

of such lesions has been given. Chromatolysis and certain other changes in the cells of the spinal cord have been reported but the causation of these conditions is not yet so well settled that we can accept them as evidences of a primary organic disease. Chromatolysis may be caused, so far as yet appears, by a variety of causes and its significance is not determined. Whether the decubitus or bed-sores, which occur so suddenly and rapidly in epileptic status, can be considered as evidence of any spinal condition is also undecided. That they are connected with trophic disturbances there is no doubt. Even if the seat of this disturbance is in the spinal cord, it must be considered as a terminal condition rather than the outward manifestation of a well-defined organic affection of the cord which has been of the same character as that which produces the characteristic symptoms in the cerebrum. It is not a primary epileptic lesion, but a terminal affection.

#### CONCLUSION.

Since the paper was written I have received this statement from Dr. Southard: "Microscopic examination of a number of spinal cords from epileptics has yielded some interesting findings. These warrant more extended and systematic study." One case shows the effects of a terminal exhaustion state on the spinal cord. In the series of cords examined Marchi degenerations of a diffuse non-systemic character were found in almost every case. One case showed considerable fibrillar gliosis.

I believe that we have here an important field for further investigation and it is to call attention to this that this article is written.

#### DISCUSSION.

DR. HOWELL T. PERSHING, Denver, Colo., asked Dr. Bullard whether the cells of the anterior horns are more implicated than those of other parts of the cord. It is in these cells, Dr. Pershing said, that he would expect secondary changes such as are known to occur in the cortex of epileptics.

DR. W. N. BULLARD, Boston, said that up to the present examinations have been made of only about 15 of the cords. Dr. Southard stated that the cells of the anterior horn of the cord have shown the axonal reaction of Nissl. There was fatty degeneration of the nerve fibers in various places, but of such a character that the pathologist was inclined to believe that in many cases it might easily have escaped notice unless special search had been made in that direction.

### MANIC-DEPRESSIVE INSANITY AND VISCERAL DISEASE.\*

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The recent consolidation of the different forms of mania and of melancholia into the one disease called manic-depressive insanity is a notable achievement and at the same time furnishes one of the most important of the recent problems of psychiatry. The fusion of so widely differing symptom complexes into one type, and their presentation as a definite disease can only be justified by showing that the same pathologic process or, what is quite different, that the same cause underlies the manifestations in all cases. It is important to investigate and group the cases of so common a difficulty as the so-called manic depressive type, to find out whether

the diagnostic criteria are justified, whether the prognosis is hopeless, as to permanent cure, as is implied in the definition ordinarily given of the disease and the treatment restricted to care and palliation, or whether some cases of the disease being curable, efforts should be made to discover and eradicate the cause of the difficulty. The answer to these questions is of vital importance to every patient in whom either elation or depression is a prominent symptom.

According to Kraepelin, manic-depressive insanity is "that mental disorder which recurs in definite forms at intervals throughout the life of the individual and in which a defective hereditary endowment seems to be the most prominent etiologic factor." According to the older classification, the diseases which are included in the new one are recoverable mania, simple mania, simple melancholia, melancholia agitata, periodical mania, periodical melancholia and circular insanity. All of the melancholias are here included except the senile form, and all of the manias which are not episodes of elation in the course of other mental disorders, as for instance, paresis or dementia precox. As the essential element in all of the symptom-complexes is emotion, either elation or depression dominating the clinical picture in each of them, and as visceral conditions notably influence emotion in both health and disease, the attitude of modern psychology toward the emotions in health is of importance as a starting point for the consideration of visceral action in mental derangement.

In brief, modern psychologists consider emotion the cognition of visceral change. If, for instance, a cause of grief is followed by the corresponding emotion, this does not happen as a direct cerebral reaction. The sequence is as follows: As a result of the bad news or the misfortune the viscera, the stomach, liver, heart for instance, are depressed and changed in their functioning and the cognition of the change is apprehended as the emotion. If the viscera were non-existent or their nervous connections with the brain severed or shunted, misfortune might be apprehended intellectually but not as emotion.

