

Figs. 11, 12, 13, 14 and 15. Cells showing but slight changes beyond multiple nucleoli.

Figs. 11, 13, 14 and 15, represent cells from the polymorphous or fusiform layer.

Fig. 12, are cells of medium size from the layers of large pyramids.

Note the relative position of the primary nucleolus to the secondary nucleolar corpuscules in Figs. 11, 13 and 14, in contrast to those of Fig. 2, Plate III.

Plate III. Figs. 1, 2 and 3, after Marinesco. Fig. 4, after Achucarro.

Fig. I. Motor cell of the anterior horn of the spinal cord of a young dog intoxicated with strychnine, showing induration of the cell body, marked hypertrophy and budding of the nucleolus, and the formation of multiple nucleolar extrusions.

Fig. 2. Medium sized pyramidal cells from the ascending frontal convolution of a three months old infant, showing a central nucleolus surrounded by multiple nuclear granules.

Fig. 3. Cell from a case of experimental suppurative meningitis, showing two oblong nucleoli and one nucleolar granule.

Fig. 4. Cell from the stratum radiatum of the cornu Amonis of a rabid rabbit. Marked fragmentation of the nucleolus, and multiple nucleolar extrustions.

[1]) All drawings made with Leitz Apochromatic objective 2 mm, Compensating ocular no. 4 and Camera lucida; Nissl Stain.

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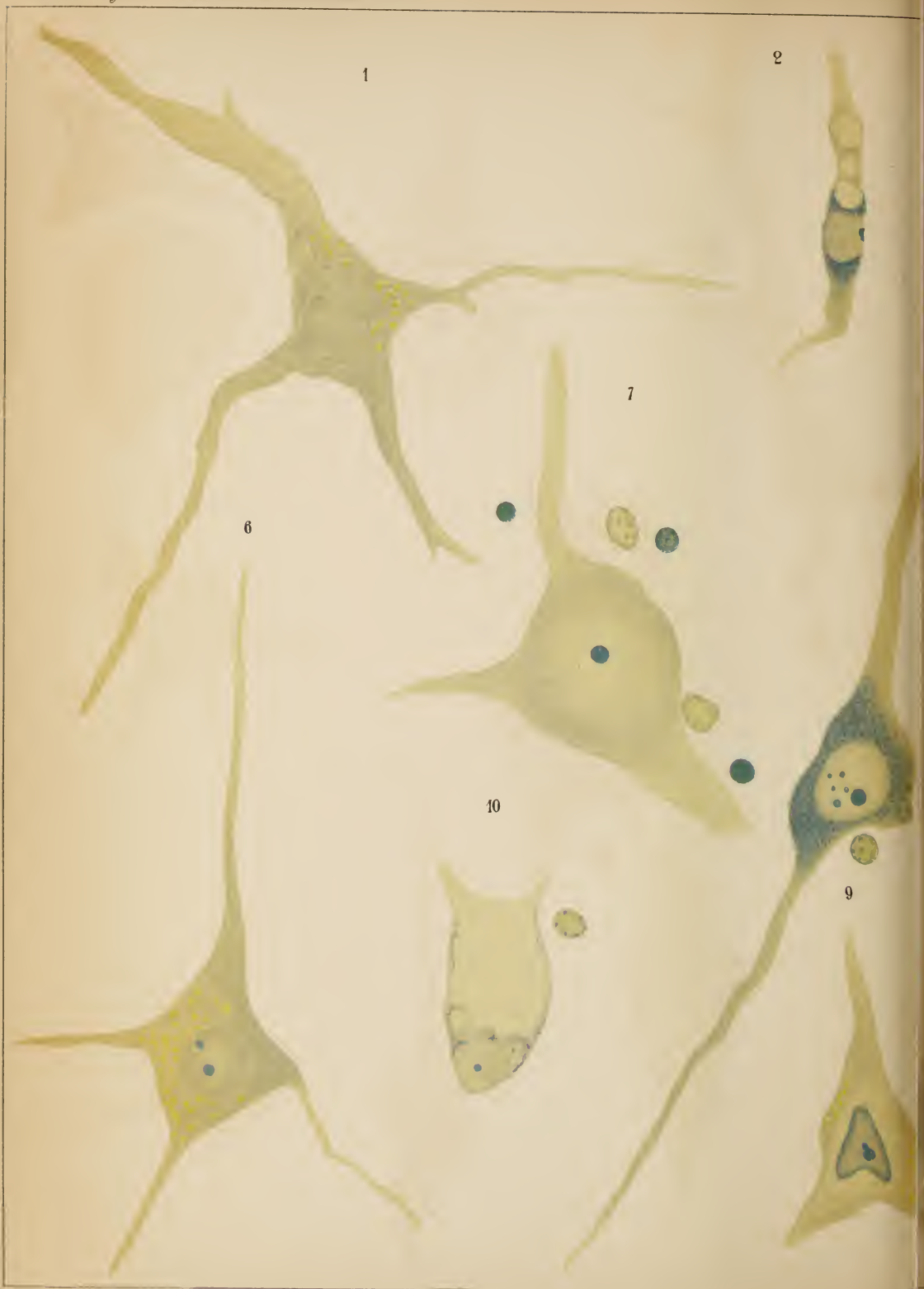

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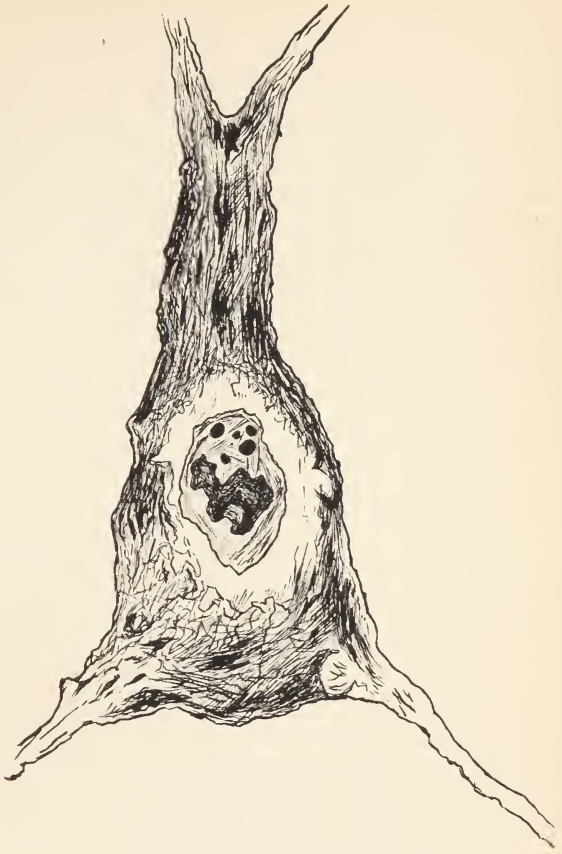

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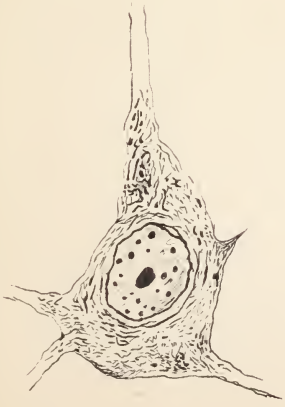

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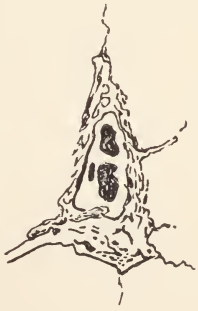

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SERUM TREATMENT OF EPIDEMIC CEREBRO-SPINAL MENINGITIS.

CASE REPORT.*

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The treatment of epidemic cerebro-spinal meningitis by means of Flexner's antiserum and the results attained, whereby a previous mortality of 75 and 80 per cent. was reduced to 20 and 25 per cent. including all types of cases in practically all stages, are now so well known that the reporting of a single case is in itself no longer of particular importance or significance. However, since the present instance is the first which has offered an opportunity for the serum treatment in Trenton and vicinity, and further, since in certain respects the treatment itself has been somewhat modified since the earlier recorded cases, a report of the present case and a brief consideration of the serum and its use may not be out of place.

The case furthermore presents a good example of all the principal points of the behavior of a severe type of the disease treated early with the serum, as well as illustrating quite typically all the essential immediate and final results of serum administration.

The case occurred in the practice of Dr. M. W. Reddan, with whom it was first seen in consultation and observed throughout.

REPORT OF CASE.

Patient—M. K., age 12 years; school girl. Previous history without importance save for the negative fact that at no time had there been any ear trouble or other significant recent illnesses which might have accounted for a secondary meningitis.

Present Illness—A very brief and indefinite prodromal period was observed on January 3, 1911; during that day the patient complained of a general tired feeling and slight headache. The actual onset occurred on the following morning (January 4), when the patient vomited frequently and repeatedly (twelve times). In the afternoon of the same day there was low fever (90 to 100 degrees). Toward evening the temperature steadily rose, there was intense headache, drowsiness and beginning retraction of the head. During the night a diffuse fine punctate erythematous rash made its appearance over the entire body, but faded quite promptly the next day. There were no convulsions, but occasional muscular twitchings and a spasmodic "cerebral cry" occurred at intervals.

