MENTAL CHANGES ASSOCIATED WITH PERNICIOUS ANÆMIA.

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It is well known that pernicious anæmia may manifest itself as a disease of the blood or of the nervous system, or that it may, at first, appear to be a morbid condition purely of the gastrointestinal tract. The occurrence of abnormalities of conduct as a symptom or even as a prodromal sign is, however, less generally recognized, and yet a considerable number of patients in whom typical pernicious anæmia is present show a peculiar mental condition. Woltmann was, I believe, the first to point out that 'These patients are different in some way from other patients: they listen to what you say, they do not argue, they raise no objections; they are almost too good.' This writer is of opinion that some persons presenting such a character are really examples of pernicious anæmia without anæmia, but he does not make clear whether he believes that all such persons will ultimately develop the typical malady.

Very anæmic patients may present signs of extreme weakness of both body and mind, but much more distinctive psychical abnormalities may arise in persons whose blood shows but little deviation from normal, and yet cure of the hæmatological malady is followed by improvement in the mental state. Barrett pointed out that psychotic manifestations of paranoid type may occur in pernicious anæmia, and that the state is symptomatic of a toxic process affecting the central nervous system. The occurrence of such distinctive psychoses as manic-depressive insanity in pernicious anæmia is probably seen only in patients with a previous psychosis. Nevertheless Cornell points out that even such a mental condition may improve when the anæmia is adequately treated. Mathieu contends that definite mental abnormalities are most frequent during the terminal stages, but that they may occur at any period of the malady, and he agrees with Langdon that an apprehensive neurosis may be a manifestation of prepernicious anæmia. Émile-Weil and Cahen point out that mental changes may occur quite independently of the anæmia, and they describe a case in which such symptoms developed just after the beginning of liver treatment, but recovered when the blood became

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normal. They state that any form of alteration of character may be observed in pernicious anæmia; even dementia may develop. As a general rule, the mental condition is a depressive one, but excitations such as paranoia and mania have been seen.

Phillips has recorded three interesting cases, and calls attention to the fact that the onset of mental symptoms may coincide with the beginning of treatment, or may develop during treatment. He describes the case of a woman, aged 43, whose uncle had died of pernicious anæmia and who herself had suffered from 'neurasthenia' for some years. In April, 1929, she had an attack of influenza and cystitis, and from then onwards complained of queer feelings in the head, insomnia and inability to concentrate. In October, 1929, she began to have delusions of persecution, and thought that her food was poisoned. In February, 1930, she was admitted to a mental home, and, at this time, she had 1,056,000 red corpuscles per c.mm., with 55 per cent. of hæmoglobin and 3,000 leucocytes per c.mm. She was treated with liver, liver extract, arsenic and hydrochloric acid, and by June, 1930, after gradual improvement, she became mentally normal; at this time there were 4,400,000 red corpuscles per c.mm., with 89 per cent. of hæmoglobin.

Phillips' second case differed from the one just described because the patient, aged 43, was diagnosed as suffering from pernicious anæmia at a time when she was an inmate of a mental home. Furthermore, one of her sisters was insane. The patient's physical and mental condition improved with liver treatment, but on discharge she ceased to take the liver and relapsed with delusions of persecution and both visual and auditory hallucinations. This would appear to be an example of a psychosis developing in a predisposed person; the attack of pernicious anæmia can be regarded as only an exciting cause.

It must be realized that similar mental states may occur in association with secondary anæmias. For example, Phillips' third case was a woman, aged 46, who had delusions of persecution and auditory hallucinations with confusion and depression, although her anæmia presented a low colour index. After three months' treatment she was discharged from the mental home apparently cured.

Unless it be realized that abnormal mental states may occur in pernicious anæmia, legal troubles may arise. For example, Hulett describes the case of an elderly man suffering from pernicious anæmia, who during the later months of his life turned against his devoted daughter, who had been his constant companion, and as a result disinherited her. Hulett was able to convince the courts that this particular form of psychosis is commonly met with in pernicious anæmia, and the will was declared invalid.

Naegeli mentions the case of a man who became so excessively brutal while suffering from pernicious anæmia that his wife was forced to divorce

him. He also refers to another case in which the patient stole billiard balls with no memory of the act afterwards.

It is rather tempting to suppose that the pathological changes underlying such mental states are similar in type to those occurring in the spinal cord in subacute combined degeneration, but there is no evidence to support this view. Woltmann states that organic changes in the cerebral cortex are just as well marked in pernicious anæmia with normal mentality as in those with mental disturbances, and he believes that one must postulate the existence of a toxin, which itself is ultimately also the cause of the terminal coma.

PERSONAL CASE.

The case which is recorded here is of interest in that complete physical and mental recovery took place.

D. S., a woman, aged 42, had been treated for 'neurasthenia' for some six months. Large doses of bromide had been given and, as the patient was never really quite awake, her husband thought that she was better. Her physical condition gradually deteriorated, and it became obvious to her relations that she was losing weight and becoming extremely pale.

