SOME CASES OF MENTAL DISORDER: A PATHO-CLINICAL STUDY.

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In recent years research into mental disorders has tended to become more and more the study of the pathology of the living. The advance of biochemistry has contributed in great measure to this practice. Although bacteriological research has, in recent years, been more extensively undertaken in connection with focal infection, it has, in the opinion of most, yielded disappointing results. The study of focal infection by bacteriological methods alone will not, I am afraid, lead us very far. Endeavour should be made to correlate its local and remote effects in disordered hæmopoiesis, disordered metabolism and disordered endocrines in relation to the internal economy of the patient. In mental disease especially this implies a knowledge of the individual's potentialities that have been predestined by heredity, and later moulded by environment—factors which largely determine the psychopathic tendencies of every one of us. The bacteriological researches of Ford-Robertson and McRae (1) strongly suggest that in mental disorders we are confronted by bacteria of a special type, which as chronic infective agents can probably only adapt themselves to a certain group of the general community having a neurotoxic susceptibility. If, then, we are to make further progress in this direction, we must search for and apply new methods of bacteriological technique, study our results, and attempt to correlate cause and effect. In this relation I shall refer to special methods which are an elaboration of my father's work, the value of which time and experience may prove. In spite of the great importance of the biochemical researches of recent years, I think it will be agreed that some of us, especially those who are clinicians, feel disappointed that so far they have not given us as much indication for scientifically applied treatment as we had hoped. May I suggest that the explanation for this is two-fold. Firstly, in forming the basis of any research the present tendency is to take mental disorders in groups, for example, dementia præcox, which has a wide range of symptoms and between which

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and other groups it is difficult to draw a line of demarcation. It seems to me that our knowledge of the somatic factors underlying mental disorder is as yet so limited that attempts to continue on these lines will lead us only hesitatingly along the path of progress. Are we not still at the stage where our efforts should be concentrated more on the individual as a problem in pathology which, when solved as far as our knowledge permits, can be correlated in the future with his or her psychogenic group? The second point is that in many instances our scientific work tends to run in too narrow channels; thus it must be frequently lacking in the invaluable support of parallel knowledge in other branches of laboratory and clinical experience. The most obvious example is the lack of adequate collaboration between the biochemist and bacteriologist. I know of no two sciences that can be welded together so opportunely. This combination can be taken a stage further: active and intelligent co-operation with the clinician and X-rays and therapeutic specialists should be sought to enable us to appreciate better the intricate problems we have to face. Some of you may, with reasonable grounds, accuse me of theorizing, and I should at this stage like to mention that before I attempted to put these considerations into practice in cases of mental disorder, I had had the opportunity of carrying out exactly similar lines of research on some hundreds of non-mental patients in hospital and private practice. The majority of them were cases obscure in ætiology and symptomatology. This scientific survey proved to me at least the value of comprehensive work on the individual, and how it enabled one to diagnose and treat many cases with some hope of success. During my two years at Wantage House (the new acute hospital attached to St. Andrew's), I have attempted to carry out what this experience has taught me, with the added advantage that the patients have been under my personal care. Further, there has been every facility for dental and general X-ray diagnosis, and, lastly, ample scope for treatment. The success of such a scheme is only possible by organization and the team spirit, and in this I have been singularly fortunate. The cases I am bringing to your notice are 4 out of some 120 which have been subjected to comprehensive overhaul. I will try to emphasize the salient features in each and correlate them with the mental disorder presented. In this way you can judge for yourselves if we have learnt anything that may in the future lead to a clearer conception of what may underlie at least some forms of mental disorder.

Before passing to them I would like to refer to a term that might with advantage be applied to mental disorder as implying much in concise language. The tissues can be divided into somatic and

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neural, and it is the relationship between the two that some of us are studying, and especially their pathology. Trotter (2) in his paper emphasizes how Nature has taken infinite pains to insulate the brain and nerves from direct contact with somatic tissues. Regarded in this way the nervous system can be said to be cut off from, but nevertheless intimately connected with, and surrounded by, the rest of the body. In health they should be constantly reacting in physiological harmony with each other, and if this harmony is perfect one system should be unaware of the presence of the other. In somatic disease, however, such harmony is frequently broken, and our nervous system protests and warns us of impending trouble. Mental disorder may, in many instances, not only be the expression but the extension of such a process. Pathological stimuli may be capable of reaching the brain by abnormal paths *viâ* the spinal cord instead of reacting upon the reflex arc mechanism. Personal observations on many cases would strongly suggest that this is possible. Assuming that some of this hypothesis can be accepted, the term "*internal environment*" as expressing the relationship of the central nervous system to the somatic tissues seems worthy of wider adoption.

CASE I.—Manic-depressive insanity, æt. 52, married. Admitted to Wantage House, December, 1927, as a voluntary boarder. Certified some days later.

History.—Family: No psychopathic history.

Personal: Childhood apparently normal; during the war subject to slight gastric trouble owing to food. In 1919 first attack of mania; under care and relieved. Second attack 1923; certified and admitted to hospital. Mania lasted for five months. Treatment, prolonged immersion baths. Became depressed and apathetic. Discharged relieved two months later. Physical health regarded as excellent.

Present illness: In November, 1927, he became excited, talkative and destructive, up most of the night. On admission he was restless, loquacious, noisy, and threatening if controlled in any way. No insight.

Physical state.—Well nourished, 2 st. over ideal weight. Skin moist, plethoric, reflexes exaggerated.

Tongue slightly coated; mouth edentulous, except for upper and lower incisors; alveolar absorption marked, gums inflamed. X-ray: Two apical foci; lines of bone rarefaction present.

Tonsils: Slightly enlarged, crypts containing thick secretion. Fauces: Rather swollen and injected.

Nasal passages: Clean, no obstruction, turbinates normal. Antra and sinuses: Clear by transillumination and X-rays.

Abdomen: Adipose. Stomach: Appetite abnormally large, thirsty; no complaint of pain or discomfort. Bowels: Had been constipated, now regular. Colon: No tonic hardening apparent. Other organs normal.

Chest: Heart and circulation good. Blood-pressure: 141/95; pulse-pressure 46.

