PRELIMINARY COMMUNICATIONS

Permeability of Membranes of Dead Fetus

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Summary

Membranes of dead fetuses showed a three-fold increase in permeability to the haemoglobin molecule when compared with normal and stored membranes. The friability of some of these membranes was markedly increased and their strength and elasticity diminished. These findings may be significant in the aetiology of the hypofibrinogenaemia and the increased incidence of amniotic fluid embolism with intra-uterine death of the fetus.

It is established that a gradual decline in the maternal blood fibrinogen level can occur in patients in whom a dead fetus is retained in utero for more than three to four weeks (Reid *et al.*, 1953; National Maternity Hospital, Dublin, 1965; Scott, 1969). Some of these patients bleed dangerously at delivery. Haemorrhage is unpredictable and hypofibrinogenaemia does not invariably mean that it will occur. The phenomenon is unexplained. It is postulated that activation of the fibrinolytic mechanism is responsible, and also that it may result from the absorption of amniotic fluid.

Steiner and Lushbaugh (1941), in describing amniotic fluid embolism, wrote: "As far as we are aware nothing is known about the effect of a dead fetus on the strength of the fetal membranes." It seems that since then no attempt has been made to show that the membranes function differently in these patients. While assessment of the function of a living membrane is fraught with difficulties, a comparative study of the permeability of two different membranes (those of a living and a dead baby) is relatively less complicated.

Materials and Methods

Because of the scarcity of clinical material a method was established by which the permeability of normal membranes could be assessed. The membranes of dead fetuses retained in utero for at least two weeks were similarly assessed as they became available. The apparatus consisted of a simple plastic diffusion chamber with a capacity of 3 ml which was inserted into a conical flask. The membranes formed a barrier between the fluid in the flask and the diffusion chamber. Haemoglobin was used because in the initial experiments it

was found to diffuse through the normal membranes in very small quantities and because it was readily available, easily measurable, and had a suitable molecular weight of 68,000.

A series of normal membranes were collected immediately after delivery and about 4 in² (26 cm²) of the unseparated amnion and chorion was immersed in Hartmann's solution. At the same time 10 ml of blood was withdrawn from the experimenter. The blood was diluted with Hartmann's solution, and high-frequency sound waves were passed through the mixture for 10 minutes to destroy the integrity of the red cells and release the haemoglobin.

The membranes were fixed in position at the bottom of the diffusion chamber, into which 2.5 ml of clear Hartmann's solution was inserted. The haemoglobin solution was put in the conical flask and the diffusion chamber inserted. The flask was then fixed to a rotating arm in a waterbath and the entire apparatus was incubated at 37°C for 12 hours. The amount of haemoglobin which diffused through the membranes was measured electrophotometrically and expressed as a percentage of the initial concentration of haemoglobin in the conical flask.

Sixteen normal membranes were tested and compared with six membranes from dead fetuses retained in utero for two to three weeks, and also with nine membranes, taken at random from the normal group, which had been stored in Hartmann's solution at 4°C for 12 to 24 hours. The pH of the initial and final solutions was measured to ensure that a consistent pattern which could explain a difference in osmotic diffusion did not occur. Volume changes were insignificant.

Results.—The percentage diffusions of haemoglobin through the 16 normal membranes were: 0.99, 0.92, 1.07, 0.95, 1.38, 1.97, 0.77, 0.63, 1.44, 1.64, 1.07, 1.20, 2.85, 5.96, 2.36, and 5.08* (mean 1.89, Student's *t* test 2.86, *P* < 0.01). The percentage diffusions through the six membranes from dead fetuses retained in utero were: 12.31, 2.71, 3.88, 6.75, 3.89, and 2.25* (mean 5.29). The percentage diffusions through the nine normal membranes before and after storage are given in the Table.

Percentage Diffusions of Haemoglobin Through Nine Normal Membranes before and after Storage at 4°C for 12-24 Hours

Before (mean 1.43)	0.92	0.77	0.63	1.44	1.64	1.07	1.20	2.85	2.36
After (mean 1.42)	1.92	0.84	0.97	2.18	1.73	1.39	0.96	1.25	1.59

Comment

There was an overall threefold increase in the diffusion of the haemoglobin molecule through the membranes from dead fetuses retained in utero when compared with normal membranes tested in identical circumstances. There was no overall increase in diffusion through the stored membranes. A further membrane stored for 100 hours allowed only 1.33% of the haemoglobin to diffuse through. There was no clear-cut explanation for the variations in diffusion.

