She did not look ill, but was panting for breath—her respiration rate was at one time as high as sixty per minute.

Her pulse was 90 and her temperature 97.0°F.

Nothing abnormal was found on examination, and X-ray confirmed the absence of any lesion in her lungs.

She had some twitching of her right shoulder.

There was no manifest tetany, but on tapping the facial nerve, spasm of the face-muscles was produced, especially at the corners of the mouth. Carpo-pedal spasms could not be produced by constrictions round the limbs. She was excreting an alkaline urine.

After a day or two in hospital her symptoms cleared up.

In neither of these cases was any organic basis found for the hyper ventilation, and so the primary lesion must be regarded as functional. Such a psycho-neurosis and post-lethargic encephalitis are generally given as the most common causes of over-breathing.

The resulting biochemical disturbance seems to be something like this :—

The reaction of the blood depends on the ratio

$$\frac{H_2CO_3}{NaHCO_3}$$

With over-ventilation the numerator is reduced, and leaves a relative alkalosis with the loss of carbon dioxide from the blood. To correct this, some of the sodium bicarbonate is redistributed in an attempt to restore the original ratio. This does not bring about complete compensation, and so there is alkalosis, although the alkali reserve has been lowered. To help to keep the blood pH correct, the kidney secretes a less-acid or, as in the second case, an alkaline urine.

Disturbance in estimated blood-calcium is not a feature in this type of tetany, though there may be a disturbance in ionisation.

While the respirations are fast they are very shallow, so that the fall in blood carbonic acid is not enough to cause apnœa.

In the first of these two cases the alkalosis was expressed in terms of open tetany. In the second case headache, nausea, and vomiting were marked, while the tetany was latent.

The thanks of the author are due to Professor Thomson and Dr. Turkington for permission to report these cases.

TWO CASES OF CHRONIC HÆMOLYTIC ANÆMIA

By J. T. Lewis, B.SC., M.D., F.R.C.P.LOND.,
Royal Victoria Hospital, Belfast.

The essential criteria of a " hæmolytic anæmia " are as follows :—

(1) A progressive anæmia.

(2) An increase in the plasma bilirubin and in the urinary urobilin.

(3) Evidence of increased activity in the bone-marrow, as shown by a high reticulocyte count, and often by the presence of nucleated red cells in the peripheral blood.

The causes of hæmolytic anæmia may be classified in the following way :—

Extrinsic—(a) Infections, e.g., streptococcal, bac. Welchii.
(b) Chemical, e.g., lead, etc.

Intrinsic— (a) Acute hæmolytic anæmia (Lederer type).
(b) Chronic hæmolytic anæmia.
(c) Rare conditions, e.g., sickle-cell anæmia, etc.

The two cases to be described fall into the group of chronic hæmolytic anæmias. This group includes several types of blood-disease, e.g., acholuric jaundice, atypical cases of Hodgkin's disease, atypical leukæmias, etc.

From a practical point of view the main interest in the group is the fact that such cases may be mistaken for Addison's (pernicious) anæmia, to which they bear a superficial resemblance.

My object in reporting these cases is to emphasize the differences between hæmolytic anæmia and pernicious anæmia.

CASE 1.—Female, aged 38. Seen in July, 1937. She had complained for some months of increasing weakness, pallor, and exhaustion. The only significant point in her history was the fact that she had for some time been taking a preparation for the relief of chronic asthma, from which she had suffered for many years. This preparation contained two unusual drugs—calcium benzylphthalate and phenylsemicarbazide. The possible significance of these will be referred to later.

Her appearance suggested a moderately intense anæmia, and her colour was distinctly icteric.

On examination, the only findings were a chronic bronchitis of the spastic type, and an easily palpable spleen. There were no enlarged glands, and her tongue did not show the features of an achlorhydric glossitis.

The urine was normal except for the presence of a marked excess of urobilin.

Blood—Hæmoglobin, 46 per cent.; red cells, 2,200,000 per cmm.; leucocytes 5,000 per cmm.; colour index, 1.05.

Film—A megalocytic, hyperchromic type of anæmia. Many nucleated red cells, both erythroblasts and normoblasts. Polychromasia marked. Leucocytes normal.

Reticulocytes—35 per cent.

Van den Bergh—Negative direct reaction, strongly positive indirect reaction.

Wassermann reaction—Negative.

Red-cell fragility—Not increased.

Fractional test-meal—Hydrochloric acid present in excess.

These findings agree with the criteria already given for the diagnosis of chronic hæmolytic anæmia.

