(Lee and White's method at 37° C., 10 minutes. Prothrombin time, 12 seconds (control, 12 seconds). The thromboplastin generation test showed defective generation with the patient's plasma. With patient's platelets and control plasma and serum, generation was normal—that is, no functional platelet defect. No circulating anticoagulant was present. Blood group B, Rh positive, phenotype CcDe, which in all probability corresponds to the genotype CDe/cDE.

Case 3

This child, a girl who died in 1949 at the age of 11 months, was not investigated by us. The following is a summary of the notes kindly supplied by Dr. J. M. Garvie. The patient was admitted to the Manor Hospital, Walsall, on October 9, 1949, with a history of bleeding from the throat for several hours. She had always bruised easily and had had a similar haemorrhage at the age of 3 months. On admission there were bruises over the limbs and head, and fresh blood was exuding from the base of the tongue. Eleven days later she developed offensive stools and went steadily downhill, dying on November 7.

Laboratory Investigations.—October 10: red blood cells, 3,250,000 per c.mm.; haemoglobin, 65% (9.7 g. per 100 ml.); white blood cells, 17,600 per c.mm. Platelets plentiful. Bleeding-time, 12 minutes. Clotting-time, 15 minutes. October 20: red blood cells, 3,500,000 per c.mm.; haemoglobin, 70% (10.4 g. per 100 ml.); white blood cells, 11,000 per c.mm. Bleeding-time, 10 minutes. Clotting-time, 10 minutes.

Post-mortem Findings.—Enlarged cerebral ventricles with thrombosis of the surface vessels of the brain. Congested lungs. Large pale liver. Patchy ulceration in the small intestine. Cause of death, toxaemia following gastro-enteritis.

Discussion

About 25 years ago von Willebrand described a haemorrhagic diathesis in 16 females and 7 males of one family in the Aland Islands, off the coast of Finland. Since that time a fairly extensive literature has arisen. The disease occurs in either sex and has one constant laboratory abnormality—namely, a prolonged bleeding-time. About 50% give a positive tourniquet test. The disease, which consists of a capillary defect with failure of normal contractility, should be differentiated from hereditary thrombasthenia or Glanzmann's disease. The latter is due to a functional platelet defect which gives rise to a characteristic pattern of abnormalities: (1) increased bleeding-time; (2) positive tourniquet test; (3) defective clot retraction; (4) defective prothrombin consumption; and (5) defective thromboplastin generation, using the patient's platelets.

The abnormalities found in the condition we describe are: —Capillary defect: increased bleeding-time, positive tourniquet test, and purpura. Antihaemophilic globulin deficiency: may or may not have increased clotting-time, easy bruising, haemarthrosis, defective prothrombin consumption, and defective thromboplastin generation.

It is obvious that differentiation of this group is of great importance to the patient, since management is influenced by the antihaemophilic globulin deficiency. Fresh plasma or blood should be used when surgery is contemplated and bleeding excessive. Generally speaking, the antihaemophilic globulin deficiency must be fairly mild, since most of the cases described have either a normal or slightly prolonged clotting-time.

We wish to thank Dr. Garvie for referring both patients to us for investigation and allowing us to use his notes on Case 3.

REFERENCES

Alexander, B., and Goldstein, R. (1953). *J. clin. Invest.*, **32**, 551.
Bigelow, F. S (1954). *J. Lab. clin. Med.*, **43**, 759.
Biggs, R., Douglas, A. S., and Macfarlane, R. G. (1953). *J. Physiol. (Lond.)*, **119**, 89.
—— and Macfarlane, R. G. (1953). *Human Blood Coagulation and its Disorders*. Blackwell Scientific Publ., Oxford.
Dacie, J. V. (1956). *Practical Haematology*, 2nd ed. Churchill, London.
Darte, J. M. M. (1955). *Amer. J. Dis. Child.*, **90**, 561.
Ingram, G. I. C. (1956). *Brit. J. Haemat.*, **2**, 180.
Ivy, A. C., Nelson, D., and Bucher, G. (1941). *J. Lab. clin. Med.*, **26**, 1812.
Koch, F., and Schulze, H. E. (1952). *Schweiz. med. Wschr.*, **82**, 924.
Larrieu, M. J., and Soulier, J. P. (1953). *Rev. Hémat.*, **8**, 361.
Lee, R. I., and White, P. D. (1913). *Amer. J. med. Sci.*, **145**, 495.
Pitney, W. R. (1956). *Brit. J. Haemat.*, **2**, 250.
Quick, A. J., and Hussey, C. V. (1953). *J. Lab. clin. Med.*, **42**, 929.
Schulman, I., Smith, C. H., Erlandson, M., and Fort, E. (1955). *Amer. J. Dis. Child.*, **90**, 526.
Singer, K., and Ramot, B. (1956). *A.M.A. Arch. intern. Med.*, **97**, 715.
Soulier, J P., Larrieu, M. J., and Wartelle, O. (1955). *Acta haemat. (Basel)*, **14**, 160.
Van Creveld, S., Jordan, F. L. J., Punt, K., and Veder, H. A. (1955). *Acta med. scand.*, **151**, 381.
Verstraete, M., and Vandenbroucke, J. (1955). *British Medical Journal*, **2**, 1533.