When first seen in consultation with Dr. Reddan the patient was lying in partial coma on the side with all extremities in marked flexion and head sharply retracted. Temperature 103⅘ degrees by axilla; pulse 122, full and bounding; respiration 42, heavy and labored. The patient was almost comatose, could not be aroused and only moaned when disturbed. Partial neurological examination showed contraction of all flexor muscles; both knee jerks exaggerated; doubtful Babinski reflex; occasional spasmodic muscular twitching and well marked Kernig's sign. Tache cerebral was readily elicited and prominent.

Lumbar puncture was done at once and 15 c.c. of extremely turbid, grayish yellow, sero-purulent fluid under markedly high tension was withdrawn; firm coagula formed promptly in the tube soon after withdrawal.

*Read before the Mercer County Medical Society, March 14, 1911.

In view of the abrupt onset, characteristic signs and symptoms and macroscopic character of the fluid alone; in the absence of any demonstrable source of secondary meningeal infection, a provisional diagnosis of epidemic meningitis was made and the anti-serum ordered at once. Microscopic examination of the fluid confirmed the diagnosis; there were innumerable pus cells and typical extra and intracellular gram negative cocci, the latter proving by culture to be the diplococcus intracellularis meningitidis.

The result of this lumbar puncture alone without serum administration is worthy of note. Following it, almost at once, consciousness began to return, and the temperature sharply declined, so that within two or three minutes questions were replied to and when the first dose of serum was administered seven hours later the patient was fully conscious, showed marked hyperesthesia and the temperature was 100 degrees by axilla.

At this second lumbar puncture, which, after repeated trials, required chloroform anesthesia, 15 c.c. more spinal fluid was withdrawn and 30 c.c. of the anti-serum injected. Following this the temperature went to normal and, with the exception of pains in the legs and back from the injection, the patient spent a fairly comfortable night.

The next day (January 6) the temperature again rose, but there was comparatively very little headache and consciousness from this time on remained perfectly clear. Lumbar puncture was again performed; 30 c.c. of still heavily turbid fluid was withdrawn and 30 c.c. more of anti-serum injected.

During the next three days, up to January 9, the temperature ranged fairly constant around 101 degrees. There was no headache; hyperesthesia was diminished and the retraction of the head, which was also less severe, and the temperature were the only essential clinical manifestations of importance. The patient on the whole was so remarkably comfortable that under other circumstances the necessity for a rather radical form of treatment might have been considered unnecessary.

The serum, however, was given daily in 30 or 45 c.c. amounts. The spinal fluid, which at first was almost purulent, had now become merely turbidly opalescent, there was a notable reduction in the pus cells and many of the organisms, which were now almost entirely intracellular, ha assumed a decidedly involutional appea ance, and the number of cultivatable coc had likewise enormously diminished.

From the second day of the disease, whe from one uncentrifuged loop of fluid fro one to two hundred colonies rapidly grev or. the fourth day (January 9) a feebl growth of only three colonies was obtaine from the entire sediment of 15 c.c. of fluic At this time six punctures had been mad and a total of 165 c.c. of serum adminis tered. Thus, both the clinical and labora tory aspects of the case were favorable an the only definite direct indication for fur ther treatment was the fact that the organ isms, although greatly diminished in num ber, involutional in type and growing ver feebly on artificial media, were still actuall present and ready to regain their previou activity. That this possibility was mor than theoretical was shown on the day fol lowing this most favorable examination o the fluid.

On the seventh day (January 10) th headache, which had previously completel disappeared, violently returned, hyperes thesia became marked and the patient wa restless and moaning. The neck was again painful and rigid. The temperature wa 102⅗ degrees by axilla. Examination o the fluid obtained by puncture on this da showed a strong rapid growth of organisms which, as compared to the last previous examination, had increased to at least twenty-five times their former numbers. It was also noted that on this occasion the tapping of the spinal canal and first escape of the cerebro-spinal fluid was immediately followed by clonic jerkings of the entire left upper extremity.

What had occurred was evidently a kindling into activity of organisms probably lurking in one of the deeper sulci and previously unreached, or only partially so, by the serum and which had given rise to a local inflammatory focus with resulting renewed symptoms of pressure and augmented infection of the cerebro-spinal fluid. This exacerbation was of short duration and subsided in twenty-four hours following the sixth serum treatment.

During the next two days, the eighth and ninth of the disease, when 45 and 60 c.c. of serum respectively were given, there was uninterrupted improvement in the symptoms; although after each serum injection there was sharp temperature reactions, and more or less pain in the legs, these were

never accompanied by any indications of pressure or discomfort other than that following the chloroform anesthesia under which the punctures were done. There was no headache, no twitchings and no cerebral cry. The number of organisms in the fluid also promptly decreased, the greatest number of plate colonies being ten from the sediment of 15 c.c. of the centrifuged fluid.

On the tenth day, after a total of 300 c.c. of serum had been injected, the spinal fluid first appeared clear. It showed a distinct light yellowish amber color and on examination showed a relatively small number of mononuclear cells (in place of the polymorphonuclear leucocytes which had previously been present) and an extremely high albumin content. In fact the spinal fluid had now come to consist very largely of the antiserum itself. In spite of this, however, a growth of twelve feeble colonies on plates was obtained. On the same day, after an interval of mild discomfort and rise in temperature a marked urticarial eruption appeared on the arms, legs and buttocks accompanied by severe itching.

Because of the character of the fluid, rather than on account of the rash, which was undoubtedly due to the serum, the daily serum injection was now first temporarily omitted. The next day, the twelfth of the disease, the final injection of 60 c.c. of serum was given while the rash was still present. In no way was the reaction from this injection different from the others save that the temperature rose a trifle higher.

Examination of the fluid from this puncture (the eleventh) showed only a few mono-nuclear cells, no detectable organisms and no meningococci colonies on the plate cultures; bacteriologically the patient was cured. The next day, however, the temperature again continued to rise throughout the day, and since the character of the last fluid was so undoubtedly favorable a possibility of some complication was thought of. Very shortly, however, during the following night this was explained by the appearance of a second rash similar to the first, which appearance was promptly followed by the temperature abruptly dropping to normal. The demonstrated bacteriological cure was clinically fully substantiated.

Following this, recovery and convalescence was uninterrupted and uneventful, the final decline being by lysis and the actual disease terminated on the eleventh day. The retraction of the head and Kernig's sign were the last symptoms to disappear, lasting through convalescence up to the twentieth day after the patient was out of bed and sitting up in a chair. Final examination showed all the special senses, motion, sensibility and mentality entirely unimpaired.

In all eleven lumbar punctures were made and 405 c.c. of serum administered in ten injections; the minimum dose being 30 c.c. and the maximum dose 60 c.c.

Aside from some general discomfort, rigidity of the neck and fever, the patient, with the exception of the one instance noted on the seventh day, was entirely free from serious discomfort and symptoms of alarming nature and at no time was consciousness other than perfectly clear throughout following the first puncture and serum injection, and the case furnishes an excellent illustration of the success of the serum treatment in even the fulminating or foudroyant type of the disease with purulent exudate when the diagnosis is made promptly and the treatment begun in the early stage with sufficient doses and daily repetition.

The accompanying charts show the course of the disease and detailed effects of serum administration.

GENERAL REMARKS ON THE SERUM TREATMENT.

Although, as before mentioned, the serum has now been in use for approximately four years, in view of the fact that there is but an unusually small literature upon its use since the earlier observations, it is not out of place to emphasize some of the more important facts bearing upon the nature of the serum, its dose and the frequency and method of administration.

Production of the Serum—When, after the epidemics which swept Europe and America from 1902 to 1905 and 1906, Flexner, as a member of a special commission, began his search for what he considered the only agent which offered any hope in combating the disease, namely, an antiserum, he himself expressed grave doubts that this result would ever be capable of accomplishment.[1] From what was then, and is now, known of the diplococcus, its pathological effects resulted from the action, not of an exotoxin freely given off by the living organisms such as in diphtheria, and thus capable of producing active antitoxins when injected into the lower animals, but by an *endotoxin*, only liberated by the actual death and disintegration of the bacterial bodies, and against which, up to what time, only the

feeblest indications of any antibody production had been detected. It was obvious that the production and use of antitoxins as previously conceived in certain other infectious diseases was not the true solution.

The only hopeful aspects of the problem were the facts that: (1) The serum of normal and experimentally injected small animals had the power of slightly inhibiting the diplococcus itself in direct test tube experiments, and that (2) the pathological effects of the organisms were limited to the cavity of the cerebro-spinal canal, thus allowing any possible antiserum to be brought into intimate relation with the seat of the disease.