Laboratory findings.—Blood: red blood-cells 4,818,000, hæmoglobin 16·2 grm. %, colour index 0·8, white blood-cells 9,200, 71% polymorphic.

Biochemical: Blood CO_2 (Van Slyke) 50 c.c %; blood-sugar 0·123 mgrm. % 2½ hours p.c.; non protein nitrogen 35·2 mgrm. %; uric acid 2·85 mgrm. %; serum calcium 10·4 mgrm.%. Van den Bergh: Negative.

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Glucose tolerance test on 50 grm. carried out simultaneously with test meal (for the latter Ryle's tube and standard oatmeal gruel were used. Resting juice and ½-hourly samples taken for a period of two hours); free HCl was absent throughout, peptic activity 1: 4, motility normal. Blood-sugar curve: Hyperglycæmia with glycosuria.

Urine: 24-hour sample 1,230 c.c. Normal chemical (quantitative and qualitative) and cytological findings.

Fæces: Stercobilin almost absent; soluble mucus excessive; assimilation fat deficient.

Bacteriological.—Dental culture: *Streptococcus anginosus* ++, pneumococcus ++, *Micrococcus catarrhalis* No. 1 ++; anaerobic culture—*Micrococcus catarrhalis* No. 2 +++. (This organism was a strict anaerobe and quite different from No. 1.)

Resting juice: *Streptococcus anginosus* ++, *Streptococcus pyogenes mitis* +, *Streptococcus pyogenes* (peroxidase type) ++, *Micrococcus catarrhalis* ++; anaerobic culture—*Streptococcus anginosus* 1 and 2 ++, *Micrococcus catarrhalis* 1 and 2 (one a strict anaerobe as in dental), each ++.

Intestine: *B. Friedländer* +++, *B. coli communis* ±, *Streptococcus fæcalis* +++, *Streptococcus fæcalis globiniticus* ++; anaerobic culture—putrefactive type of bacillus +++.

Comments.

From a clinical point of view there would seem to be little relationship between the patient's physical condition and his psychosis. In fact for the past nine years, during which he had been either melancholic or maniacal, there was nothing definite physically to which his doctors could take exception apart from his teeth, the extraction of which from time to time had not apparently influenced the onset or subsequent course of his mental trouble. The abdominal discomfort was not more than one might expect from one accustomed to overeat, and his appearance suggested robust health in spite of pyorrhœa and two loose stumps. Investigation, however, of his economy by systematic laboratory examination brought to light definite, if not serious, functional disorder, accompanied by severe focal infection and intoxication. The blood-count showed a disturbance of the hæmopoietic system and biochemical examination a reduced blood alkali reserve. Other findings were normal. There was evidence of disturbance of the parasympathetic side of the endocrine system. Sugar tolerance was much lowered on account of pancreatic and liver metabolic deficiency; hyperglycæmia and glycosuria were present. Gastric function was abnormal. Free hydrochloric acid was absent throughout, peptic secretion very low, and mucus was present in large amount. Added to this was the cultural evidence of severe infection by streptococci of the anginosus and pyogenes group and by anaerobic *Micrococcus catarrhalis*. In this case, as in many others I have studied, the resting juice showed a greater variety and severity of bacterial flora than did the teeth—an example of cumulative infection. In another paper (3) I have shown that the

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presence of hydrochloric acid and pepsin in the resting juice in sufficient concentration to act as a bactericidal barrier has an important bearing on the question of gastric infection. Study of the excreta gave evidence of biliary deficiency and defective fat assimilation in consequence. Later both became normal. No colitic mucus was found on Plombières lavage, but chemically soluble mucus was excessive, denoting a mild catarrhal condition of the colon. The bacterial flora was abnormal both in coliforms and in fæcal streptococci, while anaerobic methods showed the presence of a putrefactive organism in moderate numbers.

Progress and treatment.—Complete rest in bed and six hours' prolonged immersion athermal baths at 97° F. divided into two periods were given daily for two months. For seven weeks Plombières lavage on alternate days was given. At first sedatives were needed, but these were soon reduced. Restrictions in diet, especially farinaceous foods, were made, and 1 drm. of HCl dil. with liquor pepsini 30 min. were given as a drink with meals. Dried thyroid extract 2 gr. was tolerated well, and at the end of this period he had lost 14 lb., was sleeping better, and was much quieter, and better behaved, but still euphoric. Eight teeth were next extracted under gas, no obvious disturbance being produced. The baths were continued, but gradually reduced to one hour daily. Immunization was next tried by giving small doses of autogenous dental vaccine; no disturbance was produced. Later the intestinal vaccine was introduced, and at a dose of 800 millions and higher definite reactions were to be noted in exacerbation of the mental condition and diarrhœa for 24–36 hours. Interspaced between these doses intravenous injections of T.A.B. were given and were well tolerated with reactions up to 104° F. Ten doses were administered in all. At the end of six months his mental condition had improved greatly; he was quiet and almost reserved. The baths were omitted. The blood-count at this stage showed improvement and the blood alkali reserve was fully normal. The blood-pressure was slightly lowered, being 131·87. Improvement continued, and he was able to live a practically normal life. At the end of the eighth month he was transferred to a villa, but continued treatment as an outpatient. The autogenous vaccine was continued in order to keep up his immunity, though he had quite ceased to react. In November, 1928, he was discharged from certificate and remained as a voluntary patient.

Two months later a course of gastric lavage was given, using Senoran's evacuator and water and hydrogen peroxide as advised by Hurst (4). At first the amount of mucus was very considerable, but the quantity was greatly reduced after the sixth lavage and has

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remained so up to date with one interesting exception. The patient contracted a severe cold, which had been going for some days when he came for his next lavage, and on this occasion the amount of mucus was considerably increased. This suggested that the catarrhal condition had extended to the stomach. Up to the present he has kept perfectly well and is busy writing a book on mathematics, and it is worthy of note that he has not gone through the period of depression characteristic of previous attacks. The bacteriological flora shows much improvement.