The membranes from dead fetuses retained in utero fell into two categories: (1) those which appeared relatively normal macroscopically, and (2) those which had the consistency of perished rubber, with diminished strength and elasticity and a greatly increased friability.

It should be noted that none of the dead fetuses were retained in utero long enough to cause maternal hypofibrinogenaemia. It may be that with increasing length of retention in utero the permeability of the membranes increases to the extent of permitting the absorption of

* Histologically these membranes were complete.

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thromboplastin or other substances from the amniotic sac into the maternal circulation, resulting in the continuous consumption of fibrinogen. The increased incidence of amniotic fluid embolism with intrauterine death of the fetus may be due to the increased friability of the membranes, which are therefore more likely to split or tear, thus creating favourable conditions for amniotic fluid infusion during labour and delivery.

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MEDICAL MEMORANDA

Intracranial Tuberculosis Resembling Hand-Schüller-Christian Disease

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Tuberculosis is common among non-European immigrants to this country and often presents in unfamiliar ways (Wiseman and Mahmood, 1967). We report a case of intracranial tuberculosis in a Pakistani youth in whom diagnosis was delayed by the resemblance to Hand-Schüller-Christian disease.

Case Report

A youth aged 18 who had been in England for two years presented with a lump on the scalp, protrusion of the right eye, and thirst. He had a mild fever but was not seriously ill. There were soft subcutaneous masses about 3 cm in diameter over the right parietal bone and zygomatic arch, and a smaller mass in the right cheek. The right eye was proptosed 8 mm but there were no neurological signs. E.S.R. was 63 mm in the first hour, blood eosinophils 650/mm³. Mantoux reaction was positive with 1 unit of purified protein derivative, but he may have had previous B.C.G. vaccination. Urinary concentration tests excluded diabetes insipidus.

The chest x-ray film showed an ill-defined opacity towards the left apex but was otherwise clear. In the lateral skull film there was an irregular translucency with surrounding sclerosis (Fig. A). Plain films and tomography of the right orbit showed that the superior orbital fissure was enlarged with an indefinite margin and sclerosis of the lesser and greater wings of the sphenoid bone. A right carotid arteriogram (Figs. B, C, and D) showed a large avascular extracerebral space-occupying lesion in the parietal and temporal regions.

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Biopsy of parietal and cheek lesions yielded non-caseating exuberant granulomatous tissue judged to be consistent with the clinical diagnosis of Hand-Schüller-Christian disease; no acid-fast bacilli were seen. After beginning local radiotherapy (because of increasing proptosis) the right temple swelling became fluctuant and needle aspiration showed pus in which occasional acid-fast bacilli were seen. Cultures from this and the cheek lesion eventually yielded a scanty growth of *Mycobacterium tuberculosis*.

Treatment with streptomycin, isoniazid, and rifampicin produced rapid improvement. After three months he was back at work, the subcutaneous lesions had healed, the proptosis was only 4 mm, and E.S.R. was normal. Chest x-ray examination showed no change, but the skull lesions showed signs of healing.

Comment

Isolation of the organism from two of the lesions and the rapid response to specific therapy indicate that this patient was suffering from tuberculosis. Though mimicking the classical triad of Hand-Schüller-Christian disease, he did not have diabetes insipidus (thirst perhaps being related to fever), exophthalmos was unilateral, and the osteolytic skull lesions were not typically punched out (Lichtenstein, 1964). However, variants of Histiocytosis X are common, eosinophilia occurs (Oberman, 1961), and an intracranial mass has been described (Elian *et al.*, 1969).

Tuberculosis of the bones of the skull vault is unusual (Barton, 1961). A focus of infection in the lung or elsewhere is not always found (Strauss, 1933), and Shaw and Basu (1970) have drawn attention to apparently primary subcutaneous cold abscesses. Tuberculosis meningitis and intracranial tuberculomata may present in atypical ways (Kocen and Parsons, 1970) but a large intracranial extracerebral collection, as shown by arteriography in the present case, is very unusual. This patient was fortunate not to develop meningitis, especially after radiotherapy. But spread of tuberculosis from the skull vault to involve the meninges and brain is rare (Strauss, 1933; Meng and Wu, 1942).

In contrast to the present case several patients with Hand-Schüller-Christian disease have been recorded in whom the initial erroneous diagnosis was tuberculosis (Abbasy *et al.*,

FIG. A—Lateral skull showing translucent defect with surrounding sclerosis in right parietal region. FIGS. B, C, and D—Right carotid angiogram showing large avascular extracerebral space-occupying lesion in parietal and temporal regions.