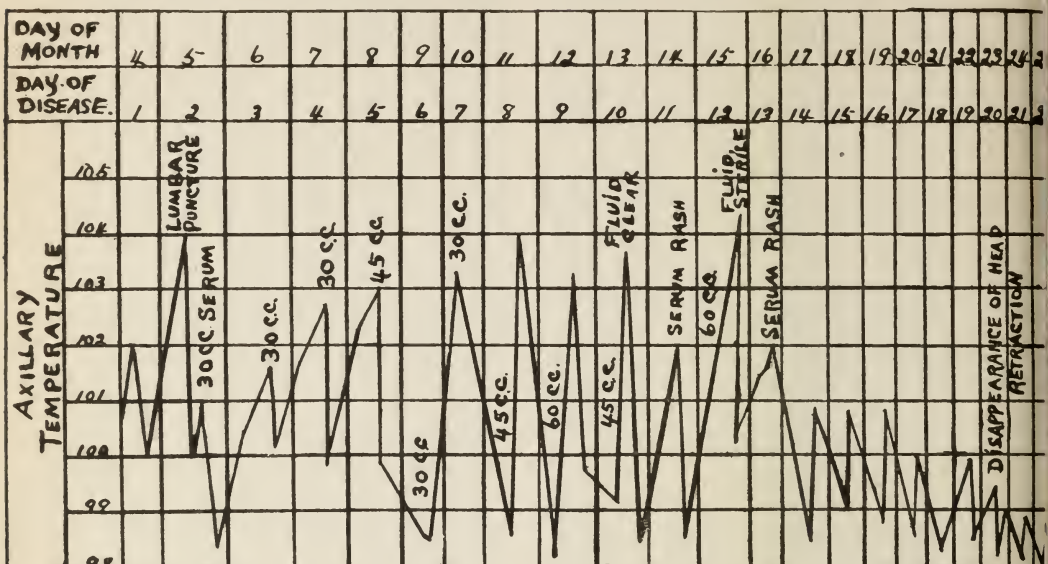

Fig. 1. Abbreviated chart showing temperature range, course of disease and serum administrations. Note that in the earlier stages with the disease at its height the serum injections were followed by a drop in temperature, while later when the process was under control the physiologic rise due to the serum itself is plainly evident.

It is unnecessary and irrelevant to here describe the many experimental steps by which an efficient anti-serum was finally produced. It is sufficient to summarize that after injecting cultures, first killed by heat and later living, alternately with similar injections of the autolysates or extracts from bodies of diplococci a true antiserum was obtained.

This serum was derived from a horse which had been treated continuously in the manner outlined for over a year and was found to protect and cure monkeys artificially inoculated with diplococcus intracellularis and to have a similar affect upon spontaneously acquired infections in human beings[2].

Nature of the Serum—In outlining t nature and principles involved in the acti of the serum, an understanding of which indispensable for its correct administratic the point of essential importance whi must be grasped is made most clear by fi definitely stating what it is not.

In any antiserum produced as is the an meningitis serum, by injections of both th organisms and their toxins, even though th latter be endotoxins, it is obvious that suc a serum will necessarily have some ant toxin content, and so undoubtedly does th antiserum of epidemic meningitis ; but it *not* to be classed as an antitoxic serum i any sense of the word, and if it be used o the principle governing the administratio of antitoxins, such as diphtheria, its employ ment can only be met with disappointmer and failure.

In the earliest test tube experiments was found that the action of even the weak est of the antisera at first produced was du to the direct action of the anti-bodies upo the organisms themselves; that is, an actu retardation or destruction of the organism such as would be accomplished by chemic antiseptics. The same action was observe when both cultures and antiserum were ir jected into the peritoneal cavity of guine pigs and into the spinal canal of monkeys.

In the animals that recovered, the flui removed at intervals, was found to becom

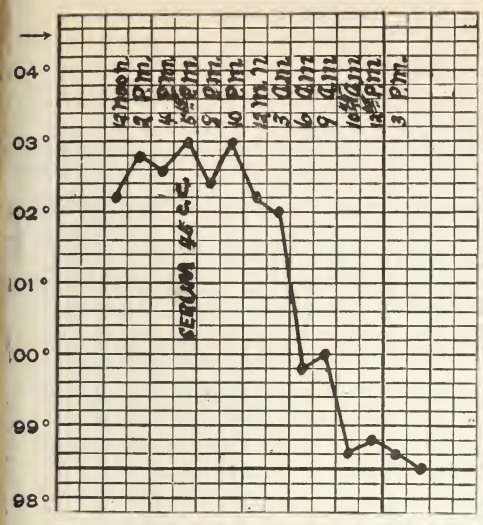

Fig. 2. Detail of Fig. 1, showing marked fall in temperature after serum administration on the fifth day which marked the beginning of definite bacteriologic improvement.

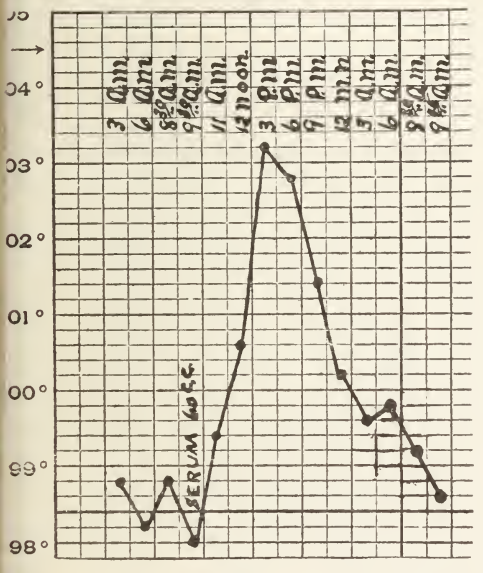

Fig. 3. Detail of Fig. 1, illustrating the physiolog-temperature reaction due to the serum at a later stage (ninth day).

progressively poorer in diplococci; that the latter assumed degenerative involutional forms, could no longer be cultivated on artificial media and greater numbers were taken up by phagocytic blood cells, whereas, as shown by the illness of the animals, the bacterial toxins were at best but partially neutralized. This is exactly what occurs in spontaneous human infections similarly treated.

The antiserum, then, is not an antitoxic, but a *bacteriocidal* or *bacteriolytic* serum; one which exerts its influence by actually killing the diplococci, but only doing this when coming with efficient strength into actual physical contact with the bacterial bodies themselves; theoretically, "one active bacteriocidal particle at least for every infecting organism" being necessary.

For the sake of clinical application we may go even further, and say without error in principle, that the serum is, to coin an expression, a "biological antiseptic" for the diplococcus in the same sense that bichloride of mercury and carbolic acid are chemical antiseptics for organisms in general, and that the principles which must govern the use of both classes are the same: direct action, efficient concentration, repeated application.

Method of Administration—It is needless to mention that the necessary direct action of the antibodies is obtained by injecting the serum into the spinal canal.

Although in some of the earlier cases subcutaneous injections were tried, Flexner never intended the serum to be used by means other than lumbar puncture. This is done in the usual manner between the third and fourth lumbar vertebræ with due regard to surgical precautions and under either local or general anesthesia.

In adults or with patients in coma the former is sufficient, but with children or highly sensitive individuals, it is not without practical import to note that there is likely to be much less general disturbance and a decidedly smaller risk from mechanical injury if the small amount of chloroform necessary to secure temporary relaxation is used.

After having entered the spinal canal and withdrawn sufficient fluid the serum is injected through the same needle. One of two methods may be selected for injecting the serum: By means of a syringe with a capacity of at least 30 c.c. as originally used, and the other by gravity later developed by the workers in the Rockefeller Institute and the New York Board of Health Research Laboratory.

In either method the puncture needle is the same, and if nothing better is obtainable may consist in an ordinary aspirating needle. It is much better and in every way more preferable, however, to use some form of regular lumbar puncture needle provided with an accurately fitting trocar which can be withdrawn after the spinal canal is entered. An excellent instrument

of this description is the Quincke lumbar puncture needle made in two sizes by Tiemann & Co., of New York City, its only drawback being absence of a hand grip.

If the syringe method is to be used, the puncture having been made and sufficient fluid allowed to escape, the syringe, previously loaded with the serum heated to body temperature, is connected with the needle, either directly or by means of coupling attachments, and the serum very slowly and carefully injected.

In the gravity method the syringe barrel is connected with about two and a half feet of suitable sized rubber tubing at the end of which is a coupling attachment fitting the end of the puncture needle when the trocar is withdrawn. After the fluid has begun to escape from the needle the latter and the tubing of the syringe barrel may be connected at any time, allowing the fluid to fill the tubing and escape into the lowered syringe barrel, from which it is emptied as often as necessary. The serum is then placed into the barrel of the syringe and the latter gradually elevated so as to allow the serum to slowly enter the spinal canal as in an ordinary hypodermoclysis.

In selecting which method to use, injection or gravity, the nature of the case has some influence. With very heavy, sticky exudates, when even at the risk of causing pressure the serum must be forced in, syringe injection is obviously the only one available. On the other hand, in cases with an exudate that runs with ordinary freedom injection by gravity offers many advantages. In the first place by connecting the length of rubber tubing with the needle and lowering the attached syringe barrel below the level of the patient a much larger amount of fluid will escape by the pressure of gravity thus produced. Secondly, any amount of serum can be injected by simply pouring additional serum into the syringe barrel as the latter becomes empty, without the inconvenient necessity of disconnecting and reloading when the injection syringe is used. Also, although no pressure results can occur if the syringe injection is properly done, the rate of flow in the gravity method is likely to be more uniform and easier to control.

Whichever method is used, certain well-known precautions as originally laid down by Flexner[3] are to be observed:

1. To allow the spinal fluid to escape spontaneously.

2. To only inject serum equal to the quantity of cerebro-spinal fluid withdrawn the only exception being in desperate case with an exudate that will not flow and i which a risk of pressure from the injectio must be run.

3. To warm the serum to body tempera ture before injecting.

4. To make the injection as slowly, grad ually and uniformly as possible with avoid ance of all force and pressure.

Dose and Frequency of Administration— From what has already been noted with re gard to the mode of action of the seru and from what is so readily demonstrabl of the pathologic anatomy of the disease, i is obvious that sufficient concentration, *i. e* quantity, and repeated action are essential in efficient serum treatment.

