studied on two occasions, and both curves showed a shift to the left of the same magnitude as before treatment.

The seeming contradiction between our findings on the one hand and those of Eder *et al.* (1949) and Waisman *et al.* (1952) on the other may be resolved by postulating the existence of two or more kinds of congenital methaemoglobinaemia not completely distinguished by methods at present available. On very different grounds Lutembacher (1947) and Hörlein and Weber (1948) have made similar suggestions. An alternative explanation is that it is not methaemoglobin itself but some other factor which is responsible in congenital methaemoglobinaemia for the abnormality of the oxygen dissociation curve. From our findings it would seem that this factor must be influenced differently by ascorbic acid and by methylene blue. It was found by Litarczek *et al.* (1931) that glutathione exerts an influence on the oxygen dissociation curve, and it seems to us that glutathione has been inadequately investigated in methaemoglobinaemia.

The mode of inheritance of familial methaemoglobinemia is still uncertain. A family tree suggestive of a Mendelian dominant character has been reported by Baltzan and Sugarman (1950). On the other hand, Gibson and Harrison (1947) and Codounis (1952) each described a family in which inheritance as a recessive character seems more likely. In our family, too (Fig. 1), inheritance as a recessive character seems the more probable.

Summary

The oxygen dissociation curves of two cases of familial congenital methaemoglobinaemia have been studied.

A shift of the curve to the left was found in both cases. This indicates impaired efficiency of oxygen delivery to the tissues in addition to what is attributable to loss of oxygen capacity due to the presence of an inert pigment.

Treatment with methylene blue restored the curve to normal. After treatment with ascorbic acid the curve remained abnormal.

These observations and published reports of similar studies are discussed. It is concluded either that there is more than one kind of congenital methaemoglobinaemia or that the alteration in oxygen transport in the condition is due to some factor other than methaemoglobin itself.

We are grateful to Professor L. J. Davis for his advice and criticism in the preparation of this paper; to Dr. J. H. Wright and the late Mr. A. M. Clark, who gave us the opportunity to study Case 1; and to Dr. H. J. R. Kirkpatrick and Dr. D. W. D. MacLaren, whose help enabled us to study Case 2. One of us (D.J.V.) was enabled to undertake this work by scholarships from the E.C.A. for Greece and from the University of Thessaloniki. The expenses of the investigation were met in part by a grant from the Board of Management of Glasgow Royal Infirmary and in part by the Rankin Fund of the University of Glasgow.

REFERENCES

- Adair, G. S. (1925). *J. biol. Chem.*, **63**, 533.
 Baltzan, D. M., and Sugarman, H. (1950). *Canad. med. Ass. J.*, **62**, 348.
 Barcroft, J., Dwyer, H., Meakins, J. C., Parsons, T. R., and Parsons, W. (1926). *Quart. J. Med.*, **19**, 257.
 Codounis, A. (1952). *British Medical Journal*, **2**, 368.
 Darling, R. C., and Roughton, F. J. W. (1942). *Amer. J. Physiol.*, **137**, 56.
 Douglas, C. G., Haldane, J. B. S., and Haldane, J. S. (1912). *J. Physiol.*, **44**, 275.
 Eder, H. A., Finch, C., and McKee, R. W. (1949). *J. clin. Invest.*, **28**, 265.
 Evelyn, K. A., and Malloy, H. T. (1938). *J. biol. Chem.*, **126**, 655.
 Gibson, O. H. (1943). *Biochem. J.*, **37**, 615.
 — and Harrison, D. C. (1947). *Lancet*, **2**, 941.
 Hitzenger, K. (1932). *Wien. Arch. inn. Med.*, **23**, 85.
 Hörlein, H., and Weber, G. (1948). *Dtsch. med. Wschr.*, **73**, 476.
 Litarczek, G., Aubert, H., Cosmulesco, I., Comanescu, V., and Litarczek, S. (1930). *Sang.*, **4**, 188.
 — and Nestoresco, B. (1931). *C.R. Soc. Biol. Paris*, **106**, 110.
 Lutembacher, R. (1949). *Presse méd.*, **57**, 276.
 Peters, J. P., and Van Slyke, D. D. (1931). *Quantitative Clinical Chemistry*, vol. 2. London.
 Valtis, D. J., and Kennedy, A. C. (1954). *Lancet*, **1**, 119.
 Waisman, H. A., Bain, J. A., Richmond, J. B., and Munsey, F. A. (1952). *Pediatrics*, **10**, 293.

