MENTAL DISORDERS ASSOCIATED WITH PERNICIOUS ANÆMIA.*

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SINCE the introduction of the liver treatment for pernicious anæmia some four years ago that disease has received considerable publicity. It has been generally recognized as having three main clinical manifestations. Thus it may show itself as a blood disease, as a gastro-intestinal disease, or as a nervous lesion (subacute combined degeneration of the cord). It is, however, by no means generally recognized that pernicious anæmia has yet another way of manifesting itself, *viz.*, by the occurrence of mental disorder. The object of this paper is to emphasize this fourth aspect of pernicious anæmia. In this country the subject has not hitherto received the consideration which is due to it. Nevertheless, a number of observers in other countries have shown, both by their own personal observations and from statistics, that mental disorders are frequently met with in the course of pernicious anæmia. The degree of mental affection varies in different cases. There may be merely a modification of character, with irritability and changing mood. W. Richardson would include in this mild group many patients described as uncooperative.

In cases where the mental disturbance is more pronounced, the psychosis most frequently met with is of the paranoid type, with delusions of persecution and suspicion, these delusions being more particularly directed against those who are responsible for the patient's welfare.

What is very remarkable is the frequency with which delirium occurs in this disease. Cabot found it in 44% of his cases. The delirium is especially marked at night. The patient develops terrifying hallucinations, with extreme agitation and restlessness; he reacts to his delusions and hallucinations by becoming grandiose, abusive and aggressive. There is nearly always some clouding of consciousness. It will be noted that this mental syndrome resembles that of the toxic group of psychoses.

The relationship of pernicious anæmia to the psychoses has been

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exhaustively studied from the medico-legal point of view. If one bears in mind the mental symptoms enumerated, it is easy to understand how the testamentary capacity of the patient may be called in question. As an example I may quote from the case recorded by Dr. A. G. Hulett, of New Jersey, who was called upon to act as medical witness in a disputed will case. The testator had died of pernicious anæmia, and a certificate was given to that effect. During the latter months of his life he had turned against his favourite daughter, who had always been his devoted companion and had been in constant attendance on him. In a codicil to his will, made just before his death, this daughter was disinherited, the estate being left to distant relatives In the litigation that ensued Dr. Hulett was fortunately able to convince the court, not only of the frequency with which mental complications may arise in the course of pernicious anæmia, but also of the particular form of psychosis most commonly met with in that disease.

The time of onset of the mental disorder is variable It was formerly thought to be a terminal condition, but it is now realized that it may occur at any stage of the disease It has been known to supervene during treatment. Sometimes it occurs in the early stages of the disease, as in the case reported below. When this happens errors of diagnosis are liable to be made. Thus the patient may be labelled as "hysterical" or "neurasthenic" while the underlying disease escapes attention. The results of such mistakes are disastrous for the patient, who is denied the benefit of modern methods of treatment.

The following case is interesting in that it demonstrates the presence in one subject of all the four manifestations of pernicious anæmia referred to above. Moreover, what seems to me particularly worthy of note is the fact that the mental symptoms correspond closely to the specific mental syndrome described by the majority of observers.

CASE I.—Miss A—, æt. 43, was admitted to St. Andrew's Hospital as a voluntary patient in February, 1930.

Family history.—Uncle died of pernicious anæmia, eldest sister died of phthisis.

Personal history.—For some years she had suffered from poor physical health and "neurasthenia," with occasional attacks of pyrexia. Appendicectomy in 1926. In April, 1929, had severe attack of influenza; also a severe attack of cystitis; complete physical breakdown. Queer feelings in the head; insomnia; unable to concentrate. In August, 1929, paraplegia said to be "hysterical." Cystitis improved. In October, 1929, condition diagnosed as "astasia-abasia"; slight pyrexia (? toxic); delusions of persecution; thought food was poisoned, refused food in consequence; mentally confused; delusions of unseen agency; irritable and lacking in control; abusive to her nurse. For some time before admission she had complained of numbness of the feet; her ankles became puffy on occasion. Wassermann reaction negative.

State on admission.—Mental: She was mildly confused and depressed; sometimes said she wished she were dead; kept her eyes shut when speaking; frequently became restless and agitated. Delusions of persecution; imagined her food was poisoned; blamed her nurse without cause. She had periods of tranquillity, when she showed insight into her condition.

Physical: She was emaciated; weight 6 st. 11 lb. Anæmic. Skin had a lemon tint; glossitis present. Teeth—some fairly recent extractions, but X-ray examination showed apical infection of three teeth. Heart—hæmic bruit over apex and pulmonary areas. Lungs clear; spleen enlarged; scar over appendix region.