This theory, which can not be further elaborated at this time, receives powerful support from observation of the simplest illnesses and departures from visceral health. As examples, depression from liver disease or dyspepsia and elation in tuberculosis have long been familiar. The rich dyspeptic who is depressed, and as a result has delusions of poverty and the loss of friends, and the emaciated consumptive who looks for speedy recovery and is better every day until he dies, are mild prototypes of the manic-depressive form of insanity which, in its severe forms, fills our asylums. The interval between mental health and delirious mania is bridged by transition forms which vary through all possible intervening states of mild depression, depression with agitation, depression with delusions, depression with suicidal impulses, with hallucination, simple exaltation, exaltation with delusions and incoherence of ideas until the most serious forms of all are reached, the cases of alternating or of rhythmically recurring mania and melancholia. The question whether the mild and the severe cases are essentially the same is not purely an academic one. If they differ from each other only in degree, and if the milder forms are dependent on visceral disease and are curable the severer cases need not be considered necessarily hopeless. If the severe cases differ in kind and are essentially incurable the dividing line should be determined.

\* Read in the Section on Nervous and Mental Diseases of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

Turning now to the mild cases, it is to be remarked that the ordinary accompaniment of visceral disease is depression. Exaltation is less common, or at any rate less obvious, but may be found even in cases of gastric and intestinal disorders. One of the commonest examples is furnished by the dyspeptic who finds himself elated and working at higher pressure than normal, and recognizes the condition as the sign of an undigested meal. Such patients can foresee the ensuing mild melancholy, remediable by a purge and subsequent care in diet. Quite as typical and almost as common are the women who find their duties increasingly hard, who cry easily, find life a burden and their friends hard to face, and along with this simple melancholy may or may not have backache, headache, indigestion and loss of weight. Every neurologist who has a care for the physical well-being of his patients has referred many such to the gynecologist and seen simple melancholia cured never to return or to return only with the recurrence of the physical cause.

The following case is one of a type more severe but almost as common as is the preceding:

CASE 1.—The patient, a woman, aged 28, after a summer spent in the woods camping and fishing and afterward in unusually good health, took up an amount of teaching that involved moderate over-strain. She soon began to be sleepless and depressed, she developed delusions that she was pregnant and that she had committed various unpardonable sins and procured a revolver with a view to committing suicide.

When seen she had grown steadily worse for two or three months. She had the usual coated tongue and pallor of the melancholic, tired easily, had no energy and no pleasure in life and was much occupied with her delusions. Examination revealed serious disease of both uterus and ovaries. Great improvement in the mental condition was apparent within a few days after an operation undertaken to relieve the pelvic conditions. The patient gained steadily in strength and cheerfulness for about a year and is now, two and one-half years after the operation, in good health.

My only excuse for citing so common a case is to point out the fact that it and similar cases are included in the group of manic-depressive insanities. In my experience such patients retain their mental health if the affected viscera do not again become diseased. One such patient, who made a good recovery from both her melancholy and her delusions, had a year or two after operation a recurrence of mental symptoms in connection with an attack of the grip. She specifically returned to mental health and remains well five years after pelvic treatment.

The clinical picture of agitated melancholy is, in my experience, often met in connection with gastric and intestinal disease. Mild melancholy is an almost regular accompaniment of indigestion, and this, under exceptional conditions, may rise to a condition of frenzied depression, with intractable nervousness and insomnia. One such patient, a man sixty-three years of age, in whom the attacks of mental alienation followed dysentery, responded readily and rapidly to purgation, milk diet and the salicylates, when hypnotics and sedatives were powerless to give more than the slightest relief. In this case agitation and depression were as extreme as I have ever seen them in an asylum case and the symptomatic diagnosis of melancholia agitata, in my opinion, amply justified by the conditions present.

Maniacal cases furnish the more intractable examples of the manic-depressive complex. Two patients have given interesting, although incomplete confirmation, of the suggestion that mania is visceral and sometimes due to curable visceral disease.

CASE 2.—This patient presented the clinical features of acute mania in the puerperium. The flight of ideas, singing, rhyming, word salad and excitement, and elation day and night were typical of mania in the stage of delirium. After improvement had begun, supporting a heavy retroflexed uterus, was followed by sudden increase in lucidity. Three days later the patient had a relapse and it was discovered that she had removed the pessary. When it was inserted improvement was at once apparent. A curetting was refused by the relatives, and the patient was removed to an asylum and several years later was still there with chronic mania.