BLOOD CHANGES ASSOCIATED WITH DISSEMINATED TUBERCULOSIS

REPORT OF FOUR FATAL CASES AND REVIEW

BY

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Although anaemia is common to all forms of tuberculosis it is rarely severe (Wintrobe, 1951), and usually normochromic or hypochromic. Chapman and Whorton (1946), in a clinico-pathological study of 63 cases of generalized miliary tuberculosis, noted a moderate normochromic anaemia in 84%. The lowest haemoglobin level was found to be 43%, the level in the majority ranging from 65% to 85%. The white-cell count was persistently low for two weeks or more in 11 out of a total of 49 patients in the above series, a relative neutrophilia being usually associated with leucopenia. The haematological picture in two cases resembled aplastic anaemia, and the presence of immature white cells and nucleated red cells in one case suggested a leuco-erythroblastic anaemia. Dyke (1924) recorded a case with generalized miliary tuberculosis associated with aplastic anaemia. Rosenthal (1928) has reported on aplastic anaemia as a complication of miliary tuberculosis, and referred to the haemorrhagic diathesis sometimes resulting from thrombocytopenia. Crail *et al.* (1948) described four cases of miliary tuberculosis associated with myelofibrosis and suggested that tuberculosis was the predisposing factor in the marrow changes. The same authors stated that the bone marrow in miliary tuberculosis shows, in the early stages, hyperplasia of all haemopoietic tissue, followed later by hypoplasia or aplasia.

Bone-marrow infiltration by disease in miliary tuberculosis seems to be not uncommon, Chapman and Whorton (1946) describing its presence in 33 out of 37 cases at necropsy. They believed that the presence of miliary tubercles in bone marrow did not necessarily predispose to depression of blood formation. Doan and Sabin (1927) produced extensive tuberculous lesions of the bone marrow of rabbits following the intravenous injection of virulent tubercle bacilli. There was an initial depression of marrow function, as judged by peripheral blood studies, followed, in animals that survived, by compensatory hyperactivity and finally by functional and morphological recovery.

In the rare condition of tuberculous splenomegaly, cytopenic states are recognized as being due to a hypersplenic mechanism, the bone marrow being normal or hyperplastic (Engelbreth-Holm, 1938). Polycythaemia has also been recorded in association with tuberculous splenomegaly (Guild and Robson, 1950).

Leukaemoid reactions accompanied by leucocytosis and the presence of immature white cells in the peripheral blood, making a differentiation from myeloid leukaemia difficult, is mentioned by Forkner (1938). Gardner and Mettier (1949) described a lymphocytic leukaemoid reaction of the blood associated with miliary tuberculosis.

Muller (1943) reviewed in detail the clinical significance of the blood changes associated with tuberculous infection.

The following four cases of generalized tuberculosis are reported in view of the profound haematological

changes which accompanied the disease, and because of the problems entailed in diagnosis.

Case 1

A housewife aged 22 was admitted to the Leeds General Infirmary on November 11, 1949. Her main complaints were increasing weakness, nervousness, sweating, and loss of weight for one year. Her past history and family history were negative. On examination she was extremely pale. Her skin was hot and moist, temperature 102.5° F. (39.2° C.). She was very nervous, with a tremor of the outstretched hands, and she had lost weight. There was no thyroid enlargement or exophthalmos, and, apart from tachycardia, no other abnormalities were discovered on clinical examination.