This case illustrates how entirely hidden the disorders of the internal environment may be unless they are especially looked for. His present satisfactory recovery strongly suggests that general alimentary infection and its resulting toxæmia were important contributory factors, which he could only overcome by scientifically applied treatment based on the findings.

CASE 2.—Mr. A. B—, recurrent confusional insanity, single, æt. 29. Admitted (transfer) to Wantage House, February, 1928. Certified March, 1924.

History.—Family: Father committed suicide at 50. Mother became weak-minded. Second cousin committed suicide. Paternal aunt insane; melancholia, with delusions.

Personal: In infancy convulsions, at 9 pneumonia. Brilliant at school, university scholarship at 17. War 1917–1919. Wounded, blown up. University 1919–1922. Consular service 1923.

Present illness: March, 1924, acute mental breakdown preceded by love affair. Transferred to St. Andrew's, May, 1925. During his 21 months of residence he suffered from periodical attacks of confusion lasting for two to three weeks, but occasionally for much longer. He was noisy, abusive, restless and destructive. Incoherent in speech, deluded and sometimes hallucinated. It was observed that his physical condition, which as a rule was outwardly good, deteriorated prior to the attacks. For some months before his transfer from the main hospital to Wantage House, treatment by rest, baths and purges tended to shorten the attacks. At the time of his transfer he was quiescent and quite normal in conduct.

Physical state.—Physique good, muscular, but 11 lb. under ideal weight. Skin rather coarse and greasy, tending to acne on back. Reflexes and pupils normal.

Tongue slightly coated; breath sour; gums healthy. X-rays: One devitalized tooth, no obvious apical focus.

Tonsils: Both slightly enlarged, a few crypts present filled with muco-pus; fauces inflamed especially around tonsillar areas.

Nasal passages: Dirty, much mucoid secretion; septum deflected but no obstruction. Right middle turbinate enlarged.

Antra and sinuses: Clear by transillumination and stereoscopic X-rays.

Stomach: Appetite good but occasionally mild digestive disturbance.

Bowels regular except during attacks; some tonic hardening of the descending and pelvic colon; cæcum palpable but not contracted, slightly tender to deep pressure.

Chest, heart and circulation good. Blood-pressure 127/78; pulse-pressure 49.

Laboratory findings.—Blood: Red blood-cells 5,184,000, hæmoglobin 16·3 grm. %, colour index 0·79, white blood-cells 6,200, 38% lymphocytic; blood CO_2 (Van Slyke) 64 c.c. %. Van den Bergh: Direct, negative; indirect, trace.

Glucose tolerance test: 50 grm. normal curve. No glycosuria.

Fractional gastric test meal: No free HCl in resting juice, none secreted until one hour; maximum tide 10° at 1¾ hours; motility deficient; pepsin 1–16 at 1 hour (normal 1–64). Gastric mucus small in amount.

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Urine: 24-hour sample, normal findings.

Fæces: Very offensive odour, stercobilin very deficient, soluble mucus excessive; assimilation, neutral fat deficient.

Bacteriological.—Tonsillar culture: *Streptococcus anginosus* +++ *Micrococcus catarrhalis* ++. Anaerobic culture—diphtheroid No. 1 (strongly metachromatic type) +++, diphtheroid No. 2 (clubbed type) ++.

Resting juice culture: *Streptococcus anginosus* No. 1 +++, ditto No. 2 +.

Intestine: *B. coli communis* +++, *Streptococcus fæcalis* ++, *Streptococcus fæcalis globiniticus* +. Anaerobic culture—diphtheroid No. 1 (strongly metachromatic type) ++, ditto No. 2 (clubbed type) ++, leptothrix +++.

Comments.

Clinical examination in this case again yielded disappointingly negative findings, although one was forced to the conclusion that his physical condition was generally unsatisfactory and that he was subtoxic. Analysis of the laboratory results gave, however, definite evidence of internal environmental disorder and severe focal infection by anaerobic species of bacteria. The blood-count was low normal, but showed a disturbance of the differential count towards the lymphocytic side, which in the light of the bacteriological findings has, I think, some significance. Gastric function was disordered, there being present a marked hypochlorhydria, with positive culture from the resting juice. Although gastric catarrh was not excessive, I believe one is justified in assuming that the mucous membrane was infected. The blood alkali reserve was taken during the remissions and exacerbations for comparative purposes. It is interesting to note that the average during remissions was 66 c.c. %, and 58 c.c. % when in an attack. Although within the normal range, it is possible that the drop of 8 c.c. %, in his case at least, has some significance. This point suggests itself: the relatively small change towards the pathological of this particular mechanism of his internal environment may be the indication of somatic tolerance, but also of neuropathic susceptibility to some toxic state. In this connection his abnormal psychotic heredity is of interest. The glucose tolerance test showed no disturbance of glyco-synthesis, but the mildly positive indirect Van den Bergh indicated a reaction of the reticulo-endothelial system of the liver. Bacteriological analysis of his case is of interest. Aerobic streptococcal infection of the tonsils was considerable, and this organism was also isolated from the resting juice along with other species. If anaerobic methods had been omitted throughout no special ætiological importance would have been placed on these findings, but in this case, as in many others, anaerobic culture presented an entirely different picture, which has, I believe, a considerable significance.

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Two species of diphtheroid were isolated, one highly metachromatic and morphologically almost identical with the Klebs-Loeffler bacillus; the other, a sub-species, was not so numerous. This picture of focal infection does not, however end there; both bacteria were isolated in almost similar numbers from the intestine, not only once, but several times. In addition to these, anaerobic leptothrix colonies were likewise very numerous. In many cases I have been fortunate enough to be able to trace streptococci, *Micrococcus catarrhalis* and anaerobic diphtheroid species from oral sources to the stomach and then to the intestine. By so doing one is better able to realize how extensive and deep-seated chronic sepsis may become. This case is illustrative, and one where ordinary bacteriological methods would have failed, the aerobic culture of the stool showing a comparatively innocuous flora of *B. coli*, *Streptococcus fæcalis* and a sub-species. After treatment and recovery from the confusional condition the diphtheroid flora in the tonsil entirely disappeared, and that of the intestine was much modified, but the infection by no means eliminated.