CASE 3.—This was a case of recurrent mania, alternating with hebétude. Patient had been three times in an asylum for periods of five to six months, with intervals of a year to a year and one-half of mild depression. During her exacerbations she had typical exaltation, was violent and had delusions with rapid incoherent speech. She was seen at the beginning of an excited period, which came to an end, and the patient became calm after support of the uterus by a pessary. She was, however, far from normal, her general health being decidedly below par. She could bear little exertion, her digestion was poor and she was anemic and emaciated. Some months after the original operation she began to be excited and it was evident that she was again drifting into a maniacal condition. The uterus was discovered to be out of place, and reposition was followed by another subsidence of loquacity and elation.

*Operations.*—Five or six months later a recurrence of the same symptoms led to a more radical operation. The uterus was supported by being stitched to the abdominal wall and one ovary, which was discovered to be markedly sclerosed, was removed. This operation was followed by an improvement which lasted for almost a year. Then the symptoms returned and a second operation was undertaken. The left ovary, which was previously found in a comparatively good condition, had become markedly sclerotic and was removed.

*Postoperative History.*—This operation was followed by complete relief. The mental condition became normal for the first time since my acquaintance with the case. The patient, instead of being, as heretofore, pale and emaciated, grew fat and rosy. Two years and one-quarter have elapsed since the last operation and about two years since her return to health. Even this short time has already furnished a complete justification for the operation by giving the patient complete relief from her previous distressing condition, although a mild relapse just inaugurated makes it clear that cure is by no means complete.

That these cases are simply illustrations in abstract scarcely needs statement. So far as melancholia is concerned they are such illustrative cases as may be furnished by any physician of wide, or even of moderate experience, in neurology. Relapse in these cases of melancholia has been in my experience rare, temporary, and due to recurrence of visceral disease or profound toxemia. Most of the patients have remained without relapse for periods varying up to twelve years.

With regard to the cases of mania criteria are more difficult. My own cases are so few in number as to be suggestive rather than conclusive. That mania is like melancholia, essentially visceral in origin, seems to me so well established as to make its cure by correction of the underlying lesion probable, *a priori*.

The recent introduction of the term manic-depressive insanity then marks what may be called the agglutinative period in symptomatology. The time is not yet ripe for a final judgment on this nomenclature. In the absence of a firm pathologic basis for either the division or the uniting of the different symptom-complexes that compose the group, it can still be said that the name does not probably represent an ultimate clinical fact, but rather a stage between the earlier imperfect divisions and a later and better classification on a pathologic basis.

The test of a theory is its ability to account for ob-

served facts. In proportion, as it does this, it possesses the weight of probability. If then, the visceral theory of the origin of mania or of melancholia, or both, is capable of furnishing an adequate explanation of their clinical features, it will be worthy, at least, of standing until it is supplanted by a better theory, on a basis of wider experience. What may we fairly expect if emotions in both health and disease are reactions from visceral change? Not that the same visceral diseases will always produce the same emotional result. This would be contrary to what we know of such effects of visceral disease, as fever and delirium. The absorption of toxins and the visceral irritation in typhoid, malaria and meningitis, carry with them reactions of fever, of pain and of delirium, the amount of the reaction varying as widely as possible in different individuals. The psychic pain of melancholy is like physical pain in being an individual reaction and only a little less widespread. The elation of mania is less common, it is a reaction of a different species but of the same family with pain and depression. So far then as concerns their variability, elation and depression are in accord with other modes of reaction to visceral disease. They resemble these too in being alike the result of disease of different viscera. There is no viscus of pain and none of depression, no viscus of pleasure and none of sorrow.

If manic-depressive states are modes of reaction to changes in the viscera we should expect some of them to be curable and others to be incurable. We should expect cases occurring in the old to be less hopeful than those in the young. We should expect some curable cases to occur even in the aged. We should expect cases of long standing to be less susceptible of cure than recent ones for two reasons, that the underlying disease has taken deeper root and the consequent changes in the cerebral tissues and the circulation have become more pronounced. These are all facts of common observation of which I have cited a few instances.