Investigations.—X-ray examination of the chest showed no evidence of lung disease. A blood examination gave the following results: Hb, 46% (Haldane); red cells, 1,900,000 per c.mm.; C.I., 1.21; M.C.V., 105 μ^3 ; reticulocytes, 5%; white cells, 4,000 (neutrophils 51%, lymphocytes 49%); platelets, 125,000; bleeding time, 2 minutes; E.S.R. (Westergren), 50 mm. in first hour. A blood film showed the red cells to be well haemoglobinized, and macrocytosis was prominent. A relative lymphocytosis was noted, but immature cells were not seen. A sternal bone-marrow examination revealed a severe depression of red- and white-cell-forming tissue, erythropoiesis being normoblastic. The differential marrow count showed 87% lymphocytes. A Rehfuess test meal showed a histamine-fast achlorhydria. The erythrocyte fragility was normal and urine urobilinogen was absent. Further tests were reported as follows: cephalin-flocculation test, negative; gold-sol, No. 2; thymol turbidity, 7.3 units; plasma proteins, total 6.8 g. per 100 ml.; A./G. ratio, 1:6; alkaline phosphatase, 6 units; blood urea nitrogen, 13.3 mg. per 100 ml.; blood calcium, 10.9 mg. per 100 ml.; phosphorus, 4.1 mg. per 100 ml. X-ray examination of the skeleton revealed nothing abnormal. Blood culture and agglutination tests for typhoid, paratyphoid, dysentery, and *Br. abortus* were negative.

The blood picture which further examination revealed was that of a leuco-erythroblastic anaemia with evidence of severe depression of bone-marrow function. The diagnosis was obscure, and atypical Hodgkin's disease, or lymphosarcoma, and aleukaemic leukaemia were regarded as possibilities.

In view of the continuous swinging temperature treatment with penicillin was instituted. No satisfactory response was obtained. The patient was given blood transfusions and discharged home at her own request on December 11.

She was readmitted on March 16, 1950, complaining of excessive fatigability, a throbbing pain in the head, night sweats, frequency of micturition, and polydipsia. On examination she was severely anaemic; temperature, 103.4° F. (39.7° C.). Systemic examination was otherwise negative. Blood examination showed: Hb, 38%; red cells, 1,500,000; C.I., 1.26; white cells, 1,200 (polymorphs, 25%, lymphocytes 75%); platelets, 80,000. A blood film showed macrocytosis, myelocytes, and erythroblasts. The sternal marrow revealed no change, the differential cell count showing 80% lymphocytes. X-ray examination of the chest revealed normal findings. Antibiotics and blood transfusions were again prescribed, but little change in her condition resulted. The spleen became palpable just before her discharge home in May, 1950.

She was again admitted to hospital in July, 1950, when extreme cachexia, anaemia, high fever, and splenomegaly were found to be present. In view of the development of a toxic psychosis she was transferred to a psychiatric ward at St. James's Hospital, Leeds, where she developed a terminal pericarditis and died on August 7, 1950.

Post-mortem examination showed evidence of miliary tuberculosis affecting the abdominal lymph nodes, the liver, spleen, and pericardium. The lungs, kidneys, brain, and pelvic organs were normal. The bone marrow was unfortu-

nately not examined. There was no evidence of extramedullary haematopoiesis in the sections of the liver, spleen, or lymph nodes examined.

Case 2

A female brass-feeder aged 51 was admitted to St. James's Hospital, Leeds, on March 11, 1950, with a four-months history of increasing weakness, lassitude, and dyspnoea on exertion. For a similar period her appetite had deteriorated and she had complained of recurrent attacks of central abdominal pain, associated with nausea and vomiting. She had lost 3 stone (19 kg.) in weight. There was no history of previous illness or any relevant family history.

Examination showed her to be of low intelligence and uncooperative. The temperature was 101.4° F. (38.6° C.), and she was moderately anaemic. The lower pole of the spleen was 3 in. (7.5 cm.) below the left costal margin. No other abnormality was noted.