CONGENITAL HAEMOLYTIC ANAEMIA COMPLICATED BY MEGALOBLASTIC ANAEMIA OF PREGNANCY

BY

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Megaloblastic anaemia of pregnancy in association with a haemolytic anaemia is rarely found. A search of the available literature suggests that only Davidson (1952) has described it. In his report of a case in which a megaloblastic anaemia of pregnancy was superimposed on a pre-existing microspherocytic anaemia he comments on the surprising rarity of this finding in view of the greatly increased requirement of haematinic agents such as folic acid which must necessarily follow the sustained overactivity of haematopoietic tissue in chronic haemolytic anaemias.

We have observed a similar case over a period of three years; a report of the case is given below.

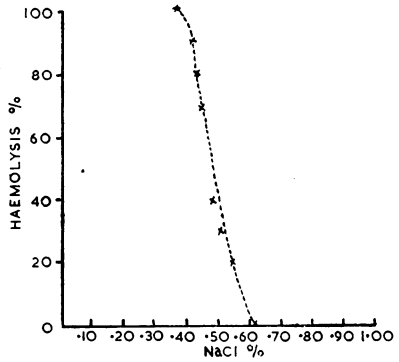
Case History

A 2-para aged 32 attended the antenatal clinic at the National Maternity Hospital on February 3, 1953. Although her family doctor had given her iron in large doses she was very anaemic and was admitted to hospital. She gave a history of diarrhoea and complained of sore tongue. The spleen was enlarged.

On admission her blood count was as follows: haemoglobin, 2.5 g. per 100 ml.; erythrocytes, 1,040,000 per c.mm.; leucocytes, 5,120 per c.mm. Sternal marrow showed a well-defined megaloblastic hyperplasia. Treatment was by transfusion (packed cells) and folic acid, 20 mg. intramuscularly daily. There was a reticulocyte response with a peak at 11% on the seventh day, following the institution of folic acid therapy. Re-examination of the sternal marrow on the 10th day after admission showed conversion to normoblastic erythropoiesis. A test meal (histamine) on March 4 showed achlorhydria. While the peripheral blood picture demonstrated a sustained improvement for 25 days after admission to hospital (Hb, 10 g.; R.B.C., 4,000,000), a transient deterioration followed. At the time the reason for this setback was not apparent. It now seems certain that a mild exacerbation of the haemolytic anaemia occurred at this period.

Between the 25th and 50th days of observation the erythrocyte count did not rise above 3,700,000, but on the 76th day it was 4,200,000 and the haemoglobin was 11.6 g. per 100 ml. On the 84th day (May 2) the patient was delivered of a living male infant weighing 7 lb. 9 oz. (3.4 kg.). She did not present herself for examination until seven months

after delivery, although she had been asked to remain under supervision. She was found to have marked splenomegaly, and a screening test on her blood showed a reticulocytosis of 10%. On December 12 the findings were as follows: Hb, 11.6 g.; erythrocytes, 4,576,000; packed cells, 39 vols. %; M.C.V., 85 cubic microns; M.C.H., 25 $\mu\mu$g.; M.C.H.C., 30%; plasma bilirubin, 2 mg. per 100 ml.; reticulocytes, 6.1%. Further investigations on January 13, 1954, included direct and indirect Coombs tests; these were negative. Tests for cold agglutinins, Ham's test, incubation fragility, and the Donath – Landsteiner reaction were negative. The osmotic fragility showed a slight but significant increase (see Chart). At this stage it was found that the patient was pregnant again (L.M.P. on December 19, 1953). The question of splenectomy was left in abeyance, but laboratory control was maintained. During the first four months of pregnancy the blood count remained reasonably good. The findings at subsequent examinations are summarized in the Table.



Osmotic fragility. P.C.V. adjusted to 45 vols. %.