If the manic-depressive insanities retain their place as a clinical entity, this must be not as symptom-complexes, but on the basis of a common pathology. That pathology must be the broad one of visceral change in general, as both mania and melancholia occur as sequences of disease of many kinds, affecting any one or several of the viscera. The precise nature of the resulting symptom-complex does not depend on which particular viscus is diseased, but apparently on the reaction mode of the person affected; just as delirium depends, not on the location or the kind of the inflammation; but that it is caused by inflammation no one doubts; that it sometimes outlasts the inflammation which causes it is also true; that the nature of the delirium is determined by the predisposition of the individual will. I think, be admitted, delirium in all these ways running parallel with the manic-depressive reactions at present under discussion.

#### DISCUSSION.

DR. W. H. HUMISTON, Cleveland, gave the condensed histories of the six cases in which he was associated with Dr. Upson.

Five of the patients were operated on for pronounced pathologic conditions found in the pelvic organs; the recoveries have been complete and the results permanent up to the present time. The one patient who refused operative measures was finally removed to an asylum where she still remains unimproved. The bimanual examination in her case revealed a large tender retrodisplaced uterus, ovaries enlarged and prolapsed. By placing her in the knee-chest position and replacing the uterus and fitting a pessary, she was made temporarily better, but on her getting out of bed and walking about the tender,

enlarged ovaries were irritated by the pessary and it was removed. Operation in this case, Dr. Humiston believes, would have given excellent results.

CASE 1.—Woman, aged 46, had had profound increasing melancholy for several years, with apathy, disinclination for society, warped views of her duties and of her relations with her family and friends, amounting to delusions. She also had lassitude, pallor, muscular weakness and retroverted, enlarged and tender uterus.

Purulent disease in tubes and ovaries was corrected by operation. The result was a return to physical and mental health, which persists after six years.

CASE 2.—Melancholia agitata, following dysentery, in a man aged 63. There was frenzied depression with insomnia and motor unrest and fear of insanity and the asylum, which might or might not, under the circumstances, be considered as an insane delusion. Steady recovery took place on purgation, restricted diet and intestinal antiseptics. There is no recurrence after 12 years.

CASE 3.—A woman, aged 28, had melancholia, with delusions of sexual and other crimes and preparations for suicide. She had had rheumatism for four or five months, with nervousness, pallor and weakness. The delusions and depressions were profound, constituting a complete psychic change from her former mental habit. Recovery was prompt and complete after pelvic operation undertaken 2½ years ago for sclerocystic ovaries, chronic catarrhal appendicitis and adherent glans clitoridis.

CASE 4.—Woman, aged 58, had profound depression, with insomnia, motor unrest and evidences of intestinal indigestion following a period of anxiety. Purgation, milk diet, and intestinal antiseptics were promptly followed by subsidence of both the depression and the agitation. Insomnia also disappeared, although previously refractory to sedatives and hypnotics. Recovery persists after 11 years.

CASE 5.—An unmarried woman, aged 28, much depressed for about a year, made several attempts at suicide. She had marked delusions. Pelvic operation was performed eight years ago for sclerocystic ovaries and retroverted uterus. The result was complete and permanent recovery.

CASE 6.—Woman, aged 49, had profound melancholy with delusions of six or eight months' duration. Pelvic operation was performed three years ago for lacerated cervix, retroflexed uterus and sclerocystic ovaries; a small myoma in the post-uterine wall was not removed. One relapse of a few weeks' duration followed an attack of grippé, a few months after operation. Recovery was otherwise complete and the patient is now well after three years.

CASE 7.—Woman, aged 27, had delirious mania in the puerperium, accompanied by exaltation, singing, rhyming and ribald speech, night and day. Replacing the uterus with support of pessary was, on two occasions, followed by marked improvement, but operation was refused and chronic mania with delusions remains after seven years.

CASE 8.—Unmarried woman, aged 24, had recurrent mania alternating with periods of mild depression, the mania being characterized by typical flight of ideas, delusions, exaltation, etc. The patient has been three times in a private asylum. On two occasions supporting the retroflexed uterus gave temporary relief; finally curetting of the uterus and removal of the ovaries was followed by recovery, persistent 2½ years after the operation. The procedure has, even in this short time, fully justified itself by the condition of the patient, who is really robust for the first time since Dr. Humiston's acquaintance with her. She is now married and is taking full care of her household duties, and has gained twenty-six pounds in weight.