Investigations.—X-ray examination of the chest, stomach, and duodenum showed no abnormality. No occult blood was detected in the faeces. A Rehfuess test meal revealed a histamine-fast achlorhydria. The urine contained a trace of albumin, and hyaline and granular casts were seen on microscopical examination. Blood examination showed: Hb, 60% (Haldane); red cells, 2,500,000; C.I., 1.2; M.C.V., 109 μ^3 ; reticulocytes, 5.4%; white cells, 2,600 (neutrophils 81%, eosinophils 3%, basophils 1%, lymphocytes 8%, monocytes 7%); platelets, 37,000. A blood film showed fully haemoglobinized red cells, macrocytosis, and anisocytosis. Platelets were scanty. E.S.R. (Westergren) 60 mm. in first hour. The sternal bone marrow was markedly hypocellular. Apart from the reduction in absolute numbers, the differential marrow cell count showed a preponderance of lymphocytes. The predominant cell in the erythroid series was the normoblast, and few early forms were seen. No megaloblasts were identified. Erythrocyte fragility was normal, lysis beginning at 0.44% of saline and complete at 0.32% of saline. Schumm's test was negative. Urobilinogen was not present in the urine, and the faecal urobilinogen was normal at 117.1 mg. per 100 g. The serum bilirubin was 0.8 mg. per 100 ml.; plasma proteins, 6.8 g. per 100 ml., A./G. ratio, 1:6; thymol turbidity, 4 units. An intravenous pyelogram demonstrated a normal renal tract and the blood urea nitrogen was 15 mg. per 100 ml.

At this stage the essential findings were persistent pyrexia, splenomegaly, and pancytopenia associated with a severe depression of all blood-forming elements in the bone marrow. There was no evidence of the nature of the underlying disease.

On April 1 a painful lymph-node enlargement which was hard and tender developed on the left side of the neck. There was no sore throat or obvious focus of infection. The symptoms abated within the next two days, but as the enlarged gland persisted it was removed on April 23. Histological examination showed caseation and epithelioid reaction characteristic of tuberculosis. Scanty tubercle bacilli were demonstrated in the section. Further chest radiographs revealed nothing abnormal and tubercle bacilli were not isolated from the sputum.

The abdominal pain and vomiting cleared shortly after admission to hospital, but otherwise her condition remained unchanged. The pyrexia was not controlled by penicillin, and blood transfusions were given in an attempt to improve the blood picture and the patient's general condition. Repeated blood examinations, however, continued to show the presence of anaemia, macrocytosis, leucopenia, thrombocytopenia, and reticulocytosis. No further clinical evidence of tuberculosis appeared.

On May 12 the patient was transferred to a convalescent home, but owing to her rapid deterioration she was readmitted to hospital 11 days later. She was pyrexial and cachectic; splenomegaly was pronounced; B.P. 115/75. Systemic examination revealed nothing abnormal. Blood examination: Hb, 58%; red cells, 3,000,000; reticulocytes, 4.3%; white cells, 3,100 (polymorphs 78%, lymphocytes 9%,

myelocytes 6%, metamyelocytes 4%, monocytes 3%); platelets, 50,000. Nucleated red cells were present in a blood film.

On May 27 she became restless, and early the next day was semicomatose. The blood urea nitrogen was raised to 68 mg. per 100 ml. and death occurred 24 hours later.

Post-mortem examination showed evidence of miliary tuberculosis involving the liver, spleen, kidneys, adrenal glands and bone marrow. The primary focus was present in a Fallopian tube. No evidence of extramedullary haematopoiesis was observed in the spleen, liver, or lymph nodes.

Case 3

A motor driver was admitted to the Leeds General Infirmary on October 22, 1948. His medical history began in April, 1948, when he developed a severe frontal headache which persisted for about 10 days and was followed by an erythematous eruption which first appeared along the hair margin of the forehead and spread to involve the right eyebrow, the pinnae, and the shoulder regions. Pustular formation followed. The eruption gradually disappeared, but about a month later he developed a severe pain in the right knee and ankles, associated with pyrexia and profuse sweating. There was no swelling of the joints, and salicylates afforded only very slight and temporary relief. He also developed a dry cough, a tightness in the chest, constipation, and marked weakness. During the next eight weeks he was confined to bed and lost 35 lb. (15.9 kg.) in weight.