She was admitted to the Chelmsford Hospital on November 12, 1931, and was seen to be wasted and to have a definitely pigmented skin. The face was distinctly brown in colour, but the pigmentation was not an even one: some areas were much paler than others. The skin of the chest and abdomen showed similar patchy pigmentation. Apart from a hæmic murmur, absence of the lower abdominal reflexes and pallor of the skin and mucosæ, no physical abnormality was detected on clinical examination.

The patient was peculiarly uncooperative, which is a feature emphasised by Richardson as being usual in cases of pernicious anæmia with slight mental change. Her uncooperativeness was peculiar in that it consisted in inability or disinclination to give information about herself; but, on the other hand, she was extraordinarily amenable and would obey instructions without any trouble. No other abnormality of conduct was observed during the first two days of her stay in hospital.

On November 14, her blood showed:—

Red corpuscles	...	...	...	2,880,000 per c.mm.
Hæmoglobin	...	...	...	62 per cent.
Colour index	...	...	...	1.08.
Leucocytes	...	...	...	2,200 per c.mm.
Neutrophils:—				
Young cells	...	0.5	per cent.	} 51.5 per cent.
Band forms	...	5.0	„	
Polymorphs	...	46.0	„	
Eosinophils	...	...	...	1.5 „
Basophils	...	...	...	0.5 „
Monocytes	...	...	...	13.5 „
Lymphocytes	...	...	...	32.0 „
Normoblasts	...	...	...	1.5 „
Polychromasia, punctate basophilia, anisocytosis and poikilocytosis: present, but not extreme.				

Arneth-Cooke count: Class I 15 per cent.

„ II 42 „
 „ III 35 „
 „ IV 8 „

This gives a weighted mean of 2.46.

The average size of the red corpuscles was 8.39μ .

It is clear that the blood picture is that of pernicious anæmia, and the only unusual feature is the high percentage of monocytes.

Intramuscular injections of liver extract (Exhepa pro injectione) for five successive days was ordered, together with six phials of Exhepa by mouth daily. After the second injection, that is on November 15, she appeared to be rather miserable, but no information could be obtained by questioning her. The next day she said she could hear voices outside her room and that these kept repeating that her husband had given himself up to the police. Her condition was peculiar in that there appeared to be no affective tone associated with the auditory hallucinations, and she was neither pleased nor distressed at the information; she lay quietly in bed and made no spontaneous remarks. If, however, she were asked a question, she did not, as a rule, reply to it, but promptly gave further information as to the voices. Occasionally she asked the nurse whether there was something wrong or whether she (the patient) had done something she ought not to have done.

On November 18, she made a fatuous attempt to cut her throat with the small blade of a blunt penknife, but only succeeded in scratching the skin. She was neither annoyed nor distressed when the knife was taken away from her.

She appeared to be rather lonely in her single room and, was, therefore, moved into the general ward. Unfortunately her bed was next to a radiator, and within a few hours of her transference to the ward she began to hear voices emerging from this, which she attributed to an arrangement on the part of the nursing staff, although she did not blame them or suggest that she would like to be moved. The voices now usually informed her that there was a large fire which had either burnt down her own home or was in process of destroying the War Office or Fleet Street. At no time during the day was she sensible and, as she slept badly, she continued her ramblings at night.

On the tenth day after starting treatment she became a little more responsive. If asked a question she might reply quite intelligently, although perhaps two or three minutes elapsed between the asking of the question and the commencement of the answer. Even so, she did not always reply completely; her answer might be interrupted by the voices whose information she then passed on to the questioner.

On the thirteenth day the Sister in charge of the ward was able to cut short the voices from the radiator by informing the patient that she herself or one of her nurses had put out the fire. On this day (November 27) the blood showed:—

Red corpuscles	...	...	...	3,100,000 per c.mm.
Hæmoglobin	...	...	...	68 per cent.
Colour index	...	...	...	1.09.
Leucocytes	...	...	...	5,600 per c.mm.
Neutrophils:—				
Band forms	...	6.0 per cent.	}	80.5 per cent.
Polymorphs	...	74.5 „		
Eosinophils	...	...	...	1.5 „
Basophils	...	...	...	0.5 „
Monocytes	...	...	...	10.0 „
Lymphocytes	...	...	...	7.5 „

The Arneth-Cooke count gave a weighted mean of 2.51; the average size of the red corpuscles was 8.19μ , and polychromasia and punctate basophilia were well marked.