Progress and treatment.—On admission, mental condition quiescent, patient bright and normal, under observation. On the 27th day, without much warning, he developed a characteristic attack of confusion, during which he was restless and talkative, noisy and deluded. Sleep was very poor, he became constipated, and examination of the throat showed considerable increase of the inflammation. Athermal baths 30 minutes in duration were given daily and Plombières lavage on the occasions the bowels failed to act. The motion was constipated, very offensive and slimy. On the seventh day of the attack 50 million T.A.B. was given intravenously and a good reaction followed. Next day he was a little better mentally. Two further doses were given at an interval of three days. At the end of ten days the acute phase was over. He was quiet and almost rational, reaching normality nine days later. He was then tested for reactive response to a small dose of the autogenous tonsillar and intestinal vaccine. The first produced a slight return of the confusion for twenty-four hours. An increased dose given five days later resulted in a definite return of symptoms which lasted several days. While still confused another T.A.B. was given and a good reaction followed. Next day he was almost normal. In all, eight T.A.B. pyrexial injections were given at about seven days' interval, and the autogenous vaccine interpolated. It was interesting to note the mental exacerbations to the latter and the cutting short effect of the former. During one of the later T.A.B. reactions I had the opportunity of observing during the short period of maximum temperature the return for a

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few minutes of his more acute mental picture. Four months after admission it was evident that the cycle of attacks had been broken. He remained quiet and normal for seven months, able to be actively engaged in all forms of recreation. In January of this year he had a slight return of confusion and talkativeness which under hydrotherapeutic treatment lasted barely ten days. Since then he has kept well physically and his conduct is satisfactory. It is unfortunate and yet interesting, especially to those more interested in the psychological aspects of his case, that he retains some of his delusions which concern his identity and one of his near relatives. When he is well he is most reticent about his ideas and his behaviour is not affected. Only with the onset of confusion does he give expression to them. One wonders, if he had had the opportunity of being treated at the onset of his long illness, whether he might not have been once more a useful member of the community.

His physical health has much improved and has been maintained; from time to time immunization is carried out along with stimulative hydrotherapy and occasional intestinal lavage.

CASE 3.—Miss C. D—, dementia præcox, single, æt. 27. Admission to Wantage House December, 1927. Certified 1925.

History.—Family: Paternal aunt, melancholia, æt. 75.

Personal: Two sunstrokes; at puberty "anæmia" and "nerves." No history of gastric trouble, but never had much appetite.

Present illness: Mental symptoms two years ago; no remission since. On admission she was confused, very restless and resistive, at times violent. Delusions prominent. She said "there were Chinamen and knives in the mattress." Rambling and incoherent, emotional at times, habits defective, refused food, sleeping badly.

Physical state.—Very thin, being 2 st. under ideal weight. Face showed stigmata of degeneration. Skin dark, almost pigmented, dry. Mucous membranes anæmic. Left ear scarred from hæmatoma. Condition obviously toxic. Reflexes exaggerated. Pupils equal, reacted to light and accommodation.

Tongue thickly coated; general sordes, breath most offensive; gums inflamed; molars well filled. X-ray: Two devitalized, one with large apical focus.

Tonsils: Small, firm; crypts contained muco-purulent secretion; peritonsillar injection marked. Fauces: Œdematous and very inflamed.

Nasal passages: Dirty, muco-pus present. Turbinates slightly enlarged, no obstruction.

Antra and sinuses: Clear by transillumination and stereoscopic X-rays.

Abdomen: Muscular rigidity marked, no tenderness. Bowels very constipated, 2–4 days. Descending and pelvic colon showed extreme tonic hardening, portions being no thicker than one's finger.

Heart-sounds slightly accentuated. Blood-pressure 102/76; pulse volume poor and pressure 26 indicating low cardiac reserve. Extremities cold with some peripheral stasis.

Chest: Poorly developed, sounds normal.

Laboratory findings.—Blood: red blood-cells 4,176,000, hæmoglobin 13·5 grm. %, colour index 0·9, white blood-cells 5,900, differential count normal. Biochemical: Blood CO_2 68 c.c. %; non-protein nitrogen 35·2 mgrm. %; uric acid 2.35 mgrm. %. Serum calcium 9·2 mgrm. %. Van den Bergh, both reactions negative.

Glucose tolerance test 50 grm.: Fasting level 89 mgrm. %; 1 hour 156 mgrm. %, 2 hours 207 mgrm. %; at one hour 0·5 % urine sugar; no other sample available owing to incontinence.

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Fractional gastric test meal: Free HCl absent throughout; mucus very excessive in most samples; hypermotility; peptic activity, resting juice 1–16 and at one hour 1–8.

Urine: 24-hours sample about 740 c.c.; albumen, faint trace; other findings negative or low normal; fæces, soluble mucus excessive, stercobilin deficient; assimilation, fat deficient; Plombières lavage showed moderate degree of colitis.

Bacteriological.—Dental culture from molar with apical focus, *Streptococcus pyogenes* (peroxidase type) two varieties, both ++, *Streptococcus salivarius* +++, diphtheroid ++.

Resting juice: *Micrococcus catarrhalis* ++, *Streptococcus anginosus* +, *Streptococcus pyogenes mitis* ++, *Streptococcus pyogenes* (peroxidase) No. 2 as in dental culture +++.

Intestinal: *B. coli* +, *Streptococcus fæcalis globiniticus* +; anaerobic culture, *B. coli* +, diphtheroid two types, both metachromatic, each ++, diphtheroid 3rd type ++, *Streptococcus fæcalis globiniticus* as in aerobic culture ++, *Streptococcus pyogenes* (peroxidase type) +.

Comments.