Date (1954)	Gestation (Weeks)	Hb (g./100 ml.)	R.B.C. (mill.)	P.C.V. (Vols.%)	M.C.H.C. (%)	Retics. (%)	Bilirubin (mg./100 ml.)	Marrow	Fragility	Therapy
		Blood Findings								
25/5	22	8·7	2·08		37·8	3·4				
8/6	24						1·2	Normo.		2 pints (1,140 ml.) whole blood
15/6	25	4·5	1·26	12	37·5	0·2	0·9			2 pints (1,140 ml.) packed cells
22/6	26	5·5		15	36·6	1·8		Megalo.		Folic acid started
26/6	26					8·8		Normo.		
28/6	27	9·6		31	31	4·5				
24/7	31	9·7	3·0			8·0				
30/8	36	10·8	3·6	31	35	4·8	1·2		Haemolysis begins 0·5% NaCl	
4/9	37	11·5	3·3	32	30	8·8				
12/9	Readmitted to hospital									
10/10	Delivered, living infant, pseudohermaphrodite, survived one week									
21/10		12	3·4	34	35	3·6				
11/12		12·4	4·1	33	37	7·0	3·2			

On December 11 there was well-marked microspherocytosis, and a further osmotic fragility test on that day showed haemolysis commencing at 0.58% NaCl, complete at 0.4%. The patient was advised to have a splenectomy, and this was performed on January 24, 1955 (Mr. E. O'Malley). Before operation the direct and indirect Coombs tests were repeated with a variety of test sera with negative results. The sternal marrow showed normoblastic erythropoiesis and the plasma bilirubin pre-operatively was 2.2 mg. per 100 ml. Histopathological examination of the spleen supported the clinical diagnosis. A suspected accessory spleen removed during operation proved to be a regional lymph node in which there was intense haemosiderosis. Recovery was uneventful, and on the patient's discharge from hospital on February 18 her blood count was as follows: Hb, 15.7 g. per 100 ml.; erythrocytes, 5,240,000; packed cells, 47 vols.%; M.C.H.C., 33.6%; leucocytes, 5,120; reticulocytes, nil; bilirubin, 0.6 mg. per 100 ml.; platelets normal. This improvement in the blood picture was maintained, and in July she became pregnant again.

Her progress was followed with keen interest, but during the entire antenatal period the haemoglobin level did not fall below 13 g. per 100 ml. In February, 1956, there was a transient erythrocytosis. On April 24 she was delivered of a living male infant weighing 6 lb. 2 oz. (2.8 kg.). There was a mild thrombophlebitis in the puerperium which responded well to anticoagulant therapy, and on May 14 she was discharged. At the time of writing she remained well.

The patient has one brother and a sister living. So far, only the sister has presented herself for investigation. No evidence of congenital haemolytic anaemia was found in her blood.

Summary

The case is reported of a patient in whom congenital haemolytic anaemia was twice complicated by megaloblastic anaemia of pregnancy. Following splenectomy a third pregnancy was successfully completed without anaemia being evident at any stage. The rarity with which this combination has been reported is commented upon.

We wish to thank Professor Sir Stanley Davidson for his kindness in examining one of the sternal marrow films from this patient. We acknowledge also the co-operation of the staff of the department of pathology, the Mater Misericordiae Hospital, Dublin, and the technical assistance of Mr. C. J. Conway, pathology department, the National Maternity Hospital, Dublin.

REFERENCE

Davidson, L. S. P. (1952). *Edinb. med. J.*, **59**, 315.

Medical Memoranda

Subcutaneous Emphysema Occurring After Labour

Subcutaneous emphysema occurring during or immediately after labour is rare (Reckitt, 1922; Charbonnet, 1925). Simmons described the first case in 1784. The majority of cases have occurred in young primigravidae following a prolonged or difficult second stage, and in whom there has been no demonstrable pre-existing pulmonary disease. The mechanism of causation is obscure. The condition has been reproduced experimentally by injection of air through the buccal mucosa (Watson, 1885). It is probable that most cases are due to intrapulmonary alveolar rupture with passage of air along the perivascular sheaths to the mediastinum. The condition has been reported to follow hard and prolonged labour (Faust, 1940), to follow easy labour (Wiland and Crowder, 1951), and to follow labour complicated by bronchopneumonia (Roth, 1943).

CASE REPORT

The patient was a primigravida aged 21. The last period was on February 16, 1955, and the expected date of delivery November 23, 1955. Her blood was group B, Rh-positive. She was 64 in. (162.5 cm.) tall and weighed 101 lb. (45.8 kg.) when 12 weeks pregnant. The external pelvic measurements were normal. The antenatal period was uneventful, the maximum recorded blood pressure being 120/70 mm. Hg. There was no albuminuria or oedema. At the 36th week *x*-ray examination confirmed that the head was engaged. At the 38th week her weight was 122 lb. (55.3 kg.).

On November 23 the patient was given a routine medical induction of castor oil, 2 fl. oz. (60 ml.) by mouth, followed by an enema saponis and hot bath. Vague uterine contractions were noted eight hours later; these continued irregularly during the next 24 hours. At 1.30 a.m. on November 25 strong regular (1:15) uterine contractions were noted. At 3 a.m. 100 mg. of pethidine was given intramuscularly, and this dose was repeated at 7.30 a.m., at which time the contractions were strong and regular (1:10),