In June he was admitted to the County Hospital, Driffield, as a suspected case of tuberculosis. On examination at that time he was noted to have lost weight and to be severely anaemic. His temperature was 101.4° F. (38.6° C.), B.P. 120/90. Systemic examination gave no abnormal findings. Various investigations, including x-ray examination of the chest and gastro-intestinal and renal tracts, blood culture, agglutination tests, plasma chlorides, and proteins, showed normal findings. Liver-function tests, however, suggested some impairment of function. Blood examination revealed a pronounced pancytopenia and macrocytosis, but no immature cells were observed on examination of a blood film. The sternal bone marrow was of normal cellularity and had a normal myeloid-erythroid ratio. Treatment with penicillin, liver extract, and folic acid failed to have any effect on the temperature or blood picture, and the patient was transferred to the Leeds General Infirmary for further investigation.

On examination on October 22 he was cachectic, pyrexial, and anaemic. The liver was palpable three fingerbreadths below the right costal margin. There was no splenomegaly. Examination of other systems revealed no abnormalities.

Investigations.—Blood examination showed: Hb, 54%; red cells, 2,600,000; C.I., 1.04; P.C.V., 26%; M.C.V., 100 μ^3 ; M.C.H.C., 30%; white cells, 1,300 (neutrophils 65%, eosinophils 1%, lymphocytes 32%, monocytes 2%); platelets, 90,000; E.S.R., 41 mm. in first hour. The blood film showed macrocytosis and one nucleated red cell per 100 white cells; clotting-time, 4 minutes; prothrombin time, 19 seconds. Bone marrow was of normal cellularity with a normal differential count. Sternal biopsy showed normal bone marrow. Agglutination tests for typhoid, paratyphoid A and B, and *Br. abortus* were negative. The plasma proteins totalled 6 g. per 100 ml. (albumin 1.9 g., globulin 4.1 g., per 100 ml.; A/G ratio 0.46); thymol turbidity, No. 8; gold-sol, No. 5; blood cholesterol, 100 mg. per 100 ml. Blood culture was negative. Repeated sputum examinations for tubercle bacilli were negative.

The patient's condition remained stationary during the first week and then rapidly progressed downhill, with high fever, sweating, tachycardia, and exhaustion. Penicillin failed to control the fever, and in view of the past history of dysentery while on active service in India and the enlarged liver a course of emetine hydrochloride was prescribed although no diagnostic proof of amoebiasis had been obtained. No response to treatment occurred. Right-sided pleural effusion was confirmed by an x-ray film of

the chest, which also revealed a patchy increase in density of a nodular type throughout both lung fields. The report stated that "the appearances are not typical of miliary tuberculosis, but such a lesion cannot be excluded." Further attempts to isolate tubercle bacilli were unsuccessful, and the patient died two weeks after admission to the infirmary with the diagnosis still in doubt.

Post-mortem examination showed massive caseating tuberculous lesions affecting both lungs. Widespread crude tubercles from 1 to 10 mm. in diameter were found in the lungs, liver, spleen, and kidneys. There were submiliary tubercles in the adrenal glands, a gross tuberculous lesion of the prostate, and localized tuberculous peritonitis with adhesions over the liver and spleen. Extensive pleural adhesions were noted on the right side, and effusions were present at both bases.

Case 4

A housewife aged 61 was admitted to the Leeds General Infirmary on November 1, 1951. Her symptoms began after an attack of tonsillitis 10 months previously, when she complained of increasing lassitude, weakness, anorexia, and slight loss of weight. During the six months before admission she had become much paler and complained of severe palpitations and breathlessness on exertion. No obvious bleeding had been noticed, but for two weeks she had been troubled with a burning epigastric discomfort following meals which was inconstant and never severe. She had had no previous serious illnesses and the family history was one of good health.

On examination she was seen to be extremely anaemic and dyspnoeic on the least exertion. The cervical lymph nodes on the left side were enlarged and a solitary enlarged left axillary node was palpable. Haemorrhages were present in the fundus oculi on both sides. The skin over the abdomen was dry and loose and the tip of the spleen was palpable. There was no hepatomegaly. Examination of other systems revealed no abnormality. The temperature was 100.4° F. (38° C.), pulse 92, and B.P. 140/70.