Although there was no great improvement in the number or quality of the red corpuscles, the presence of neutrophilia suggested that a remission was about to occur. During the next week the periods of 'listening in' to the radiator became shorter and less frequent, so that sometimes five or six hours would elapse before the patient again made any statement about the voices. Her physical condition was still poor, but was definitely improving and she was, therefore, allowed to get up and sit by the fire with the other patients at some distance from the radiator. At no time did she mention the voices when mixing with the other women, but when she returned to bed occasionally heard brief communications. Twenty-six days after the beginning of treatment she became perfectly normal and heard no further voices, but was still rather uncooperative. The next day she was almost talkative, but perfectly reasonable, with no apparent recollections of her delusions. She was discharged from hospital on December 19, 1931, with the following blood count:—

Red corpuscles	...	...	...	3,584,000 per c.mm.
Hæmoglobin	...	...	...	72 per cent.
Colour index	...	...	...	1.0.
Leucocytes	...	...	...	7,600 per c.mm.
Neutrophils:—				
Band forms	...	25.0 per cent.	}	75.5 per cent.
Polymorphs	...	52.5		
Eosinophils	...	...	...	0.5
Basophils	...	...	...	0.5
Monocytes	...	...	...	11.5
Lymphocytes	...	...	...	10.0

The Arneth-Cooke count gave a weighted mean of 1.61, platelets were very plentiful and polychromasia was well marked.

The high percentage of immature neutrophils suggested the possibility of a septic focus, but, as careful examination did not reveal one, it was presumed that this phenomenon was due to simple hyperactivity of the marrow.

An opportunity presented itself for the patient to have a holiday with relations, and she was, therefore, instructed to report in three weeks. As the response to liver had not been very good, the Exhepa was stopped and the patient was given desiccated stomach (Capsol Eugastrol) three times a day during her holiday. On January 9, 1932, her blood showed:—

Red corpuscles	...	...	...	4,840,000 per c.mm.
Hæmoglobin	...	...	...	98 per cent.
Colour index	...	...	...	1.0.
Leucocytes	...	...	...	5,000 per c.mm.
Neutrophils:—				
Band forms	...	7.5 per cent.	}	75.5 per cent.
Polymorphs	...	68.0		
Eosinophils	...	...	...	0.5
Basophils	...	...	...	1.5
Monocytes	...	...	...	5.5
Lymphocytes	...	...	...	17.0

The patient's general condition was now good, and she gained weight. There did not appear to be any recollection of her previous delusions. Pigmentation was still present, but was much less intense. Appetite and sleep were good, and

indeed no indications of illness were detected. The patient was seen again on March 5, 1932, and still appeared to be quite well. In September, 1932, she was still perfectly normal.

COMMENT.

It appears that it might be profitable to examine the blood in all cases of mental disorder in which there is even the slightest clinical evidence of anæmia. Unfortunately the number of cases of the present type recorded in the literature is still small, and it is therefore difficult to give any guidance as to prognosis, but the case described here shows that complete restoration may occur. It is particularly interesting to observe that the disappearance of the mental symptoms preceded the cure of the anæmia.

The very fact that suitable treatment of the blood may be followed by cure of the mental condition suggests that such patients should be kept in their own homes or in the wards of a general hospital for a month or two instead of being certified immediately. If this were done, much distress might be avoided, as presumably the considerable percentage of cases would be saved from the stigma of insanity. It seems almost certain that, if the pernicious anæmia and the mental symptoms have persisted for a long time, the latter will not respond to treatment, even if the former be adequately dealt with. In the last stages of a case in which treatment has been long delayed, complete dementia will inevitably develop.

REFERENCES.

- BARRETT, A. H., 'Mental disorders and cerebral lesions associated with pernicious anæmia,' *Amer. Jour. Insan.*, 1913, lxi, 1063.
- CORNELL, B. S., *Pernicious Anæmia*, 1927, 205.
- ÉMILE-WEIL, P., and CAHEN, R., 'Contribution à l'étude des désordres mentaux au cours de l'anémie pernicieuse,' *Presse méd.*, 1928, ii, 945.
- HULETT, A. G., 'Psychological and medicolegal aspects of pernicious anæmia,' *Med. Jour. and Record*, 1928, cxxvii, 1.
- LANGDON, F. W., 'Nervous and mental manifestations of pernicious anæmia,' *Jour. Amer. Med. Assoc.*, 1905, lxv, 1635.
- MATHIEU, P., *Syndromes neuro-anémiques*, 1925, 36.
- NAEGELI, O., *Blutkrankheiten und Blutdiagnostik*, 1931, 371.
- PHILLIPS, N. R., 'Mental disorders associated with pernicious anæmia,' *Jour. Ment. Sci.*, 1931, lxxvii, 549.
- RICHARDSON, W., 'Pernicious anæmia; results of treatment with liver and its derivatives,' *New Eng. Med. Jour.*, 1929, cc, 540.
- WOLTMANN, H. W., 'Brain changes in pernicious anæmia,' *Arch. Int. Med.*, 1918, xxi, 791.
- Id., 'Nervous system in pernicious anæmia,' *Amer. Jour. Med. Sci.*, 1919, clvii, 400.
- Id., 'Mental changes associated with pernicious anæmia,' *Amer. Jour. Psychiat.*, 1924, iii, 435.