Clinically this case showed severe toxæmia with defective metabolism and general endocrine deficiency. Amenorrhœa since commencement of illness. Cardiac weakness was evident along with hypotension. Teeth not obviously infected, but X-rays showed one extensive apical focus. The flora of the tonsils, fauces and nasal passages, although not examined bacteriologically, was without doubt represented by that found in the resting juice. The laboratory findings were in keeping with the clinical, but showed that she was the victim of achlorhydria and a very severe gastritis. The glucose tolerance curve was unusual and suggested slow absorption, but at two hours a hyperglycæmia occurred. At one hour slight glycosuria resulted with only 150 mgrm. % of blood-sugar. The low blood-calcium of 9·2 mgrm. % may, however, explain this in causing renal permeability to sugar. Four months later this test was repeated and a practically normal curve resulted, but slight glycosuria again occurred. The blood alkali reserve as estimated by the CO_2 combining power of the plasma gave a high normal figure, but later, as her physical condition further deteriorated, it fell to almost pathological limits—53 c.c. %. The non-protein nitrogen and uric acid figures did not indicate any obvious renal involvement, in spite of the albumen which appeared in all samples of urine except the one on admission. The admission twenty-four hours' sample did not contain abnormal constituents, but later sugar, acetone and albumen appeared.

The fæcal sample was offensive and indicative of disordered bowel function. Later the cerebro-spinal fluid was taken, but showed nothing abnormal; the colloidal gold curve gave, however, the following mildly positive luetic type of curve: 112310000. Whether it has any significance is doubtful. The bacteriological

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findings gave evidence of severe focal infection, the gastric infection alone was sufficient to cause serious toxæmia, and this state of affairs was probably in existence for years prior to her breakdown. The infective condition of the mouth and respiratory passages probably augmented and maintained the gastric mucous membrane as a large focus of infection.

The anaerobic intestinal flora, as in the other cases, was most abnormal. No fewer than three types of diphtheroid were isolated and the sum total constituted a neurotoxic infection of great severity. The omission of tonsillar cultural examination did not give me the opportunity of tracing the path of infection as I had been able to do in other cases. If time had permitted, a more detailed investigation of the blood, urine and stool during the period of her residence might have thrown further light on the disordered internal environment. As it will be seen, she proved unresponsive and a failure in every way.

Progress and treatment.—For the first six weeks prolonged immersion baths were given at 97–98° F. for six hours daily. Intestinal lavage was also given each day, and during the course colitic mucus appeared in moderate amount, and later diminished. Sedatives were given at night. At the end of this period, her confusion had improved to some extent; she was still deluded. Her skin and general appearance had improved considerably, but she lost some weight. After ascertaining the gastric condition, HCl and pepsin were given as a drink with meals, but had no effect on her appetite. A course of artificial sunlight was tried in the hope of improving assimilation and raising her resistance. Little or no skin reaction was produced. She was quieter after each treatment but only for a few hours. Fifteen exposures were given in seven weeks, cod-liver oil being given at the same time. At the end of the treatment there was no gain in weight, but her physical condition had shown further slight improvement.

She was less confused but remained restless and resistive. It is necessary to mention that intestinal lavage was continued and given every second day on account of the severe constipation. Two teeth were extracted without affecting her mental state. An attempt was then made to immunize her by an autogenous dental vaccine. Small but increasing doses were given for a period of three months. Owing to the mental condition it was very difficult to judge whether reactions occurred; at the end of this period she, however, was much clearer mentally and could converse at times quite coherently. She remained deluded and restless, but was more cooperative. Her physical health was definitely better and she gained weight. Having got thus far a T.A.B. injection was tried, but with a poor

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reaction, maximum temperature 99° F., pulse good. No effect on her mental condition was observed. Four days later another intravenous injection was given, again with a disappointing reaction and no improvement. In fact her delusions were more marked and her behaviour deteriorated. One more intravenous injection was, however, tried. Practically no reaction occurred, her temperature rose from subnormal to normal, the pulse was rapid and feeble and she looked ill. Mentally she became worse. After a brief interval the autogenous intestinal vaccine was tried, small doses being given at five to seven days' interval. Again, owing to her constant restless and confused condition possible reactions were difficult to ascertain, but occasional rises of temperature to 99° F. followed. After two months' immunization she showed definite improvement and more than regained the lost ground. A month later she once more relapsed, at a time when larger doses of vaccine were being given. Her mental and physical condition grew worse and the treatment was discontinued. On November 6, 1928, she developed œdema of the ankles and showed more definite heart weakness. Indican, acetone, sugar and albumen were present in the urine in small amounts. The cerebro-spinal fluid was taken at this time. Tube-feeding had to be resorted to. Before giving the feed the stomach was washed out, using Senoran's evacuator. Three separate lavages were made by introducing 1½ pints of water containing 3 oz. of hydrogen peroxide. This treatment was carried out on eight successive days. On all occasions the amount of gastric mucus was tremendous. The patient was transferred to the main hospital on November 28, 1928; no improvement had been brought about mentally or physically. This case was a dismal failure in spite of treatment, which had been based on a fairly sound knowledge of the underlying physical disorders. Due consideration must be taken, I think, of the duration of the illness, its severity, and the extreme nature of the alimentary focal infection in assessing the powers of recovery. Too much should not be expected with our present limited knowledge of the treatment of such cases. The patient's resistance was very poor, in fact overwhelmed, and the mechanism of the brain completely disorganized. Nevertheless there was some response to specific stimulation, as her temporary improvement showed. The difficulty of observing reactions and thus controlling the vaccine dosage probably allowed one to overstep the small margin without any warning of its approach until too late. The T.A.B. injections were a failure for the same reason and probably did harm. Her subsequent course I have not been able to trace, as her relations decided to have her under care at home. The prognosis in the case was bad, but I think rendered more hopeless

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when the underlying disorders of her internal environment were revealed. From each case we may learn something, and the chief lesson from this one can be summed up in a few words: Diagnose and treat early.

CASE 4.—Miss E. F—, recurrent confusional, single, æt. 18. Admitted (transfer) to Wantage House, November, 1927. Certified, November, 1926.

History.—Family: Uncle insane. Mother alcoholic.

Personal: No serious illnesses; appendicitis, recurrent septic throats.

Present illness: In the summer of 1925 she became worried, morose, sometimes restless and excited at night. Turned against her mother and threatened suicide. Later she developed hallucinations, and, the voices and visions affecting her conduct, she became noisy and violent.