Dr. Humiston believes that the majority of cases of melancholia, without family history of insanity, in which pronounced pathologic conditions in the pelvis exist, can be cured by resorting to surgical procedures.

DR. FRANCIS X. DERCUM, Philadelphia, declared that he is firmly convinced that manic depressive insanity is primarily a neurosis. The overwhelming factor of heredity, the absence of visceral complications and the variability of visceral complications when present, justify no other inference than that the disease is a nervous disorder and that visceral symptoms when

present are merely complications. Recovery from insanity, subsequent to operations of various kinds is, of course, not unknown. Recovery has been known to follow accidents, such as injury to the head, after operations of various kinds, after infections and after indeed anything that may profoundly modify the general nutrition. The well-known influence of typhoid fever in bringing about recovery in insanity, is a convenient illustration. If manic depressive insanity is dependent on visceral lesions, these lesions ought to be of definite character. In view of the overwhelming factor of heredity how, he asked, are we to attribute any importance to such conditions as retroversion of the uterus. The truth is that retroversion is in many cases merely a retention of the primary position of the uterus and is not of itself really pathologic. Attempts to attribute manic depressive insanity to diseases of the digestive tract or to other visceral affections meet necessarily with the same fact, namely, the entire absence of a close etiologic relationship.

DR. ALFRED GORDON, Philadelphia, referred to the work of a French surgeon, Dr. Picqué, who made an exhaustive study of this subject. The work was done in one of the asylums of Paris and from a study of the record of these cases one is impressed with the fact that while some of the patients improve, the majority have recurrences, in spite of the correction of the retroversion of the uterus or any other pelvic disease. To Dr. Gordon it seemed difficult to connect, in any pathologic sense, as cause and effect visceral complications, or defects in the viscera with the psychoses, discussed by Dr. Upson.

DR. HENRY S. UPSON, Cleveland, Ohio, said that he is well aware of the unpopularity with many physicians of the theory that psychoses are dependent in any way on visceral disease, but it seemed to him that the bad repute of surgical intervention in these cases is due preëminently to the one fact that some early good results were obtained by operation on the pelvic viscera. Because the ovaries had been removed in some cases and melancholia cured, it was thought, formerly, that melancholia was an ovarian disease and that a cure would follow in all cases. There was too much enthusiasm, which resulted in disappointment, because recovery did not take place in all cases in which the ovaries were removed. It is a mistake to think that manic-depressive insanity in all these cases is the result of any one pathologic process, or has any well-defined syndrome in all cases. Dr. Upson believes that such statistics as Dr. Gordon mentioned ought not to be given too much weight, because such observations are usually made by a surgeon with the idea that manic-depressive insanity is a surgical disease and may be relieved by surgical procedure, especially in one class of cases.

### THE OPSONIN INDEX IN MEDICINE.\*

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In 1895, Denys and Leclef<sup>1</sup> first called attention to the effect of blood serum on phagocytosis by leucocytes. They were the first to produce reliable experimental evidence that substances which alter microbes in such a way as to permit their being ingested by the leucocytes exist in the blood serum of immunized rabbits. From careful experiments *in vitro* they concluded that in an immunized rabbit the leucocytes obtain their power of engulfing the bacteria from some other property of the serum. The immunized animal fights the bacteria, first, by the direct action of its serum; second, by its leucocytes.<sup>2</sup> The latter always owe to the serum the commencement of their power.

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

1. "Sur le mécanisme de l'immunité chez le lapin vacciné contre le streptococcus pyog.," *La Cellule*, 1895, vol. xi, p. 198.

2. A summary of their conclusions follows:

(a) The serum of normal rabbits exercises no bactericidal action on the *Streptococcus pyogenes*.