It is again to be emphasized that the ac tion of the serum is practically strictly tha of a local antiseptic and that the field re quiring its action is relatively an enormou one.

With the pathologic picture of an intens and frequently purulent inflammation in volving the serous covering of the entir central nervous system in mind, it is easy t realize the importance which necessaril exists between the mere relative extent o surface involved and the quantity of thera peutic agent required, however active th latter may be.

When, still further, it is recalled that th surface to be dealt with is not one per fectly smooth and easy of access, but one i which innumerable narrow fissures an sharp anatomical angles and corners whic may be blocked by exudate and thus offe the best of refuge for the infecting organ isms, it is equally obvious that in practicall no case is one administration of even a larg quantity of serum sufficient or safe, but tha in any number of given cases, four, five six or even ten or more doses may be re quired.

What, then, in the light of more recen experiences with the serum is the amoun and frequency of the dose? The good ol trite dictum that the dose must depend or the nature of the individual case and cir cumstances here still holds good. But as a general proposition it may be said that th dose is large, much larger than formerly given; that it should be frequently and sys tematically repeated; and that cytologic an bacteriologic examinations of the spina fluid withdrawn at each puncture are th only really safe criteria in treatment.

As before indicated, the doses used in th

earlier cases were small, as was natural with an untried agent, and although even with these, excellent results were obtained, we see records made at that time of cases long drawn out and some with fatal termination in which the outcome might have been different had larger and more frequent doses been employed[4].

Flexner, in giving his directions for the use of the serum in 1908[5], said: "The quantity of antiserum to be used at a single injection should not exceed, for the present, 30 c.c. * * * The injection should be repeated every 24 hours and for three or four days or longer. * * * One hundred and twenty c.c. of the antiserum have been injected into the spinal canal in four days without causing unpleasant symptoms."

It is now known that 45, 60 and even 90 c.c. of serum can be injected at one dose with impunity and that even the largest dose may be repeated daily for at least ten days if necessary.

The best general rule, if any general rules are permissible, in either chemical or biological therapeutics, is to administer as much serum, to within a few c.c., as the maximum amount of cerebro-spinal fluid that it is possible to withdraw by ordinary gravity at the time of administration.

Thus, in all but infants and very young children the maximum dose of 30 c.c. recommended in 1908 practically becomes the minimum, and 45 and 60 c.c. repeated daily for a week are not unusual doses. From what has been recorded the very few bad results from the serum appear to be due to the phenomena of anaphylaxis, in which a large dose and frequent repetition bears no part, as will be mentioned later.

As a guide to the necessary duration of the treatment the clinical condition of the patient and the presence or absence of certain signs and symptoms, particularly those of pressure, are naturally of considerable importance, but as before stated the only rational guides to treatment are the laboratory findings of the cerebro-spinal fluid. This is clearly evident when it is known how readily a few organisms temporarily in abeyance may rekindle the entire process in a clinically convalescent patient.

When the fluid becomes clear and shows a total or almost complete replacement of the original polymorphonuclear leucocytes with cells of mononuclear type with absence or only a very limited number of highly involutional organisms which do not grow on suitable artificial media, it is usually safe to discontinue the serum administration.

The one exception to this is in cases of the chronic basic type, in which from occlusion of the formenia of Magendie, Key and Retzius the spinal fluid from lumbar puncture becomes clear and sterile, while the symptoms continue. Such cases, however are recognizable from the combined clinical picture of marked head retraction, stupor, fever, etc., together with a clear fluid. In such cases craniotomy with puncture of the ventricles and injection of the serum are not only rational measures, but have actually met with success when not too long delayed.

Affect of the Serum in Clinical Cases—Since the physiological effects of the serum have been stated so often, and since they have not been found to differ essentially in later years, with the exception of some reports of fatal accidents, from those observed when the serum was first used it will be sufficient to here merely enumerate the effects which may be looked for after administration in ordinary favorable cases. With the exception of certain grave results, they are all well illustrated by the case here previously cited.

The effects may be divided into three classes: (1) The fairly frequent, but not grave, undesirable symptoms; (2) the usual favorable effects; (3) the rare grave, unfavorable results.

1. *Transient Untoward Effects*—Immediately following the lumbar puncture and serum injection the patient very frequently complains of what are evidently neurologic pains, particularly in the legs and knees, and there is likely to be some general feeling of discomfort if the patient has been fully conscious previously. All of these subjective complaints are of short duration, rarely lasting longer than six to twelve hours and are of no significance. Likewise if the fever was low or only moderate there is often a sharp elevation of temperature accompanied by a corresponding rise in the pulse and respiratory rate. When this rise occurs it is likely to continue for about twelve hours, when the temperature again falls. Such temperature reactions apparently cause the patient no discomfort.

A third and perhaps more significant symptom is the occasional appearance of a serum rash. This is in every way similar to that produced by the administration of diphtheria antitoxin and occurs in the form of a more or less marked urticaria accompanied by severe itching. It belongs to the

syndrome of the serum sickness of Von Pirquet and Shick, and may be associated with rise of temperature and general discomfort.

The entire reaction, however, rarely lasts longer than twenty-four or thirty-six hours, and although it is due to the form of anaphylaxis, the presence of either rash or general reaction of this type should not be looked upon as a contraindication to further treatment should the condition of the case demand it. That with certain methods of administration there may occur more serious phenomena of anaphylaxis has been shown; this is mentioned under the grave results of the antiserum treatment.

2. *Favorable Effects*—These have been so frequently mentioned that their mere enumeration is here sufficient. The favorable results are noticed chiefly by the improvement of certain clinical features and the character of the cerebro-spinal fluid.

Clinically the most notable indications are frequently observed in the mental condition of the patient. If previously comatose or delirious there is the most striking clearing of consciousness. After a lapse of only two or three hours following a single dose of serum even the most marked mental disturbance is often replaced by a completely rational state, and the patient is able to converse intelligently and clearly. There is likewise amelioration of the intense headache, pain in the neck and back, general hyperesthesia and increased comfort of the patient in general. The temperature, if previously high, usually drops, sometimes abruptly, the ultimate decline more frequently being by lysis. As already seen, however, there is frequently to be expected a temporary physiologic rise in temperature due to the serum itself. The physical signs of the meningeal irritation are usually the last to disappear, retraction of the head and Kernig's sign frequently persisting for a week or more after convalescence is definitely established.

The effect on the cerebro-spinal fluid is, after the first two or three administrations, to cause a very perceptible clearing of the turbidity, a decrease in the polymorphonuclear leucocytes; and as seen in stained films and cultures, to bring about marked disintegration of the displococci, an increased phagocytosis and a progressive reduction in the numbers of cultivatable organisms.

3. *Grave Results of the Serum Treatment*—In a very great majority of all cases, treatment with the antiserum has been found to be strikingly free from all manifestations of a serious nature; and, considering the enormous numbers of cases treated, were it not for a few recorded instances to the contrary, it would almost seem that a general rule could be stated in this regard. But, since there are at least four cases on record with serious outcome, it is necessary to briefly mention the possibilities of such an occurrence.

Since the phenomena of anaphylaxis, the chief danger in all serum administrations, is dependant upon the repeated injection of a foreign serum (or proteid) into the organism under certain circumstances, it is evident that the administration of the antimeningitis serum (a horse serum) might, under proper conditions, bring about a similar reaction.

In one of the earlier cases Flexner[6] records such a case, where in an infant eleven months old, the fourth injection of serum, given forty-two days after the first and sixteen days after the third injection, was followed by convulsions, prolonged rigidity and elevation of temperature, though without a fatal outcome. More recently, Hutinel[7] has recorded four cases in which serious nervous symptoms with rapid fatal termination followed a serum injection made three, five and forty-four days, respectively, after the first administration.

With regard to these fatal cases, which are ascribed to anaphylaxis, it is important to note in all instances of experimental enaphylaxis, as well as in the serum disease of Von Pirquet and Shick, that a period of incubation must elapse between the first or "sensitizing" dose of serum and the second dose, which produces the symptoms. On the other hand, experimentally at least, it is impossible to produce the anaphylactic syndrome unless the injections be properly spaced; and continued daily administration of the foreign serum are capable of even bringing about a condition of anti-anaphylaxis or anaphylactic immunity.

In the fatal instances referred to, a varying, but distinct, interval between doses is observable, but, since in many hundreds of cases the injections have been similarly spaced without any ill effect, no definite statement can be made concerning the probable dangers in allowing any particular interval to elapse between doses.

In view, however, of what is known of the nature of anaphylaxis, it would seem that there is sifficient ground to believe that

this phenomena is much less likely to occur if the serum is administered at short intervals; and this serves as another indication for daily injections aside from the fact that such a plan of treatment is clinically and pathologically indicated.

CONCLUSION.

In conclusion it is unnecessary to again emphasize that which is so well understood regarding the urgency for the early administration of the serum. What is of more importance is the method of diagnosis and the treatment itself with regard to frequency and size of dose.

The clinical features of frank epidemic meningitis are so characteristic that a diagnosis on these grounds alone is often, or even perhaps frequently, possible. There is, however, only one method by which as early and absolute diagnosis can be made in either frank or obscure cases alike, and that is by lumbar puncture.