She showed insight into her condition and felt that she had lost control and that her mind was going. She deteriorated, and in November, 1926, was admitted to St. Andrew's Hospital. Her mental condition was reported as confused, emotional, phrases reiterated again and again, auditory hallucinations marked. She was well nourished, and there was apparently nothing to take exception to in her physical health. Later examination by a neurologist pronounced that there was no organic disease of the brain and she was free from any sign of disease elsewhere, but that endocrine disturbance associated with her periods might have a bearing on her mental condition. During the course of the year remission followed exacerbation at fairly regular intervals. The attacks of restlessness and confusion gradually became more frequent and severe, their onset sudden and the confusion subsequently deepening into a trance-like state lasting sometimes for a week. Her physical state deteriorated; she had lost 19 lb. since admission. Treatment was baths, sedatives, laxatives and endocrines.

Mental condition.—In remission, slightly confused and restless but able to talk and answer questions fairly rationally.

Physical condition.—Looked ill and toxic, development poor, amenorrhœic for months. 1 st. 2 lb. under ideal weight. Skin pale, sallow, slight pigmentation on body. Complained of headache, variable, but when severe localized to the occipital region. Pupils dilated, equal, reactive. Reflexes sluggish. Endocrines general hypo-function, especially thyroid and gonads.

Tongue coated, breath offensive, gums healthy, teeth very good; X-rays showed no apical foci.

Tonsils: right, no enlargement, secretion small; left enlarged, irregular, crypts filled with *débris* and muco-pus. Fauces: very injected, peritonsillar flush marked.

Post-nasal spaces inflamed, secretion excessive. Nasal passages inflamed, turbinates slightly enlarged, mucoid secretion present.

Antra and sinuses: Clear by transillumination and stereoscopic X-rays.

Abdomen flaccid. Complains of gastric discomfort after food having become worse, no abnormality of stomach to be made out. Bowels: Constipated, descending and sigmoid definitely hardened and slightly tender to firm pressure. Other organs normal.

Heart normal. Pulse soft, regular, feet cold; blood-pressure 113/84, pulse-pressure 29.

Chest normal.

Laboratory findings.—Blood: A count was taken a few hours prior to an attack. Red blood-cells 4,464,000, hæmoglobin 13·3 grm. %, white blood-cells 15,700, differential count 70% polymorphs. Biochemical: Blood CO_2 47 c.c. %, non-protein nitrogen 26·06 mgrm. %, uric acid 1·8 mgrm. %, calcium 10·85 mgrm. %. Van den Bergh negative.

Cerebro-spinal fluid taken while patient was unconscious. Pressure raised, cells lymphocytic, 5·6 per c.mm., globulin *nil*, albumen 0·0264 %, sugar 62 mgrm. %, non-protein nitrogen 12·2 mgrm. %, chlorides 0·7%.

Glucose tolerance test, 50 grm. carried out 24 hours after consciousness was regained. Fasting blood 112 mgrm. %, at ½ hour 191 mgrm. %, 1½ hours 171 mgrm. %, no glycosuria.

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Fractional gastric test meal: Resting juice 6° free HCl; no secretion of free acid until 1 hour, then only 8°, maximum 12° at 2 hours; peptic activity 1–2 at 1 hour; gastric mucus excessive.

Urine: 24-hour sample collected immediately following recovery from first attack. Low specific gravity, albumen trace, ammonia 0·625%, other findings low.

Fæcal: Stercobilin deficient, soluble mucus excessive; colitic mucus, as ascertained later from Plombières reports, was present in moderate amount. Assimilation, fat deficient.

Bacteriological.—Left tonsil: *Streptococcus pyogenes mitis* ++++, *Streptococcus pyogenes* (peroxidase type) ++, *Micrococcus catarrhalis* No. 1 ++, diphtheroid clubbed type +. Anaerobic culture—diphtheroid (metachromatic type) ++, *Streptococcus anginosus* +, *Micrococcus catarrhalis* No. 2 (strict anaerobe) ++.

Resting juice: Culture obtained at second test-meal. No free acidity, *Streptococcus pyogenes mitis* ++, *Streptococcus pyogenes* (peroxidase type) +, leptothrix +; no anaerobic culture made.

Intestinal: *B. coli communis* ++, lactose non-fermenter, *Proteus* +, *Streptococcus anginosus* ++, *Streptococcus pyogenes* peroxidase type ++, *Streptococcus fæcalis globiniticus* ++. Anaerobic culture—diphtheroid No. 1 (clubbed type) ++, diphtheroid No. 2 (metachromatic type) ++, leptothrix ++, *Micrococcus catarrhalis* (strict anaerobe) +.

Comments.

The clinical picture can be summed up in two words—intense toxæmia—and yet detailed examination did not give any obvious clue to the cause of her serious condition. Symptoms such as gastric pain would have passed as hypochondriacal delusions. The endocrine disorder represented by absent menses was probably only one manifestation of a complex of disordered functions. The laboratory findings, on the other hand, expressed in no uncertain terms the state of the internal environment. The secondary anæmia and polymorphic leucocytosis of 15,700 showed the reaction to bacterial toxins, which, as it so happened, must have been reaching a climax of intensity prior to an attack. The low CO_2 reading of 47 c.c. %, indicating acidosis, is also clearly in keeping with events. The blood calcium gave a normal figure, but subsequent examinations throughout the illness showed a deficiency. The glucose tolerance test taken after the first attack was only slightly outside strictly normal limits, but the test-meal showed a very definite hypochlorhydria and an accompanying gastritis. A repetition of the test eleven months later confirmed this, but the signs of inflammation had much improved. The twenty-four hours' sample of urine and others were surprisingly negative, but later definitely pathological constituents appeared. The stool, as in other cases, was offensive, biliary excretion was deficient, catarrh excessive and assimilation lacking. The cerebro-spinal fluid with its negative findings helps to support the supposition that the effects on the central nervous system were purely toxic, *viâ* the blood-stream or lymphatics. The bacteriological findings are of special interest if not of considerable importance. They show

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particularly clearly how the whole of the upper respiratory flora can be traced to the stomach and then to the intestines. The streptococcal flora represented by the anginosus and pyogenes groups were isolated from the stool and were identical with those in the tonsils. Of the anaerobes, not only had the two diphtheroids become firmly implanted as a bowel infection again derived from the tonsils, but so also had the *Micrococcus catarrhalis*—a fairly rare occurrence in my experience. The leptothrix was the only organism not definitely accounted for. With evidence of generalized focal infection of this kind it is hardly surprising that some serious disorder should result. This patient, as with many others in my experience, was seriously ill not only mentally, but also physically.