(b) The serum of a rabbit on whom a certain degree of im-

In 1897, Bordet<sup>3</sup> was unable to confirm their results. In the same year Mennes<sup>4</sup> showed that the immunity of guinea-pigs inoculated with toxins or cultures of pneumococci depends on a modification of their serum whereby an active phagocytosis is induced, and that this is not due to any special activity of the leucocytes. In 1902, Leishman<sup>5</sup> devised a method of quantitatively estimating the phagocytic power of blood to staphylococci. In 1903, Wright and Douglas<sup>6</sup> introduced the word "opsonin" (*opsono*, I prepare the food for) to characterize the substance in normal blood which they believed prepared the microbes for ingestion by the phagocytes. They were able to show that this substance exists in the serum, that it is partly thermolabile, being largely destroyed at 60 C. in ten minutes, and that it acts on the bacteria and not on the leucocytes.<sup>7</sup>

In 1904, Neufeld and Rimpau,<sup>8</sup> independently of Wright, alluded to the two well-known elements in immune sera (i. e., antitoxin and bactericidal substances) and stated that they had found a third element which they claimed sensitized the bacteria, but did not act on the leucocytes. They treated leucocytes with antistreptococcus serum for a certain time, suspended them in normal serum, and found that they did not ingest virulent streptococci (note that they employed virulent organisms). On the other hand, after treating virulent streptococci with antistreptococcus serum and then washing them free from the serum with salt solution, they found leucocytes could then actively ingest these sensitized microbes. They obtained corresponding results with pneumococci. They proposed to call their sensitizing substances "bacteriotropic" substances. To these substances Wright and Douglas have given the name "immune opsonins."

munity to streptococcus has been conferred by vaccination, will delay the development of streptococcus for several hours and will sometimes exhibit a true bactericidal power.

(c) Leucocytes from a normal rabbit added to the serum of a normal rabbit exhibit only a feeble phagocytic power to streptococcus. The leucocytes die before their usual term of life.

(d) Leucocytes from a normal rabbit added to the serum of a vaccinated rabbit energetically destroy streptococcus. The leucocytes preserve their normal duration of life.

(e) Leucocytes from a vaccinated rabbit added to its own serum act the same as above (d).

(f) Leucocytes from a vaccinated rabbit added to the serum of a normal rabbit act as above (c).

(g) If a dose of streptococcus, lethal for a normal rabbit, is injected into the pleura of a vaccinated rabbit, the serum prevents the development of a pleurisy.

(h) If a dose of streptococcus capable of producing erysipelas in a normal rabbit is injected under the skin of a vaccinated rabbit the infection is prevented especially by leucocytes.

3. *Ann. de l'Institut Pasteur*, 1897, p. 201, note.

4. "Antipneumokokken Serum und der Mechanismus der Immunität des Kaninchens gegen den Pneumokokkus," *Zschr. f. Hyg.*, 1897, vol. xxv, p. 413.

5. "Method of Estimating Phagocytic Power," *Brit. Med. Jour.*, 1902, p. 73.

6. *Proc. of Royal Soc.*, vol. lxxii, p. 357.

7. The following experiments were responsible for their conclusions:

(a) Staphylococcus emulsion + washed corpuscles + NaCl solution at 37 C. for 15 minutes = no phagocytosis. Add serum; phagocytosis occurs.

(b) Three vols. washed corpuscles + 3 vols. serum at 37 C. for 15 minutes, then heated to 60 C. (destroying the thermolabile opsonin). Cool + 1 vol. emulsion staphylococci at 37 C. for 15 minutes, result is little or no phagocytosis.

(c) Three vols. serum + 1 vol. emulsion staphylococci at 37 C. for 15 minutes, then heated to 60 C. + 3 vols. corpuscles at 37 C. for 15 minutes, result is marked phagocytosis. Hence, action of serum is mainly to modify the bacteria in such a way as to render them a prey to the phagocytosis.

The organisms which are thus acted on are staphylococci, streptococci, gonococcus, pneumococcus, *Micrococcus melitensis*, vibrio of Asiatic cholera, and colon, pest, typhoid, tubercle, anthrax, proteus, and dysentery bacilli.

8. Neufeld and Rimpau: "Ueber die Antikörper der Streptokokken und Pneumokokken Immunserum," *Deutsch. med. Wochschr.*, 40, 1904, Sept. 29, p. 1458; also *Zschr. f. Hyg.*, 1905, vol. ii, p. 283.