Investigations.—Blood examination showed: Hb, 32%; red cells, 1,300,000; C.I., 1.23; white cells, 4,000 (polymorphs 28%, bands 3%, lymphocytes 64%, monocytes 4%, eosinophils 1%); platelets, 110,000. The blood film revealed macrocytosis, anisocytosis, and poikilocytosis. The bleeding-time was 3½ minutes, and the clotting-time 4½ minutes. The sternal bone marrow showed 98% lymphocytes, many of them immature. A Rehfuess test meal demonstrated a hyperchlorhydria and x-ray examination of the chest was normal.

In view of the haematological findings, together with the enlarged lymph nodes and splenomegaly, the probable diagnosis was thought to be aleukaemic lymphatic leukaemia. Blood transfusions corrected the anaemia. The patient was discharged home on November 28.

She was readmitted on January 7, 1952, in view of progressive pallor, weakness, and dyspnoea. Examination showed considerable weight loss, severe anaemia, and widespread purpura. The enlarged lymph nodes in the neck were more prominent and the spleen was palpable. There was no hepatomegaly. Blood examination revealed a pancytopenia, the Hb being 52%; white cells, 4,000 (polymorphs 45%, lymphocytes 45%, bands 10%); platelets, 70,000. A further bone-marrow examination was not performed. Blood transfusions were again given, but a rapid downhill course followed, and the patient died on January 26.

Post-mortem examination revealed widespread caseating tuberculosis involving the cervical and axillary lymph nodes, the lungs, spleen, and liver. In addition considerable infiltration of these organs by lymphoid cells was observed, indicating a coexisting lymphatic leukaemia.

Comment

The four cases described above presented with profound haematological abnormalities. A pancytopenia was present in all from the outset. Anaemia was severe; in three

patients the haemoglobin was below 50%, the lowest reading being 32%. Macrocytosis was present in all, and the bone marrow showed marked depression of haematopoiesis in three cases.

In Cases 1 and 2 the bone-marrow picture suggested aplastic anaemia, although, as is not unusual, aleukaemic lymphatic leukaemia was difficult to eliminate by marrow aspiration alone. Persistent reticulocytosis and a leuco-erythroblastic anaemia in the absence of myeloid metaplasia indicated that some marrow function remained. A possible explanation for the leuco-erythroblastic anaemia may have been infiltration of the bone marrow by the tuberculous process. Chapman and Whorton's series, however, indicated that a leuco-erythroblastic picture was rare, while miliary spread to the bone marrow was a common finding. In Case 3 the bone marrow was normal, and the absence of splenomegaly contraindicated a hypersplenic mechanism as the cause of the cytopenia. Case 4 was remarkable in that, although clinically showing many haematological features similar to those of the other cases, post-mortem examination showed that it differed in that widespread visceral infiltration with lymphoid cells was present, indicative of a co-existing lymphatic leukaemia. Although lymphatic leukaemoid reactions have been reported (Gardner and Mettler, 1949) to be associated with miliary tuberculosis, the presence together of leukaemia and generalized tuberculosis must be extremely rare. Forkner (1938) has reviewed this subject. Of much interest was the fact that the patient's previous history was one of good health and there was no suggestion of previous tuberculosis. A possible explanation for the dual findings may have been the presence of a latent focus of tuberculosis which was exacerbated by the developing leukaemia, with resulting widespread dissemination.

From the clinical standpoint the cases presented were primarily problems in diagnosis, of which the cardinal feature was the presence of marked haematological changes, together with pyrexia and progressive weight loss. In only one instance was a definite diagnosis reached before death (Case 2), following the appearance and biopsy of an enlarged lymph node in the neck. Case 1 showed no clinical evidence of tuberculosis at any time during the course of the disease, while routine investigations for tuberculosis in Case 3 were negative, although latterly the x-ray findings of the chest were suggestive. A clinical diagnosis of aleukaemic lymphatic leukaemia was made in Case 4, and it was not until necropsy that the enlarged lymph nodes and spleen, in life considered to be due solely to leukaemic infiltration, were found also to be the seat of extensive tuberculous disease.