Progress and treatment.—Within a few hours of admission a severe attack developed. The symptoms were so remarkable that they are worth giving in detail. She became restless and noisy, having to be held in bed. She complained of severe epigastric pain, flatulence, intense occipital headache and diplopia. Her distress and fear of her impending fate made her cry out in agony of mind and body. The pupils were greatly dilated and sluggish in reaction, head retracted, facial expression drawn and anxious. Suddenly she screamed, "Save me. I'm going!" and almost immediately the head and body extended fully in extreme opisthotonos, and, with one convulsive movement, she precipitated herself out of bed deeply unconscious. For four days she remained in this state, and during this time she exhibited regular muscular movements, the head turning from side to side for long periods, arms and legs likewise being affected. Later she became noisy and sedatives were given. On the evening of the fourth day consciousness was regained and she was able to speak. She complained of gastric pain and earache, but the headache had gone. The leucocyte count had fallen to 12,400. It was four days before another exactly similar attack occurred. While unconscious a T.A.B. intravenous injection of 50 millions was given, with maximum temperature 101° F., the temperature falling to normal twenty-four hours later. Morphia ¼ gr. was given during the night as in the previous attack. Complete consciousness was regained in the early morning, and she was quiet and rational during the day, but still complained of gastric pain. The duration of this second attack was obviously shortened. The same night she became restless and noisy and slept very little. In the morning it was obvious she was working up to a third climax and a second T.A.B. was given. The reaction was severe, maximum temperature being 104·6° F., preceded by a period of collapse with vomiting. She continued to be noisy during the day, but did not lose consciousness. Towards night she quietened, and with ¼ gr.

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morphia slept for eight hours. Next morning she was exhausted and dazed. The fourth attack occurred two days later and lasted forty-eight hours, but this time there was no dramatic onset. She was restless and noisy, but capable of being aroused and understanding more or less what was said to her. Complete consciousness was regained and she was quite rational, expressing herself as feeling much better. Twenty-four hours later an even more modified attack occurred, its interest lying in the fact that it was similar in every detail to those of twelve months before. She was obviously hallucinated, and kept sitting up in bed repeating phrases over and over again. On being roused she would stop and try to answer questions. This observation is, I think, illustrative of a symptomatic regression occurring in a process of recovery—a feature I have been able to note in more than one case. The fifth and last attack occurred, again much modified, and a third T.A.B. was given during it. Maximum temperature was 102·4 and there was diarrhœa and vomiting. Next morning she had completely recovered. For three weeks there were threatening periods of restlessness, occipital headache and gastric pain, but the combination of immersion baths, Plombières lavage, mild sedatives and two well-borne T.A.B. reactions prevented recurrence. After a period of eight days the sixth T.A.B. injection was given on the evening of January 3, 1928, as it looked as if another attack was imminent. The reaction on this occasion was peculiar. Collapse was severe and she looked ill, the temperature failing to rise until next morning. Vomiting and diarrhœa occurred frequently during the night, but with the rise of temperature in the morning (maximum 101° F.) her general condition improved. All signs of the mental disturbance had gone, but in place of this she complained of feeling acutely ill physically. Gastric pain, vomiting, abdominal tenderness and frequent stool were prominent symptoms. The throat was greatly inflamed and covered with muco-purulent secretion, and a moderate degree of tracheitis developed. These symptoms persisted for nearly three weeks, but gradually abated in severity.

Five blood-counts were taken, the first being made on the morning of January 4, 1928.

Jan. 3.	6.40 p.m. T.A.B.				
,, 4.	White blood-cells	97,200.	Polymorphs	82%.	Red blood-cells 5,520,000.
,, 5.	,,	63,000.	,,	89%.	
,, 6.	,,	28,000.	,,	86%.	
,, 7.	,,	9,300.	,,	70%.	
,, 9.	,,	7,400.	,,	68·5%.	

On Jan. 4th and 11th, examination of the urine showed

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albumen and acetone in small amount. Indican was estimated as ++++, and it is worthy of note that on no other occasion was this found. It is evident that these findings, along with the clinical picture, indicated a crisis such as occurs in an acutely toxic illness. In pneumonia, for example, leucocytic mobilization, if sufficient, overcomes the invader in this manner. In this case, I think we have a picture of an economy saturated with a toxin of a special type producing a psychotic symptomatology which tended to obliterate more or less the underlying and causal somatic disorders in terms of physical signs and symptoms. The conversion of her condition from one of acute mental to acute physical illness was nothing short of dramatic. I have observed this phenomenon in many cases, but usually it is more gradual. Without special treatment the patient had poor chances of spontaneous recovery, as the history of her decline shows. That her life was in danger during this crisis I have little doubt, but it was the turning-point, and led to gradual but complete recovery. For a month she required most careful nursing, her gastric and intestinal condition giving great trouble. Mentally she was emotionally unstable, and on one occasion she expressed her former delusions. Except for this single recurrence she had complete insight. The treatment during this time consisted of baths, Plombières, injections of collosol ferro-manganese, small doses of a compound detoxicated intestinal vaccine and strict diet. Under this *régime* she made good progress. For the next three months treatment was directed towards stimulating her powers of recovery, and consisted of autogenous vaccine injections, endocrines, thyroid and ovary, the latter by injection, and a course of artificial sunlight. The acid drink of HCl and pepsin taken with meals proved to be of great value; without it pain and flatulence occurred. At first she proved to be very sensitive to the tonsil and intestinal autogenous vaccine. Reactions were noted by soreness of the throat, slight headache, increase of gastric discomfort, loss of appetite, and these were accompanied by languor, some depression and emotional upset for twenty-four hours. Sleep was usually disturbed. Later the reactions were much less obvious. At the beginning of June she was sent out on trial, her mental condition having greatly improved. She was bright, less emotional, and her delusions and hallucinations had disappeared. Physical re-examination showed marked improvement all round and weight had been gained. The laboratory findings were satisfactory, but not yet fully normal. In four months' time the patient returned for general overhaul. She had kept well, but continued to show at times her emotional instability and difficult temperament. Weight had been gained to the extent of 2 st. The biochemical and

