PERNICIOUS ANAEMIA WITH RETURN OF HYDROCHLORIC ACID AND FERMENTS AFTER TREATMENT

BY

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An absence of free hydrochloric acid in the gastric contents is one of the most constant features of pernicious anaemia, since achlorhydria is present in approximately 99 per cent. of cases. While it is true that an absence of the intrinsic factor (Castle)¹ and a lack of hydrochloric acid do not invariably accompany one another, it may be safely said that the finding of even a trace of free hydrochloric acid is sufficient to warrant the most serious doubts in regard to the diagnosis of pernicious anaemia. Equally important, as indicating the primary part played by the secretion of the stomach in the aetiology of pernicious anaemia, is the well-recognized fact that no matter how complete or how prolonged a remission may be, the secretion of hydrochloric acid fails to return. This has been clearly demonstrated in hundreds of cases of pernicious anaemia by workers in every country. The case reported below, in which all the cardinal features of pernicious anaemia were present, regained the power of secreting normal gastric juice. The rarity^{2,3} of this occurrence would appear to warrant the publication of an individual case.

CASE RECORD

The patient, a male aged 39, had for the past ten years been a tea planter in India. His mode of life in the Tropics was unsatisfactory in every way, especially in regard to the constant abuse of alcohol and tobacco. His health was further undermined by repeated attacks of malaria. He returned to this country on sick leave some six months before he came under my charge. During this period he suffered from

weakness and general ill-health, and was easily tired. A blood count made on one occasion gave the following results: February 16th, 1932—red blood cells, 2,190,000; haemoglobin, 52 per cent.; white blood cells, 5,400.

Despite the fact that an anaemia of a macrocytic type was already present, his medical adviser was influenced, by the history of malaria and by the finding of an enlarged spleen,

to consider that the blood condition was a post-malarial anaemia. No parasites were found in the routine examination of blood films, but their absence could be explained by the quinine therapy which had been given. Large doses of iron and ammonium citrate over many weeks failed to produce any clinical or haematological improvement whatsoever. Accordingly the patient was referred to me for investigation on June 16th, 1932.

State on Examination and Treatment

The patient complained of weakness, lack of appetite, and breathlessness on slight effort. For more than a year his health had been failing. Nutrition was satisfactory. Skin and mucous membranes were extremely pale, with a definite icteric tint. Cardiovascular system—apex 3½ inches from mid-line in fourth interspace. Pulse rate 90. Haemic murmurs present at all areas. Urinary system—no albumin or bile, urobilin++. Respiratory and nervous systems satisfactory. Haematopoietic system—lymphatic glands not enlarged. Liver four fingerbreadths below costal margin in the nipple line. Spleen, hard and easily palpable four fingerbreadths below the costal margin.

Blood count on June 16th, 1932: red blood cells, 1,250,000; haemoglobin, 30 per cent.; colour index, 1.2; white blood cells, 4,375; reticulocytes, 1 per cent.

There were five megaloblasts and four normoblasts present per 100 white cells. Megalocytosis and anisocytosis were prominent features of the blood picture. Cells were oval in outline, and hyperchromic. The Price-Jones curve showed the typical picture—namely, a broadening of the base and a shift of the peak to the right. The van den Bergh reaction was: direct—negative; indirect—positive. The icteric index was 8.

The patient was given two tubes daily of a fish-liver extract made in Aberdeen. A reticulocyte crisis started on the third day and reached 18 per cent. on the fifth day, returning to normal in twelve days. As soon as the reticulocyte crisis was well developed—that is, on the tenth day—fish-liver extract therapy was stopped. Apart from the usual hospital diet the patient received nothing further in the way of specific therapy (mammalian liver or liver extract, gastric tissue products, vitamin B preparations, etc.), or drug treatment (iron or arsenic), or gastric lavage. The remarkable potency of the remedy employed for this short period is evidenced by the doubling of the blood count in twelve days and the trebling of it in twenty-one. Minot stated in a recent paper that a gain of 2,500,000 red cells in a month represented the maximum increase which could be expected. In this case this result was obtained in three weeks. Thirty-three days after admission the patient left hospital with a blood count of 4,100,000 red cells and 85 per cent. haemoglobin. The liver and spleen had markedly diminished in size, and his general health and appearance were excellent.

Gastric Analysis

First Examination, June 18th, 1932.—The fractional test meal revealed a complete absence of acid and a low total acidity. Pepsin was absent from both the fasting juice and one hour sample (Fuld's method).⁴

Second Examination, July 9th, 1932.—Fractional test meal—free hydrochloric acid absent. Histamine 0.5 mg. was injected, and half an hour later a sample of gastric juice was obtained which contained free hydrochloric acid. The amount of acid was scarcely sufficient to be titratable, but Gunzberg's test was definitely positive. The post-histamine sample contained 4 units of pepsin.

Third Examination, October 27th, 1932.—Fractional test meal showed a normal gastric secretion—namely, thirty-seven units of free hydrochloric acid in the three-quarter and one hour samples, four units of pepsin in the fasting juice, and sixteen in the one hour sample.

In view of the fact that the stomach had regained its power to secrete hydrochloric acid and pepsin, it was not unreasonable to assume that the intrinsic factor (Castle) was also being produced—in which case the pernicious anaemia might be held to be cured, an occurrence of the greatest rarity. Accordingly the patient was informed of our opinion, and it was explained to him that, provided he gave up alcohol and led a physiological life, he need take neither

liver, liver extract, nor any specific remedy for pernicious anaemia. This he has done for the past six months, and without any treatment whatsoever he has maintained perfect health, with a blood count around 4,500,000 red blood cells, and a haemoglobin percentage of 90. When last examined (December 21st, 1932) both patient and doctor were entirely satisfied with the result.