In view of the present chemotherapeutic agents available for the treatment of tuberculosis it is essential that an early diagnosis be made. As in the above cases, in the presence of pancytopenia with or without depression of the blood-forming elements in the bone marrow, together with pyrexia and loss in weight, and in the absence of any other causative factor, tuberculosis should be considered. The presence of lymphadenopathy demands a biopsy in order to differentiate from Hodgkin's disease, or lymphosarcoma, and aleukaemic lymphatic leukaemia. In addition to routine diagnostic procedures, the bone marrow should be examined for the presence of miliary tubercles either following trephine biopsy or by the technique described by Schleicher (1946). Culture of blood obtained by bone-marrow aspiration, together with guinea-pig inoculation, should also be carried out in an attempt to demonstrate the presence of tuberculous disease.

Summary

Four cases of disseminated tuberculosis are described associated with pancytopenia and macrocytosis. The bone marrow in one was normal, but in three cases a profound depression of the blood-forming elements in the bone marrow, with a preponderance of lymphocytes, was present. In two a leuco-erythroblastic anaemia was

observed, and aleukaemic lymphatic leukaemia together with generalized tuberculous disease was observed at necropsy in one instance.

The difficulties entailed in diagnosis are described and suggestions made regarding the procedure likely to prove helpful in similar cases.

I wish to thank Professor R. E. Tunbridge and Dr. S. J. Hartfall for permission to publish details of cases under their care.

REFERENCES

- Chapman, C. B., and Whorton, C. M. (1946). *New Engl. J. Med.*, **235**, 239.
 Crail, H. W., Alt, H. L., and Nadler, W. H. (1948). *Blood*, **3**, 1426.
 Doan, C. A., and Sabin, F. R. (1927). *J. exp. Med.*, **46**, 315.
 Dyke, S. C. (1924). *Lancet*, **1**, 1048.
 Engelbreth-Holm, J. (1938). *Amer. J. med. Sci.*, **195**, 32.
 Forkner, C. E. (1938). *Leukaemia and Allied Disorders*. Macmillan, New York.
 Gardner, F. H., and Mettler, S. R. (1949). *Blood*, **4**, 767.
 Guild, A. A., and Robson, H. N. (1950). *Edinb. med. J.*, **57**, 145.
 Muller, G. L. (1943). *Clinical Significance of the Blood in Tuberculosis*. Commonwealth Fund, New York.
 Rosenthal, N. (1928). *J. Lab. clin. Med.*, **13**, 303.
 Schleicher, E. M. (1946). *Amer. Rev. Tuberc.*, **53**, 115.
 Wintrobe, M. M. (1951). *Clinical Hematology*, 3rd ed. Kimpton, London.

CARDIAC ARREST UNDER ANAESTHESIA DURING INDUCTION OF LABOUR WITH "PITOCIN" DRIP

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The intravenous use of the oxytocic principle of the pituitary seems now to be established practice in obstetrics, and successful results are causing it to be more widely used. A recent fatality, which appeared to result directly from the administration of a continuous intravenous "pitocin" (oxytocin) drip, is recorded to draw attention to the fact that there are circumstances in which the practice is not free from danger.

Case Report

A 40-year aged 41, who was two weeks past her expected date of delivery, was admitted to hospital because of painless vaginal bleeding. The blood loss was estimated at about half a pint (285 ml.).

There was no abnormality of the heart or lungs, the blood pressure was 130/60, and the urine was free from albumin. The vertex was presenting and the head was high. A provisional diagnosis of placenta praevia was made, and it was thought advisable to examine her under anaesthesia, with full preparation to proceed to caesarean section if this should seem necessary. Blood was cross-matched for the patient. She was given an injection of atropine, 0.65 mg., one hour before the time fixed for operation.

Because the preliminary examination would necessarily delay the delivery of the foetus should caesarean section be undertaken it was thought best to avoid thiopentone altogether and to use only cyclopropane and oxygen in a closed circuit. Induction was smooth and uneventful, and within five minutes it was possible for the obstetrician to begin his examination. At the same time an intravenous drip of 5% glucose-saline was set up.