Central nervous system: Functions of cranial nerves normal; some pallor of discs. Muscles of legs small and soft; extreme weakness of both lower limbs; ataxia very marked—patient unable to stand without support on either side. Knee-jerks and ankle-jerks +; plantar reflexes extensor on both sides; lower abdominal reflexes absent; loss of joint sense in both limbs. Sensation to cotton-wool and pin-prick unimpaired; tuning-fork vibration sense absent up to knee (both legs). There was no loss of tone of the muscles of the upper limbs; muscles of the trunk moderately strong; there were scars over the left buttock (from recent bed-sores). A blood-count showed: Red blood-cells, 1,056,000 per c.mm.; white blood-cells, 3,000; hæmoglobin, 55%; colour index, 2·6; anisocytosis and poikilocytosis marked; microcytes, megalocytes, megaloblasts, normoblasts, polychromasia all present. A test meal confirmed the presence of achylia gastrica. Examination of the fæces showed the presence of those streptococcal elements characteristic of pernicious anæmia.

Diagnosis.—The case was clearly one of pernicious anæmia with achylia gastrica, subacute combined degeneration of the cord and mental disorder.

Treatment.—Fresh liver treatment was started at once, ½ lb. of liver being given daily in various forms. As the patient did not tolerate this treatment well, liver extract had to be substituted. She was also given liquor arsenicalis, beginning with small doses, gradually increased. She also had dilute hydrochloric acid (5j doses) with glycerin of pepsin *t.d.s.* She was given plenty of fresh fruit. The bowels were regulated, and medinal was given for insomnia when required. The patient's health was too poor to justify the extraction of the infected teeth at this stage.

Progress of the case.—Mental: The patient's mental state varied considerably, periods of agitation alternating with periods of comparative tranquillity. Delusions of persecution were very persistent. She said we used hypnotism, mesmerism or suggestion, and that we could read her thoughts and influence her conduct. She would become restless, noisy and abusive under the influence of her delusions. In June she developed delirium of a persecutory type. There were terrifying hallucinations affecting all the senses, especially marked at night. She complained that all kinds of horrible animals—spiders, wasps, insects, bats, mice, etc.—came through her window and got into her bed. She told me she could hear, see, feel, and sometimes even smell them. It was this, she said, that caused her to scream with fright. She believed that the hospital authorities staged all these things in order to test her sanity. She would rage and storm at the nurses, and sometimes at the doctor. Everybody, she said, was against her. Though sometimes threatening, she was never actually violent. The delirious state lasted with varying intensity for some weeks, when it gradually abated. The delusions of persecution persisted, but she reacted to them differently. Thus she became domineering and dictatorial. She would shout out orders to the nursing staff and generally abuse them. In October the patient began to show some improvement in her mental state. The tranquil intervals became more prolonged, and the periods of agitation shorter and less marked. The mental confusion was also less obvious, and she took more interest in her surroundings. As her general health improved, her outlook on life became happier. In November there was still further improvement. The delusions of persecution gradually disappeared, and she showed much better insight into her condition. About the middle of December not only had all the patient's suspicions and delusions disappeared, but she began to express her gratitude for the kindness and attention she had received during her mental illness. From that time the patient's insight has been perfect and she has cooperated in the treatment to the best of her ability. She displays a very keen interest in her increasing weight, and rejoices in her

renewed health and strength. She is rational in conversation. She reads a good deal and enjoys the various entertainments. In short, the patient's mental state is now normal. She realizes, however, that if she were to stop taking liver she would have a relapse. She is therefore willing to stay on at this hospital until suitable arrangements can be made for the continuance of the treatment elsewhere.

As might be imagined, there have been many difficulties in the treatment of this case. In her more irritable moods she would refuse the special diet prescribed; and on occasions she would even refuse all food and medicines. However, during her more tranquil periods she was open to persuasion, and was more willing to cooperate. Advantage was taken of this fact to explain to her as fully and discreetly as possible the nature of her illness and the object of the treatment. It is all-important to gain the patient's confidence. In one of her reasonable moods she herself volunteered to return to the fresh liver treatment instead of continuing with the liver extract. It was found that her variations of mood were in some way related to the intermittent character of the blood counts. In spite of ups and downs the blood picture gradually improved, as is shown in the accompanying table:

Table (abridged) showing Improvement in the Blood Count.

Date.	Red blood-cells.	White blood-cells.	Hæmoglobin.	Colour index.
11.2.30	1,056,000	3,000	55%	2·6
26.2.30	1,432,000	2,100	55%	1·9
12.3.30	1,920,000	3,300	65%	1·6
24.3.30	1,420,000	4,200	64%	2·0
23.4.30	3,320,000	2,500	55%	0·8
20.5.30	3,920,000	4,700	62%	0·8
4.6.30	3,696,000	7,900	85%	1·1
11.7.30	3,728,000	4,600	64%	0·8
21.8.30	3,392,000	4,800	65%	0·9
25.9.30	3,456,000	4,500	68%	1·0
3.11.30	4,160,000	3,800	78%	0·9
15.12.30	4,592,000	4,000	91%	0·9
23.1.31	4,400,000	3,800	89%	1·0

By degrees the red cell count increased from 1,056,000 to 4,592,000 per c.mm. Meanwhile there was remarkable improvement in the general health, as is shown by the increase of the patient's weight from 6 st. 7 lb. to 9 st. I may mention that hydrochloric acid was discontinued early in the treatment, and only given when some digestive symptoms seemed to indicate its use. Arsenic also was not given continuously, but it was found a useful adjuvant when there was a slight fall in the red cell count. The infected teeth have been removed after local anæsthesia. From the commencement of the treatment the patient has been as much as possible out of doors. The amount of open-air exercise has, of course, increased in proportion as her health and strength have improved. At the present time the patient's general health is remarkably good. She has a fresh complexion; her tongue is clean. The hæmic murmur disappeared early in the treatment; the lungs are now clear: there is no enlargement of the spleen.