When it is appreciated that in this procedure, in itself both easy and safe, can be found an explanation for meningeal manifestations of any inflammatory origin whatever, it is at once obvious that lumbar puncture alone is the one reliable aid in detecting a condition upon the correct and early diagnosis of which successful treatment entirely depends.

With regard to the principal points in the treatment developed since the earlier cases the whole matter is summarized by regarding the entire cerebro-spinal canal in epidemic meningitis as a potential, or actual, surgical pus cavity, which is to be treated according to the two great surgical principles; free drainage and unstinted antisepsis. And that, while the agent to be used is a highly specialized biologic product, it is nevertheless an antiseptic in a clinical sense and is to be used as such; in frequent doses and in large doses, until by exact methods of examination it is found that all the infecting organisms have been reached and destroyed.

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(6) Flexner, Simon, and Jubling, J. W., *Journal of Experimental Medicine,* Vol. X., No. 1.

(7) Hutinel, V. *Presse Medicale,* Vol. XVIII., No. 52. *Abstract Journal* of the American Medical Association, Vol. LV., No. 6, page 538.

REPORT OF CASE OF PRIMARY TUBERCULOUS INFECTION THROUGH INTESTINE WITHOUT INTESTINAL LESION

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The almost innumerable observations and researches on the various phases of tuberculosis, more particularly in recent years, have gradually but surely led to the conclusion that not only is infection primarily contracted through the alimentary system far more frequently than was previously supposed; but a number of competent observers have expressed a positive opinion that the danger from ingestion of the bacilli is even greater than by inhalation, and that many apparently primary tuberculous processes in the lungs or elsewhere in the body are in a large percentage of instances in reality but the manifestation of an infection occurring through the intestinal tract.

Clinically such conclusions are based largely on the frequent occurrence of intestinal lesions in artificially fed infants, but the direct proof of this route of infection naturally rests on animal experiments.

Chauveau,[1] who was the first to demonstrate the infectivity of the human bacillus for cattle clearly proved this method of infection, as did later Nocard,[2] Tjaden[3] and Cipollina,[4] by using kittens, young pigs and monkeys as well as cattle in their feeding experiments.

The still further disputed question of whether a lesion of the intestinal mucosa is necessary for infection by

1. Chauveau: Compt. rend. et mém. du Cong. p. l'étude de la tuberc. chez l'homme et chez les animaux, Paris, 1891, p. 51.
2. Nocard: Schweiz. Arch. f. Thierh., September, 1902.
3. Tjaden: Centralbl. f. Bakteriol., February, 1903.
4. Cipollina: Berl. klin. Wchnschr., Feb. 23, 1903.

this channel has also been approached in a similar manner. Dorbroklonski[5] introduced cultures of tubercle bacilli into the stomach of normal guinea-pigs, and from a most careful microscopic as well as macroscopic examination of the entire digestive tract concluded that living bacilli were capable of passing through the perfectly normal intestinal mucosa of guinea-pigs and that no lesion of any description was necessary. Similarly Ravenel[6] was able to recover virulent bacilli from the chyle of previously healthy dogs fed with cultures mixed with melted butter as early as three and one-half to four hours after feeding.

From these and various similar experiments it would appear undoubtedly that not only is the intestine frequently the portal of entrance for the bacilli, but that in the lower animals, at least, infection may occur through a perfectly normal intestinal mucous membrane.

In man, however, this is particularly difficult to demonstrate because at autopsy there is most frequently present either, on the one hand, an advanced stage of the disease with multiplicity of lesions which makes it impossible to detect with certainty the primary source of infection or, on the other hand, a rapidly fatal process confined to the lungs alone.

The findings in the present case noted in a routine post-mortem examination under circumstances which rendered a particularly careful examination of the parts affected necessary are of interest from the fact that, while the conditions noted arose in a wholly natural manner, they resemble those produced in the experiments quoted and bear closely on the results.

Subject of Examination.—This was a colored man, aged 32, a patient of the State Hospital at Trenton for three years previous to his death. He was a general paretic, dull, stupid and much deteriorated, and untidy and filthy in his habits. He was placed in a ward occupied by other negroes, many of whom were similar in general behavior. His mental condition and habits offered excellent opportunity for infection by the intestinal tract. His last illness was cardiac weakness from chronic

5. Dobroklonski: Arch. de méd. expér. et d'anat. path., Paris, 1893, Series 7, ii, 253.

6. Ravenel: Pub. Health Reports and Papers, Am. Pub. Health Assn, Columbus, 1904, xxix, 404.

myocarditis. There was no loss of weight or other suggestion of any constitutional disorder.

Autopsy.—Examination of the thorax showed the pericardium and pleuræ to be normal. The heart muscle was the seat of atrophic and interstitial changes. The lungs were both considerably engorged and the dependent parts showed some partial lobular consolidation. No nodules, pleural scars or thickenings were present. There was no macroscopic indications of tuberculosis and the peribronchial glands were not unusual. The general abdominal cavity was likewise negative. Both the parietal and visceral peritoneum was free from adhesions or exudate. The liver and kidneys were affected with early interstitial changes.

The pancreas, adrenals, bladder and prostate showed nothing abnormal.

For the reason that, at the time the autopsy was made, an outbreak of typhoid fever was feared in the institution, an unsuspected case having been discovered at autopsy shortly before, special attention was given to the intestinal tract, spleen and mesenteric lymph-glands. The latter in the region of the lower three feet of the ileum were greatly enlarged, about six or eight of the glands being as large as walnuts; others were about the size of a pea, and a few similarly enlarged glands were found at the root of the mesentery.

Typhoid was immediately suspected, although the spleen was quite small and firm, and the intestine was most closely examined, both externally and internally, for any variety of lesions.

Practically nothing was found. The mucosa of the duodenum, jejunum and large intestine showed indefinite areas of blood stasis only.

The mucosa of the ileum was smooth and pale throughout; there was not the slightest indications of injection, erosion, ulceration or enlargement of Peyer's patches or solitary follicles. The serous coat everywhere appeared normal.

A careful examination of a smear preparation from an enlarged mesenteric gland showed tubercle bacilli in limited numbers and a large part of the ileum opposite the affected lymphatics was saved for microscopic examination. The other organs, including the brain, heart, lungs, kidneys, pancreas, adrenals, and lymph-nodes, were examined microscopically.

Cultures on agar were taken from the liver, spleen, bile and mesenteric glands; colon bacilli only were found.

Microscopic examination of the pancreas, adrenals, liver and kidneys showed no lesion of importance in connection with the special findings. There was a moderate grade of chronic interstitial overgrowth in liver and kidneys, but no indication of tubercle formation.

Sections from all of the more suspicious looking areas of the lungs showed merely an engorgement and edema with a moderate cellular alveolar exudate; an early simple broncho-pneumonia incidental to the cardiac condition without any special characteristics.

A satisfactory examination of the intestine was possible, the autopsy being performed only two and one-half hours after death. Extended examination of sections from the ileum at different levels along the lower third, including the entire circumference, showed the mucous membrane to be the seat of early post-mortem alteration, but entirely free from erosion or ulceration. No indication of infiltration or hyperplasia was found in the submucous lymphoid tissue or follicles. The intestinal findings were pronounced negative only after prolonged search.

Two organs contained tuberculous lesions, the spleen and mesenteric glands. In the latter the process was fairly well advanced, the largest glands showing massive central coagulation necrosis with very little unaffected tissue remaining; the smaller glands showed numerous giant cells and scattered solitary tubercles in which tubercle bacilli were demonstrable after alcohol fixation.

The spleen, though macroscopically negative, showed a condition somewhat similar to that in the more slightly affected lymph-nodes, though even less advanced.

Scattered through the pulp were fairly numerous incipient tuberculous foci, represented by small collections of epithelioid cells, with an occasional giant cell or minute area of necrosis. The number of lesions was considerably greater proportionately than the apparent age of even the more advanced individual tubercles. The lesions in the spleen suggested a very recent but rather severe infection. As before indicated, no lesions in any way suspicious of tuberculosis were found elsewhere.

Notwithstanding the fact that no lesions, tuberculous or otherwise, were found in the intestine, the case is regarded as one of primary infection through this organ.

It is realized that tuberculosis of the mesenteric glands *per se* is not necessarily an indication that the channel of infection was the intestine, and that these are not only frequently but commonly infected in processes of a general nature.

On the other hand, it is certainly a recognized characteristic of tuberculous infection generally that involvement of the regional lymphatics is the best guide to the original point of infection; and this applies more particularly to cases such as the present, in which the infection is recent and the areas limited.

This view is based not merely on human autopsy findings, which in themselves are sufficiently numerous to support the view, but on exact experimental methods as well.

Among the investigations in human subjects may be mentioned the work of Heller,[7] who, in order to approach the question of primary intestinal tuberculosis, examined the bodies of 714 persons dead of diphtheria, and based his opinion that about 31 per cent. of the tuberculosis found was primarily intestinal on the tuberculous condition of the mesenteric glands.

On the experimental side, among others, are the works of Tjaden[8] and Schottelius,[9] who in all their animals fed with tuberculous material found a marked tuberculous mesenteric adenitis as well as larger lesions of the lungs, pleura and other viscera.