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bacteriological tests showed further improvement except that the hypochlorhydric condition of the stomach remained, but the degree of gastritis was very much less. At this stage she went to live at home and was discharged from certificate. At the end of November, 1928, owing to her own emotional instability and introspective outlook she was unable to cope with a very difficult environment. She rebelled, and attempted violence to herself by jumping out of a window. She was taken firmly in hand and returned as a voluntary patient. There was little evidence of physical deterioration except that she was constipated and her periods, which had just begun, had again stopped. In a few days she was much more balanced, and treatment on vaccine, endocrine and stimulative hydrotherapeutic lines was given during her two months of residence. Strict but kindly discipline brought about a better outlook and she remained bright and active. On leaving, the laboratory findings had reached a high normal level, the intestinal flora had much improved, but the abnormal elements were still to be found. Having regained her physical health and menstrual function she is now leading a normal family life, but away from home, where re-education and adjustment of her mentality to her environment is being carried out under careful guidance.

Concluding Comments.

These few cases help, I think, to emphasize how complex if not elusive are the problems of the physical disorders underlying insanity. It is evident that little information could be gained by clinical examination alone, and, without knowledge gained by special methods such as have been applied to the cases under consideration, little but symptomatic treatment could have been given. Without in the least wishing to criticize, it is obvious that in three of these cases treatment based on clinical examination alone over a long period had failed to bring about improvement or recovery. My observations on some 120 cases, all investigated in the same manner, lead me to believe that the individual or psychotic tendencies, especially if they be strongly hereditary, fail to reveal at all clearly the underlying pathology of the internal environment by ordinary signs and symptoms. The gastritis in Cases 1 and 3 is an example. The absence of this normal reaction permits to pass unrealized by physician and patient alike the true nature of his illness. In others, again, a more definite physical symptomatology may exist, but there will come a time when this is finally overshadowed by the masking effect of disordered cerebral function. In my experience many of the so-called hypochondriacal delusions

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are the attempt of a disordered intelligence to express what may be actually the truth, but again, without special knowledge, we have no means of adequately diagnosing and treating such cases. What bearing have the four cases upon the much discussed question of focal infection in relation to mental disease? Kopeloff and Kirby in their recent article in the *Journal of Mental Science* (5), in defending their own conclusions on the functional psychoses, emphasize certain fundamental aspects of the present position. They submit three important questions:

(1) Is focal infection the specific cause of the functional psychoses? Their answer is in the negative. I think you will agree that in this country we are not yet in a position to reply, but I believe that a time will come when we will be able to differentiate more clearly between cause and effect.

Then we will be less hesitant in answering this difficult problem. The method of research I have adopted is an attempt towards reaching this goal, and the cases under consideration will, I think, give some of us good reason for anticipating that certain types of mental disorder have a combined specific cause.

(2) Can surgical removal of foci of infection alone bring about improvement and recovery of patients with mental disease? Their answer again is in the negative, and I think most of us will feel inclined to agree. If it were merely a question of surgery the problem would be near solution to-day. The removal of tonsils and teeth and the drainage of infected sinuses may be essential in some cases, but unfortunately the matter, as will be seen, does not rest there. Clearing the mouth of septic teeth or tonsils is in many cases only tackling a mere fraction of the actual focus of infection. Indeed, in my experience, so extensive can bacterial infection become that one could on merely logical grounds ask the surgeon to remove the entire alimentary canal. It is evident, therefore, that we must seek other means of solving the problem.

(3) Is focal infection of importance in mental disease? I have no hesitation in stating that it is of the greatest importance.

My conclusions are based on what is considered to be a reasoned scientific hypothesis. If in mental disorders special bacteriological methods enable one to associate definite types of focal infection with disordered biochemical functions, and upon treating these conditions by specific and general therapy there is an improvement in the mental and physical condition, then we may assume that we have been dealing with factors which we must regard with strong suspicion in possible ætiology. Three of the four cases I have given support this claim, and had time permitted I could cite many other examples. In mental disease there is strong evidence

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that we are dealing with special types of microbic infection superadded to what can be found by ordinary bacteriological methods. The bacteriological researches of Ford-Robertson point out that invasion of the tissues by anaerobes forms the major part of the bacteriological flora in mental patients. For the past six years I have continued this research and have had the opportunity of carrying out a large amount of control work. My results, so far, support most emphatically the opinion of my predecessor. Whether on account of susceptibility or chance, the insane, without doubt, harbour anaerobic bacteria of the diphtheroid and lepto-streptothrix group, which not infrequently infect the major part of the alimentary canal. Many of the diphtheroids are morphologically identical with the Klebs-Loeffler bacillus, but are rarely found except as strict anaerobes. We all recognize the highly neurotoxic character of the Klebs-Loeffler bacillus, even when operating in the relatively small area of the tonsil and fauces. Why, then, should we overlook the importance of this bacillus and its sub-species as an anaerobe, especially since it can be traced to an infinitely wider focus of infection? The morphological characteristics of the lepto-streptothrix bacteria suggest that they are closely allied to the diphtheroids, and are similar in their toxic effects.

The correlation of the biochemical and hæmatological data to the toxic conditions presented shows how variable the response of the individual may be. It must be in some measure dependent on physiological balance, and in mental disorders we must recognize not only somatic, but neuronic resistance. The margin of safety to toxic action on the central nervous system may be small as suggested in Case No. 2, or wide as in Case No. 4. I suggest that if we study our cases from this aspect we may get nearer to the solution of what neurotoxic susceptibility involves. I make no pretence to understand the full significance of some of the findings; many are as yet problematical. I submit them to you, however, for your criticism and advice in the hope that much may come out of little.

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