Remarks.

Central nervous system.—The severity of the disease of the spinal cord is shown by the fact that the patient had been bedridden before admission (she had actually had bed-sores), and she had also had a severe attack of cystitis. The outlook, so far as the combined degeneration of the cord was concerned, seemed anything but "rosy." The œdema of the feet and ankles which had been noticed before admission recurred from time to time. Retention of urine

also re-appeared on one occasion. This was relieved by catheter, and has not since returned. The slight pallor noticed in the optic discs disappeared with the improvement in the blood picture. In contrast to the experience of certain observers the paræsthesiæ have extended, the hands becoming involved as well as the feet. Moreover, the area over which vibration sense was absent has also increased—it now involves both the lower limbs and the pelvis. The ankle-jerks and knee-jerks are now only slightly exaggerated; the abdominal reflex is still absent; the plantar reflexes remain extensor on both sides; there is no loss of sensation to cotton-wool or pin-prick; joint sense is lost in the joints of both lower limbs.

With regard to the ataxia there has been very marked improvement. It must be remembered that on admission the patient could not stand without support on either side; movements of the lower limbs were most uncertain and irregular; muscular weakness was extreme. The patient's progress in this respect is probably due to the great improvement in her physical strength as well as to muscle re-education. The patient has been encouraged to do Frenkel's exercises. In the summer she was provided with a walking-machine which has enabled her to get about, both indoors and in the grounds, without the assistance of a special nurse.

General.—Dr. Gordon Holmes examined the case in April, 1930. Speaking generally on the subject of the prognosis in cases of subacute combined degeneration he said: "Some cases of combined degeneration of the cord improve considerably under treatment; in others treatment at the most arrests the progress of the disease, while in some cases the spinal disease advances despite the treatment." W. Richardson says that when the disease involves the central nervous system there is call for extra large amounts of liver substance. It is exceedingly important, he adds, to maintain the red cell level above 4,500,000 per c.mm. in order to prevent the progress of the degenerative process in the spinal cord. I consider that the extension of the subjective and objective phenomena, noted in this case, probably occurred during those periods of excessive agitation when the patient refused to submit to the liver treatment, and when there was a reduction of the red cell count in consequence.

Case 2.—Miss C—, æt. 43, a certified patient, admitted in March, 1929.
Family history.—One sister insane.
Personal history.—First attack in January, 1927. In 1928 pernicious anæmia diagnosed whilst in a mental hospital. Her mental state improved with liver treatment, and she was discharged from certificates. Unfortunately the treatment was discontinued, and she relapsed.

State on admission.—She was suffering from delusions of persecution. She was confused and had auditory and visual hallucinations. Later this condition merged into a delirious state. Blood examination showed that she was suffering from pernicious anæmia. C.N.S. examination showed the presence of subacute combined degeneration of the cord.

Treatment and progress.—This patient has been on liver treatment. She has shown considerable improvement at times, but there is an undoubted tendency for the mental symptoms to recur at intervals. The fact that this case has not responded to liver treatment in such a striking manner as the other two cases reported may be accounted for by the family history, which indicates a predisposition to mental disease.

The following case is of interest as being one of secondary anæmia associated with mental symptoms and treated successfully with liver diet.

CASE 3.—Miss B,— æt. 46. Admitted as a certified patient on August 10th, 1930.

She was suffering from delusions of persecution and marked auditory hallucinations. There was confusion, and she was depressed. She had attempted suicide recently. Shortly after admission she became delirious, with grotesque hallucinations. Blood examination showed her to be suffering from definite secondary anæmia with a reduction of hæmoglobin out of proportion to that of red blood-cells. There was slight anisocytosis, microcytes were present, and poikilocytosis was marked. Red blood-cells were 4,352,000.

Treatment and progress.—The patient was put on liver treatment. About the middle of September she showed considerable improvement. Insight into her condition became very good, and she was able to realize the absurdity of her former delusions. From that time on she made an uninterrupted recovery, and on November 6th she went out on trial, *i.e.*, 3 months after treatment began. She was discharged recovered a month later.

There is ample evidence to show that mental disorder is liable to occur in the course of pernicious anæmia, as also in the secondary anæmias. The mental symptoms are secondary phenomena, and when treated by modern methods they are curable, just as the underlying condition is curable. The mental disorder may disappear before the blood is completely regenerated. It is of the greatest importance to bear in mind that the mental symptoms may be so pronounced as to obscure the original blood disease. Hence a systematic examination of the blood should be undertaken in all cases where there is the least suspicion.

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