Schroeder and Cotton[10] considered that the mesenteric tuberculosis found in a calf subcutaneously inoculated with tubercle bacilli (a severe tuberculous bacteriemia) was due either to direct transmission of infection from the seat of inoculation or from bacilli coughed up from the lung and swallowed. In this animal the lungs were heavily infected.

If in the examples quoted the conclusions relative to intestinal and mesenteric lymph-gland infections can be accepted, certainly in the present case, in which no tuberculous foci, however small, were found either in lungs, bronchial glands or other organs which might create doubt, the assertion that the infection entered through the unaltered intestinal mucosa and first manifested itself in the regional lymphatics may be accepted, the only alternative being that the case was of the type of *typho-bacillose* of Landouzy,[11] which from both the clinical history and post-mortem findings seems extremely unlikely.

Two points are worthy of emphasis:

1. An unquestionable instance of primary tuberculous infection through the intestine in an adult individual, as shown by the marked foci in the regional lymphatics.

7. Heller: München. med. Wchnschr., April 15, 1902.
8. Tjaden: Deutsch. Vrtljschr. f. öff. Gsndhtspflg., xxxiv, No. 3.
9. Schottelius: München. med. Wchnschr., Sept. 30, 1902.
10. Schroeder and Cotton: Bull. 93, Bureau of Animal Industry.
11. Landouzy: International Congress of Tuberculosis, Washington, D. C., 1908; abstr. in THE JOURNAL A. M. A., Oct. 17, 1908, li, 1359.

2. The passage of active tubercle bacilli through an intestinal mucosa which to both macroscopic and microscopic examination showed no trace of a demonstrable lesion.

The presence of multiple additional foci in the spleen indicates the manner in which the infection was progressing; had the disease been allowed to continue its course it would have doubtless terminated in a diffuse miliary tuberculosis without definite suggestion of the primary source of infection. But, as previously stated, the purely accidental discovery of the condition at the exact stage when of sufficient duration to make perfectly clear the process without obscuring the true significance gives to the case the definiteness of experimental observations along similar lines, and offers a demonstrable proof and natural illustration of what must be of frequent occurrence, though seldom capable of so direct demonstration, in man.

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A STUDY OF CERTAIN PARACOLON FORMS FOUND IN POLLUTED DEEP WELLS*

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About August 1st, 1907, a new wing of the State Hospital for the insane at Trenton, New Jersey, was first put in service. The sewer from this wing was laid in a trench through red sandstone and shale and passed within fifty feet, horizontally, of the three deep wells which furnished the water supply of the hospital. These wells were approximately 260 feet deep, with iron casings extending down a foot into the hard rock. Wells thus constructed would ordinarily be regarded as being safe from pollution.

On account of a typhoid fever epidemic which had visited the hospital earlier in the summer, the only other available water supply, an open and polluted spring, had been cut off from the system and bacterial analyses of the well waters as they reached the buildings were frequently made. Twenty analyses of these waters made during the period, August 1st to August 17th, showed the absence of fermenting organisms, ten cubic centimeter quantities having been tested. *B. coli* was isolated from one ten cubic centimeter sample on August 17; from a one cubic centimeter sample on the 19th, and from three such samples on the 22nd. Thereafter it occurred in increasingly greater numbers.

*Read before the Laboratory Section of the American Public Health Association at Winnipeg, August, 1908.

Studies were made of the individual wells and *B. coli* were found regularly in 0.1 cubic centimeter in the water of that well nearest the new sewer, and in lesser numbers in the others.

Suspicion was naturally directed to that sewer. An investigation showed it to be poorly laid and in a leaky condition. Its use was discontinued on September 19th, and large quantities of bleaching powder were introduced with a stream of water. It was hoped by disinfecting the neighboring soil to repair some of the damage that had been done. A rather unusual opportunity was here offered for study. The wells were known to have been unpolluted up to August 1st, and polluted with sewage from August 1st to September 20th. After that time no new pollution was possible, the use of the sewer having been discontinued. These conditions were of so unique a character that occasion was taken to make a special study of the bacteria found in the waters and of the various methods employed for detecting pollution. Daily samples from each of the three wells were examined. Each sample was inoculated into dextrose broth, lactose bile and dextrose neutral red broth. The first medium was prepared according to the standard methods adopted by this section, the second according to Jackson's directions, and the third was like the first with the addition of neutral red.

RESULTS OF PRELIMINARY FERMENTATIONS:

For reasons which later appear the period covered by this detailed study will be divided into two periods of approximately thirty days each. The first from September 10 to October 12; the second from the latter date to November 9. During this entire period the results obtained on the dextrose neutral red broth were practically identical with those obtained on the standard dextrose broth. The former will not be considered further.

The results of the preliminary tests are tabulated below in the two periods mentioned and in a third period covering the entire time.

TABLE I

Results of Preliminary Fermentations and Isolation of B. Coli and Paracolon

Period	Volume ested c. c.	Total	Number of tests Giving Gas in			Number of Times B. coli found in				Number of Times Paracolon found in				Number of Times Colon Forms found in			
			A	B	C	A	B	C	Total	A	B	C	Total	A	B	C	Total
			Dextrose only	Dextrose and Bile	Bile only												
Sept. 10 to Oct. 12	10	109	21	56	3	2	43	3	48	14	11	0	25	16	54	3	73
	1	90	14	22	0	0	19	0	19	10	5	0	15	10	24	0	34
	Total	199	35	78	3	2	62	3	67	24	16	0	40	26	78	3	107
Oct. 12 to Nov. 9	10	88	34	14	3	0	7	1	8	30	9	2	41	30	16	3	49
	1	88	12	5	0	2	2	0	4	9	2	0	11	11	4	0	15
	Total	176	46	19	3	2	9	1	12	39	11	2	52	41	20	3	64
Sept. 10 to Nov. 9	10	197	55	70	6	2	50	4	56	44	20	2	66	46	70	6	122
	1	178	26	27	0	2	21	0	23	19	7	0	26	21	28	0	49
	Total	375	81	97	6	4	71	4	79	63	27	2	92	67	98	6	171

Note. – Dextrose results are recorded positive when gas appears within 48 hours, bile when 20% or more gas appears within 72 hours.

In this table, under column headed A, will be found results obtained on dextrose broth only, the corresponding bile test having been negative. Similarly under C the result was positive on bile and negative on dextrose. Under B are recorded results positive on both media. The division referring to *B. coli* includes those organisms which conform strictly to the tests laid down in the standard methods adopted by this section. The division referring to paracolon includes a group of forms which also conform strictly to those tests. The difference lies in the behavior of the two groups toward lactose. The former gives gas in lactose; the latter do not. It should be called to mind that gas formation in lactose broth is not an essential characteristic in the present standard method for the identification of B. coli. The third division includes both the groups and gives therefore the actual *B. coli* as at present defined.

Referring first to this third division, and taking the total period as given in the last line, we find that dextrose was fermented alone in 81 cases, and together with the parallel bile test in 97 cases,—a total of 178 times. Similarly bile was fermented 97, plus 6, or 103 times. Colon forms were isolated altogether in 171 cases. There were 178 positive preliminary tests in dextrose and 103 in bile, an apparent advantage in favor of the dextrose broth as a presumptive test. This advantage is seen to be still more striking if we consider only the 1 c.c. samples of this same period. Colon forms were isolated altogether 49 times. There were 53 positive preliminary tests in dextrose and only 27 in bile. Taking the period, October 12 to November 9, of all the samples tested, 65 fermented dextrose, 22 fermented bile, and 64 gave colon forms. In the same period of the 1 c.c. samples, 17 fermented dextrose, 5 fermented bile, and 15 gave colon forms. To better point out this rather unusual result these figures are tabulated by themselves, avoiding

the confusion of the larger table, the total colon forms being given in the last column.

TABLE II.

Relation of preliminary fermentation tests on dextrose broth and lactose bile to the final isolation of colon forms

Period	Volume tested c.c.	Number of Positive Fermentations in		Number of Positive Tests for		
		Dextrose	Bile	B. Coli	Para Colon	Colon Forms
Sept. 10 to	10	77	59	48	25	73
Oct. 12	1	36	22	19	15	34
	Total	113	81	67	40	107
Oct. 12 to	10	48	17	8	41	49
Nov. 9	1	17	5	4	11	15
	Total	65	22	12	52	64
Sept. 10 to	10	125	76	56	66	122
Nov. 9	1	53	27	23	26	49
	Total	178	103	79	92	171

Earlier in this work the fact was noted that the dextrose broth was giving much higher results in preliminary tests than the bile. This was to be expected, but it soon appeared that the dextrose results were in very close agreement with the final complete results, while the bile was very low as has been indicated. It was noted at the same time that the organisms fermenting the bile always gave strong red colonies on litmus lactose agar, while those fermenting dextrose frequently gave colonies which were red but not so strongly acid. At the beginning of the period covered by the above table, therefore, all cultures from dextrose fermentations were fished into ordinary lactose broth and into dextrose bile. As had been anticipated, those cultures which gave feeble acid production did not give gas in the lactose broth, but did ferment dextrose bile vigorously. Apparently there was present in these waters a distinct strain of organism which agrees with *B. coli* as ordinarily understood. It forms acid, but little or no gas in lactose. From that time on, then, these two types were distinguished. Tables I and II show the reason for the poor bile results. A large proportion of

these are typical forms, which, for want of a better name, are here called *paracolon,* were being dealt with. They did not ferment lactose and hence were lost by the lactose bile medium. It is interesting to note that the bile itself had no inhibiting effect upon them whatever in the dextrose bile medium.