DISCUSSION

It can be safely said that the blood picture present in this case contains every feature on which the diagnosis of Addison's pernicious anaemia rests, and there can be little doubt that, had this patient suffered from the malady previous to 1926, he would have died. The megaloblastic degeneration of the bone marrow present previous to treatment can be explained as a consequence of the gradual and progressive loss of the ability of the stomach to secrete the intrinsic factor (Castle) which is essential for the continuation of normal blood formation. In idiopathic pernicious anaemia the cause of this failure in secretion is not properly understood, but in any hypothesis submitted it would be necessary to consider the constitutional factor as of great importance. In the case reported above, which can be classified as *acquired* pernicious anaemia, the deficiency was probably due to a gastritis conditioned by the abuse of alcohol and tobacco, together with the deleterious effects of malarial toxæmia. An inquiry into the patient's dietary during the past year clearly indicates that, consequent on the loss of appetite resulting from the gastritis, the dietary became progressively more and more defective in protein intake and in foodstuffs rich in the extrinsic factor of Castle. A consideration of these points throws some light on the natural history of the disease, and the mechanism of the remissions which were of such common occurrence in idiopathic pernicious anaemia previous to the inception of liver therapy in 1926. In the majority of cases of pernicious anaemia the onset is insidious, and many months elapse before the blood level reaches the stage at which symptoms are of sufficient severity to demand medical advice. At any period previous to the complete and final failure of gastric secretion a temporary improvement in the secretion of the intrinsic factor may occur, consequent on causes unknown or known (drug therapy, or even rest). In addition, provided any intrinsic factor is present, the temporary ingestion of foodstuffs rich in the extrinsic factor will also be effective in starting a remission. The reduction of the anoxaemia and the improvement of the general circulation, which follow a rise in the blood level, will in turn benefit the secretory mechanism of the stomach, with a further increase in production of the intrinsic factor. This has actually been shown to be the case in one of Castle's patients, and I have repeatedly seen the stomach regain its secretory properties in regard to hydrochloric acid and pepsin in cases of simple achlorhydric anaemia of ten years' standing or longer, in which the blood level had been brought up to normal by treatment with massive doses of iron. In idiopathic pernicious anaemia no known method exists by which a progressive loss of the secretory power of the stomach can be stopped, and in consequence remissions are invariably followed by relapses, until death finally ensues. Where a definite cause can be found and then removed, as in the present case, a complete cure may be expected to result.

SUMMARY

1. A case of pernicious anaemia is described in which the stomach regained the power of secreting hydrochloric acid and pepsin, and in all probability the intrinsic factor of Castle.

2. The patient has maintained excellent health and a satisfactory blood level for the past six months on a

normal diet. While it is necessary to await developments for another year, it is not unreasonable to assume that this case of pernicious anaemia has been cured.

3. The mechanism of the natural remissions which occur in pernicious anaemia is discussed.

REFERENCES

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- ² Wilkinson, J. F.: *Quart. Journ. Med.*, 1932, i, No. 3, 369.
- ³ Hurst, A. F.: *Ibid.*, 1932, i, No. 1, 165.
- ⁴ Cole, S. W.: *Practical Physiological Chemistry*, 1928, eighth edition, p. 252, Heffer, Cambridge.

FORCIBLE NASAL INSPIRATION

BY

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In one of my cases of tonsillectomy by dissection in an adult I was sent for on account of bleeding on the sixth day. The bleeding was not coming from the tonsillar bed, but from the left half of the nasopharynx, from which a small amount of adenoid tissue had been removed. After cleansing with peroxide of hydrogen (10 vols.) diluted with an equal quantity of warm water, I instructed the patient to make *several forcible nasal inspirations, each followed by the gentlest expiration through the mouth*. The haemorrhage diminished very perceptibly. The blood-stilling action of the forcible inspiration depends on the fact that the powerful expansion of the chest leads to a dilatation of the hollow organs in proportion to the degree of their softness. The right cavities of the heart are the most dilated, but the general dilatation leads to blood being sucked into the thorax and a consequent lowering of pressure in the peripheral vessels, including those of the throat and nasopharynx. When the nose and mouth are completely closed the action is at its highest, and diminution of pressure in the radial artery is very obvious to the finger on the pulse.

Among other means of checking haemorrhage from the nose or throat, one which will be found most useful is a clinical application of J. Müller's experiment dating from 1838, which is described in Landois and Stirling's *Textbook of Human Physiology* (third edition, p. 89), as follows:

"If after the deepest possible expiration the glottis is closed, and the chest be now dilated with a great inspiratory effort, the heart is powerfully dilated, the elastic traction of the lungs, and the very attenuated air in these organs, act so as to dilate the cavities of the heart. More blood flows into the right heart, and, in proportion as the right auricle and ventricle can overcome the traction outwards, the blood vessels of the lungs become filled with blood, and thus partly occupy the lung space. Much less blood is driven out of the left heart, so that the pulse may disappear. Hence, the heart is distended with blood and the lungs are congested, while the aortic system contains a small amount of blood—that is, the systemic circulation is comparatively empty, while the heart and the pulmonary vessels are engorged with blood."

The procedure as applied to haemostasis is recommended by G. Krebs,¹ who gives the instruction to inspire deeply with the mouth closed and to expire gently with it open. He quotes the authority of Karl Hueter, whose explanation he gives as follows:

"The blood is thereby sucked into the thoracic cavity and the nasal mucous membrane is rendered bloodless; but at the same time, owing to the inspiratory draught towards the nasal cavity, the outflowing blood is, to a certain extent, fixed in the open lumina and closes them as it coagulates."

It may, however, lead to syncope from a lowering of the cerebral blood pressure, and it is, I believe, the