It was decided to observe the effect of the administration of liver extract (intramuscular) and large doses of iron on this case. After two months of this treatment, the examination of the blood showed :—Hæmoglobin, 65 per cent.; red cells, 3,500,000 per cmm.; reticulocytes, 26 per cent.; film—nucleated red cells still present.

It now became impossible to follow up the case further, but I am informed that she relapsed, and further liver treatment had no effect. She was given a blood-transfusion by Sir Thos. Houston, who has kindly asked me to see the case with him recently. The response to the transfusion has been remarkable. Her hæmoglobin has risen to one hundred per cent., and her film appears normal. The spleen is still slightly enlarged.

CASE 2.—Female, aged 35. Seen in September, 1937. She gave a history of failure of health for the past year, with fatigue, headache, weakness, dyspepsia, and a tendency to loose motions. She was obviously anæmic and definitely icteric. Her tongue was clean, but not smooth. There were no enlarged glands, but the spleen was palpable. Her urine contained a faint trace of albumen and a large amount of urobilin. In this case there was no history of any unusual drug, but she had had liver at intervals.

Blood—Hæmoglobin, 36 per cent.; red cells, 1,730,000 per cmm.; leucocytes, 8,200 per cmm.; colour index, 1.

Film—Marked anisocytosis and megalocytosis. No nucleated red cells seen. Polychromatic cells plentiful. Leucocytes appeared normal.

Reticulocytes—30 per cent.

Van den Bergh—Direct reaction negative; indirect reaction strongly positive.

Wassermann reaction—Negative.

Red-cell fragility—Normal.

Fractional test-meal.—Hydrochloric acid present in normal amount.

She has been treated by intramuscular liver and large doses of iron by mouth. There has been a slow but steady improvement, and her last blood examination gave the following figures :—Hæmoglobin, 62 per cent.; red cells, 4,010,000 per cmm.; film—No definite abnormality in red or white cells; reticulocytes, 5 per cent.

If there is any indication of a relapse in the future, one would certainly advise a blood-transfusion in view of the dramatic response in the previous case.

The question of splenectomy has been considered, but at the moment does not appear to be desirable.

It should be emphasised that the administration of liver to these cases has no real scientific basis, and the apparent improvement may only represent a natural fluctuation in the disease.

DIFFERENTIATION FROM PERNICIOUS ANÆMIA.

It will be seen that there are some points in common between chronic hæmolytic anæmia and pernicious anæmia. In both one finds a high colour-index (this is

not invariable in hæmolytic anæmia), megalocytosis, increased bilirubin in the blood, and excess of urobilin in the urine.

There are, however, two essential points of difference :—

(1) In hæmolytic anæmia it is unusual to find any abnormality in gastric secretion, whereas achlorhydria is almost an essential point in the diagnosis of pernicious anæmia.

(2) In hæmolytic anæmia a constant reticulocytosis is always present in the peripheral blood, even when the anæmia is rapidly progressing. A reticulocytosis only occurs in pernicious anæmia at the onset of a remission, and is transitory.

The megalocytosis of chronic hæmolytic anæmia has been frequently noted. It is certainly not due to deficiency of the specific anti-anæmic factor. In a recent paper Davidson[1] suggests that prolonged and excessive erythroblastic activity results in the formation of large primitive erythroblasts, " the descendants of which have a diameter greater than normal."

Discussion.

In attempting to classify these cases, one notices that they agree closely with a group of anæmias which have been described by Davidson and others[2]. There appear to be four possibilities :—

(1) *Drugs*—This might have an etiological bearing in Case 1. I have been unable to ascertain whether the chemicals in the " asthma cure " could produce hæmolytic effects. It is perhaps significant that the patient has now ceased to take the drug.

In the second case there is no history to suggest a chemical origin.

(2) *Atypical leukæmia.*—The absence of any immature white cells in the blood on repeated examinations, and the subsequent histories of the cases, would rule out this possibility.

(3) *Atypical Hodgkin's disease.*—It is difficult to exclude this completely, except to state that there are no other signs to suggest the disease.

(4) *Acholuric jaundice.*—It would seem that these cases can best be classified as acquired acholuric jaundice. In making this statement, one is aware that many authorities deny the existence of such a condition, and hold that all cases of acholuric jaundice are " congenital," the so-called " acquired form " being simply a delayed manifestation of the familial disease.

In the patients described there was no family history of jaundice or anæmia, but the fragility of the red cells of relatives was not tested.

The fact that the fragility in the two patients was normal does not, apparently, rule out such a diagnosis.

References.

1. Davidson and Fullerton, *Quart. Jour. Med.*, January, 1938.
2. Davidson, *Quart. Jour. Med.*, October, 1932.