An interesting point also is the relative abundance of the two types. To bring out the point the time has been divided into two periods in the tables. During the first period pollution was at a maximum, and during the second it was slowly disappearing. In the one case the lactose fermenting *coli* outnumbered the *paracoli* in a ratio of 1.7 to 1.0. In the other the ratio was over 4 to 1 in the other direction. That is to say, during the gradual improvement of the well waters the typical *coli* decreased at a much more rapid rate than did the *paracoli.* Toward the end of the study *paracoli* persisted for a considerable period after the typical forms had disappeared.

STUDY OF THE PARACOLON FORMS:

It was deemed highly desirable to obtain as complete knowledge as possible of this important group of organisms. Accordingly special studies were made upon it during this investigation.

Records were kept of the appearance of each litmus lactose agar plate from which colonies were fished. The amount of acid produced by the organism could be roughly indicated by the color given to the plates, recorded as red, pink, or no change. A total of 198 *paracolon* colonies were fished from an equal number of plates. The recorded color of these plates is given in the following table, divided as usual into two periods. During the same period 160 colonies were fished which proved to be typical *B. coli.* The recorded color of these plates was red in all cases.

A distinct change in the acid producing powers of these organisms is noticeable in this table. This seems to be directly associated with the more rapid decrease of the acid forming *coli* alluded to above. The tendency in both cases is to eliminate most rapidly those forms which most readily acidify lactose.

TABLE III.

Acidity produced by Paracolon as indicated by change of color in Litmus Lactose Agar

Period	Number of plates.			
	Total	Turning Red %	Turning Pink %	No change %
Sept. 10 to Oct. 12	104	29.8	52.8	17.3
Oct. 12 to Nov. 9	94	19.1	61.7	19.1

The evidence seems to be very definite here that those forms which have lived longest in the soil, or are farthest away from the initial sources of pollution are least able to ferment lactose. They produce acid less vigorously than the normal forms and form little or no gas. As to whether these forms represent degenerate individuals or constitute a distinct and more resistent strain remains to be shown.

Fifty strains were selected at random from the daily plates and subjected to a detailed study. They were first inoculated with lactose broth and dextrose bile media. Very feeble gas production was noted in lactose broth in a few cases. As a rule there was none. Dextrose bile was fermented vigorously, showing as has already been pointed out, that these forms are not excluded by the bile. After being on artificial media for a few weeks 70% of these cultures developed lactose-fermenting powers. This, however, was never vigorous as in normal *coli*. Their action upon saccharose was also tested. About half of them formed gas in that sugar. Or

the basis of their fermentations of lactose and saccharose the fifty strains were divided into four groups and further studies were made upon them. It became apparent that these four groups possessed several correlated properties in increasing or decreasing magnitudes, and further, that the whole division considered in respect to these characteristics lay intermediate between typical *B. coli* and *B. cloacae*. For the purpose of comparison 19 strains of *B. cloacae* were isolated from the same waters, the organism being quite abundant at that time. In the following table are shown the four groups of *paracoli,* selected in reference to their sugar fermenting powers, with a column of *B. coli* on one side and *B. cloacae* on the other. Numbers refer to per cent. of positive tests. Obviously no statistical value attaches to these results obtained on so few numbers, but the intermediate character of the group as a whole and a decided correlation of certain characteristics is distinctly indicated.

TABLE IV

Table showing the intermediate position of the four paracolon groups between *B. coli* and *B cloacae* and correlation between certain characteristics

Test	Per cent of Total Giving Positive Tests.					
	B.coli	Paracolon groups				B. Cloacae
		1	2	3	4	
Fermenting Dextrose	100	100	100	100	100	100
Fermenting Lactose	100	100	100	0	0	16
Fermenting Saccharose	?	0	100	0	100	100
Lactose strongly acid	100	67	44	29	20	0
Gelatin liquefied	0	0	14	14	60	100

In general these organisms would pass the ordinary tests for *B. coli,* and in fact they were selected on the basis of the standard tests for that organism. The liquefaction of gelatin noted occurred always between 14 and 28 days. Forms which liquefied more rapidly were classed as *B. cloacae*. The

distinction is obviously an arbitrary one, but was maintained according to present practice. On gelatin the growth was less luxuriant than usual, at times translucent. In milk acid production was less than normal. Coagulation generally occurred only after heating. Nitrate was reduced vigorously and indol produced rather weakly.

The gradual increase in the relative numbers of these atypical forms has been alluded to, as has the fact that they became relatively less active in acidifying lactose. It can be stated further that in all their characteristics they showed a definite progressive change during the period of the investigation. At first they were quite overlooked. Attention having been called to them through the low bile results they were later searched for, and identified on various platings by their slightly feebler powers of acid production in lactose. Identification at this time was quite difficult. Later, plates with pink colonies occurred more frequently. At the close of the study many plates were obtained in which no red colonies were found.

Upon fishing colonies which appeared to be otherwise typical, however, this organism was regularly isolated. The intermediate and gradually progressive characters of this organism appear to us to be of great significance.

In this same connection also, but possibly entirely independent of it, it should be stated that the appearance of *B. cloacae* was more frequent towards the end of the work and that after all other sewage species had practically disappeared, forms of proteus were frequently found.

Thus the change in characters from non-liquefying, lactose fermenting coli to liquefying non-lactose fermenting proteus was continuous and complete.

CONCLUSIONS.

We believe the results of this investigation have a greater importance than their mere scientific interest. According

to accepted standards of interpretation the pollution of these wells ceased with the disappearance of typical *B. coli.* But long after that point was reached other types presisted which were connected with the typical forms by a gradual and perfect transition. The arbitrary character of our accepted standards, necessary as it is in practice, appears to disadvantage in a case like the present one. For certain classes of work, such as the quantitative study of polluted rivers, the control of filtration processes, and legal work, a hard and fast definition of *B. coli* is needed. When we expect to find pollution we may measure it in this way better than in any other . *On the other hand, where it is desired to detect pollution, if any exists, however slight, where the least indication of pollution at present may mean serious consequences in the future; the most sensitive tests we have and the broadest possible interpretations are desirable.* In the present instance the source of pollution was known and had been dealt with. The actual amount of pollution was not serious. In fact, by excluding the one well and avoiding extra heavy drafts in the other two, and by discontinuing pumping entirely after rainstorms, this anxious period was safely tided over. But if the source of pollution had been unknown and the continued use of the water had depended upon the bacteriologist's report, great harm might have been done by a too rigid adherence to the accepted definition.

One further point of immediate importance is this: The standard methods adopted by this section allow the use of either dextrose or lactose in preliminary tests. In the confirmatory tests, however, the production of gas in lactose broth is not made an essential feature. This inconsistency should be remedied. In the present case two independent workers, both following conscientiously the present standard methods, would have come to opposite conclusions regarding the presence of *B. coli,* in 50% of the samples tested had one worked with dextrose and the other with lactose broth. Either

the definition of *B. coli* should be made to include fermentation with gas production in lactose broth, or the latter should not be used in preliminary tests. Lactose was introduced in place of dextrose, which was long the standard, to cut out certain organisms such as cloacae. The process of cutting out seems to be too severe, and in our opinion, where the fullest possible knowledge of conditions is desired, the use of dextrose broth in preliminary tests is to be recommended. For presumptive and comparative tests in such routine work, as the systematic control of filters or the regular examination of water supplies, lactose may still find useful application.

Since the original communication additional attention has been given to the organisms referred to as paracolon forms.

In a fairly large series of fecal examinations comprising about 100 examinations, made at the New Jersey State Hospital in connection with typhoid bacillus carriers, the occurrence of organisms answering to the description given above has been particularly searched for. That these are undoubtedly fecal in origin is shown by the fact that there was scarcely an examination in which forms could not be found which corresponded exactly to the various characteristics of the paracoli found in the water examinations if properly searched for. On the Drigalski-Conradi medium used in the series the initial colonies at times somewhat resembled those of the *B. typhosus*, while others would simply be regarded as a typical colon colonies unless further investigated.

It is doubtless this indefinite character of the initial growth of these organisms on lactose media even when grown directly from feces which has led largely to their neglect as indicators of fecal pollution in the interpretation of results of bacteriological water analysis.

A TYPHOID BACILLUS CARRIER

HISTORY AND AUTOPSY

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Since the comparatively recent discovery of what may be termed latent typhoid infection and its bearing on the spread of the disease, as well as its pathologic and bacteriologic significance, additional examples of this condition have been reported repeatedly.

As yet, however, the number of postmortem examinations of bacillus carriers has not been large, and the present instance is cited, not only as an example of the possibilities of transmission of infection under certain circumstances, but as an additional confirmation of the generally accepted belief in the origin of the bacilli in such cases.

HISTORY OF A BACILLUS CARRIER

The individual in question was a colored man admitted as a patient to the New Jersey State Hospital at Trenton in 1902. He was at that time sixty-seven years old, and presented then, or subsequently, nothing beyond the gradual mental and physical failure incident to his age, and was able to perform such light work as was assigned him.

During July and August, 1907, the institution was visited by an epidemic of typhoid fever, due to the contamination of a spring from a leaking city sewer, over one hundred cases resulting, with the usual mortality.

The patient (C.C.) then seventy-two years of age, became ill early in August, and responded positively to the agglutination test on the 13th. The course of the disease was exceptionally mild; the temperature was at all times low, rarely above 100 F.; and there were few, if any, subjective or objective symptoms, so that, in spite of his age and comparative weakness,

1. Park, William: Typhoid Bacilli Carriers, THE JOURNAL A. M. A., Sept. 19, 1908, li, 981.

the patient was able to be about in a little over three weeks from the time of onset. Indeed, so mild was the disease that the diagnosis was made entirely on the Widal reaction, this test being made at this time on all patients showing any signs of ill health whatever. In the absence of an epidemic it is probable that the few symptoms observed would have given no indications of the condition.

He made an uneventful recovery, and very quickly regained his usual health..

During the fall and winter (1907), following the epidemic, bacteriologic examinations of the urine of all convalescent patients (including C.C.) were made at the hospital laboratory, three examinations each of fifty-two convalescents being performed. Digalski-Conradi agar medium was used for this purpose, and in no instance were suspicious organisms isolated.

All patients were at this time kept segregated after having had typhoid and hexamethylamin (urotropin) systematically administered over a period of months. Subsequent to the urine examinations, in the spring of 1908, the Research Laboratory of the New York Health Department, under the direction of Dr. W. H. Park, undertook the examination of the feces of the same individuals, samples being sent to New York for this purpose. Three or more examinations of specimens from each patient were made, and, as already reported by Dr. Park,[1] two bacillus carriers were discovered, one being the patient C. C. Four consecutive fecal examinations of this patient during March and April each showed typhoid bacilli in large numbers. He was at once isolated and rigid disinfection of all discharges carried out. No further cases occurred. It is here of interest to note what would have been the inevitable consequences, had not these individuals been recognized.

As is now generally conceded, the opportunities and frequency of contact typhoid infection under ordinary circumstances are great, but in large institutions, particularly for the insane, these are enormously multiplied.

Where large numbers of patients are in close daily contact in dormitories, wards and dining rooms, many of whom from their mental condition are careless or filthy in their habits, the direct transference of infection, in spite of all ordinary precautions and watchfulness, is unavoidable. Nieter and Liefmann, in 1906, reported a series of typhoid outbreaks in an insane asylum due to this cause, and Friedel in the same year cites another instance in which sixty-three cases resulted in another similar institution. Liebtrau speaks of an attendant in a jail who caused four cases, but who had herself never been ill.

Following his isolation, the history of C. C. was uneventful, and nothing of note in his physical condition was observed up to his last illness, with the exception of a trifling and irregular diarrhea, alternating with mild constipation.

Although the gall bladder and small intestine were found involved at autopsy, no essential symptoms of these conditions were observed during life. C. C. continued in his usual condition, though gradually failing in strength from old age, up to within six weeks of his death when he developed an irregular temperature, accompanied by signs of thoracic disease, became progressively weak and emaciated, and died Oct. 16, 1908, one year and three months after having had the attack of typhoid.

AUTOPSY

The autopsy was performed three and a quarter hours after death. Nothing beyond a senile appearance and rather marked emaciation was noted externally. The brain was typical of senile atrophy, and close inspection of the pia failed to detect anything except the usual changes of this condition, though microscopically an interesting condition was discovered. The left seventh rib was found detached from the vertebra at the articular process, and the severed ends were surrounded by a small pocket of thick yellow pus.

The left pleura was enormously thickened, and the lung deeply engorged and firmly attached to the chest wall. The upper lobe of the right lung showed lobar consolidation, and the heart a rather severe grade of brown atrophy. The aorta and other large trunks were sclerotic and contained a moderate number of atheromata. The spleen was small, tough and fibrous, but macroscopically showed nothing further. The liver was small, mottled in appearance, uneven on the surface and thickly studded with minute grayish solid bodies and fasciculi taken at autopsy to be fibro-connective tissue.

On making a minute opening in the gall bladder for the purpose of taking cultures, a small amount of clear mucoid bile escaped; the rest of the bile, however, which completely filled the gall bladder, was dark yellowish brown, thick and partially inspissated. A dark greenish-black, smooth oval calculus, 1.5 by 0.5 cm., was present; and the mucosa was very dark and slightly thickened. The cystic, hepatic and common ducts were unobstructed.

There was a well-marked chronic interstitial nephritis, and one kidney contained a small sclerotic nodule at the junction of the cortex and medulla. The mucosa of the bladder was slightly injected, but otherwise negative.

In the intestine there were irregular areas in which the mucosa was mildly injected, and two small ulcers were found, each about 0.5 cm. in diameter. One was situated in the lower portion of the ileum, the other in the cecum. Both were circular, sharply circumscribed, involved the mucosa only, and showed complete absence of induration or surrounding reaction.

It was thought that, anatomically, we were dealing with a possible traumatic fracture of the seventh rib with secondary

infection and involvement of the left pleura, a chronic senile leptomeningitis, fibroid spleen, and a rather marked chronic interstitial hepatitis.

On microscopic examination, however, the thickened pleura was seen to contain many characteristic giant cells, and the liver and spleen were studded with numerous and closely set minute miliary tubercles, while the pia was the seat of the earliest stage of tuberculous meningitis. In fact, there had been a rapid and general dissemination of acute miliary tuberculosis, probably arising from a necrotic rib.

Whether this was primarily a post-typhoid necrosis secondarily infected with tubercle bacilli remains in doubt, though from its apparent comparatively recent occurrence this was probably not the case.

BACTERIOLOGIC EXAMINATION

Cultures were taken on lactose litmus agar from the region of the intestinal ulcers, the liver and bile. The latter were made in definite decimal dilutions from 1 to 0.00001 c.c., using sterile water as a diluting fluid, and incubated at 37.5 C.

On the plates made from the intestinal ulcers many red colonies developed, chiefly of the colon group, but none showed any resemblance to typhoid organisms, either on the plates or by subcultivation.

In twenty-four hour observations of the bile plates no colonies whatever could be distinguished on those made from the undiluted bile, or on the dilutions up to 0.0001 c.c., although a very delicate film appeared to cover the surface of the medium, which was unaltered in color. On the 0.0001 plate innumerable minute blue points could be distinguished with a hand lens, while on the plate of highest dilution (0.00001) an enormous number of distinct delicate bluish colonies could be seen, all of which were identical in appearance. It was impossible to count the colonies accurately, but it was estimated that they numbered between 1,000 and 2,000.

The plate cultures made from the liver by smearing a small bit of excised tissue over the bottom of the plate before pouring the agar, showed identical colonies varying in numbers from 100 to 1,000 on each plate. About twenty of the colonies from the bile and liver were subcultivated and tested for agglutination with a known typhoid serum tested against a stock culture of typhoid bacilli. The reaction was prompt and vigorous in dilutions of 1 to 50. A number of stains were then selected and subjected to cultural tests the results of which corresponded in every instance to those of *Bacillus typhosus*.

In stating the probable number of typhoid bacilli present in the bile in this instance, only approximate figures can be given, since the enormous overgrowth even in the highest dilu-

tion, obviously places the numbers too low, but as a conservative estimate it is safe to say that there were at least 20,000,000 per c.c., basing the estimate on the number of colonies developing on the least crowded plate.

The numbers developing in the liver cultures were correspondingly large, although from the nature of the material it is impossible to give these in as definite a manner as with fluids such as bile.

That the bacilli are found in the liver when present in the gall bladder is shown by the case reported by Levi and Kayser, who at autopsy of a bacillus carrier found them in the wall of the gall bladder, the liver and inside of calculi. In this instance the autopsy was performed nineteen hours after death, and the findings suggest that the bacilli invade the liver, postmortem, through the bile ducts.

This is believed to be the case in the present instance, for although tubercle bacilli were readily demonstrated in sections of the liver fixed in alcohol, the most careful search failed to detect the presence of either colonies or isolated bacilli in any portion of the liver tissue examined.

In an autopsy cited by Nieter and Liefmann, in 1906, they found not only the gall bladder involved and containing the organisms, but also a chronic catarrh of the lower intestine and many typical old typhoid ulcerations. This patient had suffered from chronic dysentery during life.

In the present case the patient also showed a mild catarrhal condition of the intestine, and ulcerations were present, but in no way did either lesion resemble a long-standing or chronic condition, nor were the ulcers of a nature to suggest a typhoid origin; and from the appearance of the lesions, rather than the failure to cultivate typhoid bacilli from them, they are regarded as unconnected with the infection of the gall bladder or the presence of the bacilli in the stools.

SUMMARY

The points of interest in the present case are:

The race and age of the individual (73 years at time of death).

The extreme mildness of the primary disease.

The constant presence of the organisms in the stools and their absence in the urine, following the attack.

The apparent failure of progressive and, toward the last, severe senile changes, together with an intense and widely disseminated tuberculous process to influence the course of the chronic typhoid infection.

The enormous numbers of the organisms found in the gall bladder and liver at autopsy.

The futility of hexamethylamin as a treatment for typhoid infection of the gall bladder.

And, finally, the extreme value of fecal examination of post-typhoid subjects in institutions where control is possible and the practice of rigid isolation and disinfection when carriers are discovered.

I am indebted to Drs. Sandy and Taylor of the State Hospital, under whose care the patient was, for the clinical facts, and to Dr. W. H. Park for the reports of the fecal examinations.

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