Summary

Clinical involvement of the central nervous system occurs only in a very small proportion of cases of virus infection, usually at the end of viraemia and often at a time when antibodies are already detectable. After the end of viraemia, virus multiplication appears to continue, at least for a period, in certain tissues, including the central nervous system. Encephalitis can present a histological picture, ranging from almost pure neuronal destruction to a largely inflammatory picture with minimal neuronal damage. The latter seems to be associated with the presence of partial immunity. There is experimental evidence that the administration of antibody at a critical time during the course of the infection may aggravate the inflammatory reaction, and that suppression of the immune response may ameliorate it. The possibility is discussed that the inflammatory aspect of the tissue reaction to virus infection is due to an interaction between the virus and the host immune response. Some ideas are put forward to suggest how virus infections might be responsible for some of the more chronic neurological disorders.

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Medical Memoranda

Amniotic Fluid Embolism: Case with Biochemical Findings

Brit. med. J., 1966, **2**, 1181–1182

Elective caesarean section is generally a safe operation and amniotic fluid embolism is an extremely rare complication. Only one such case has previously been reported in the literature (Barno and Freeman, 1959). The mortality from amniotic fluid embolism is over 80% (Aguillon *et al.*, 1962; Scott, 1963; Geoghegan *et al.*, 1964; Russell and Jones, 1965).

The following case presents the clinical features of amniotic fluid embolism and is, we believe, of particular interest because of the detailed evidence available.

CASE REPORT

A woman aged 37, whose two previous children had been delivered by elective caesarean section, was admitted in the 38th week of her third pregnancy on account of mild hypertension. Seven days after admission she was prepared for elective caesarean section.

Atropine 0.6 mg. was given subcutaneously one hour before operation. After preoxygenation for three minutes with a high flow of oxygen she was given thiopentone 250 mg. followed by suxamethonium 60 mg. The trachea was then intubated with a cuffed endotracheal tube without prior inflation of the lungs by face mask. On laryngoscopy there was no evidence of regurgitation of stomach contents and intubation was easy. Anaesthesia was maintained with 30% oxygen in nitrous oxide by means of a volume-cycled ventilator with a non-return circuit. Relaxation was maintained with D-tubocurarine.

The abdomen was opened through a Pfannenstiel incision and lower-uterine-segment caesarean section was performed. The child, a boy weighing 3.8 kg., was in good condition at birth (Apgar score

9 at 2 minutes). Profuse bleeding occurred after delivery of the child and the uterus did not retract well. Manual removal of the placenta was performed and the uterus was closed in the usual manner. Ergometrine 0.5 mg. had been given intravenously with the birth of the child and uterine retraction was eventually satisfactory. The loss of blood during the operation was later estimated by a haemoglobin dilution technique at 1,850 ml. Compatible blood 1,000 ml. and plasma 500 ml. were infused during the operation.

During closure of the abdomen cyanosis and distension of the neck veins were noted and there was marked resistance to inflation of the lungs. At the conclusion of the operation atropine 1.2 mg. and neostigmine 2.5 mg. were given. Spontaneous ventilation was inadequate and cyanosis persisted despite the administration of 100% oxygen. At this stage amniotic fluid embolism was suspected and blood samples were taken for clotting tests (see Table I). The blood pressure was now 80/60 mm. Hg and the pulse rate 140. Obvious signs of massive pulmonary oedema were present; this was confirmed by x-ray examination.

TABLE I.—Haematological Findings (Times are Hours After Conclusion of the Operation)

Time	Fibrinogen Titre	Thrombin Time	Prothrombin Time	Lysis at 37° C.	Foetal Red Cells	Hb g./100 ml.	W.B.C./cu. mm.	Platelets/cu. mm.
0	1:128	7 sec.	14 sec.	Complete in 2 hr.	None			
1	1:128	7 "	14 "	4–12 hr		13.4	32,700	183,000
6	1:128	7 "	14 "	No lysis after 12 hr				

Manual intermittent positive-pressure ventilation (I.P.P.V.) with 100% oxygen was restarted, attempting to maintain a slight positive pressure during expiration. Examination of capillary blood revealed a moderate metabolic acidosis (see Table II). Sodium bicarbonate 100 mEq, aminophylline 250 mg., and hydrocortisone 200 mg. were given intravenously. At the same time an infusion of low-molecular-weight dextran was started and 1,000 ml. was given.

During the next three hours the patient remained hypotensive and cyanosed despite I.P.P.V. with 100% oxygen. Her skin was cold and clammy and she showed no sign of returning consciousness. We despaired of her life. Then cyanosis began slowly to decrease, the blood pressure rose steadily till it was maintained at 120/80 mm. Hg, and she began to respond to stimuli. Throughout this time much pink, frothy fluid was aspirated from the trachea. The slow intravenous hydrocortisone infusion was continued. Intravenous frusemide 20 mg. and digoxin 0.5 mg. were also given, with a good diuretic response. Seven hours after operation the arterial oxygen tension (P_{aO_2}), which had been as low as 38 mm. Hg, had risen to 115 mm. Hg and there was no acidosis (see Table II).

Spontaneous ventilation was then allowed and one hour later the endotracheal tube was removed, oxygen then being given by mask. Oxygen therapy was stopped 25 hours after operation. The electrocardiogram was monitored throughout but only non-specific anoxic changes were noted.

TABLE II.—*The Acid-base and P_{aO_2} Findings in This Case (Times are Hours After the Conclusion of the Operation)*

Time	pH	PCO ₂ (mm. Hg)	St. Bicarb.	Base Excess	PaO ₂ (mm. Hg)	Remarks
			(mEq/l.)			
0	7.31	46	20.5	-5	—	These specimens were taken while I.P.P.V. with 100% O ₂ was continued
1	7.28	—	—	—	38	
5	7.43	40	25.5	+2	45	
8	7.40	39.5	24	—	115	
11	—	38	—	—	63	8 l. flow of O ₂ by polymask
19	7.47	42	29	+6	56	Patient breathing 27% O ₂ spon- taneously through venturi mask
72	7.42	37	—	—	69	Patient breathing air

Four days after operation the patient was seen by a consultant cardiologist with a view to excluding any underlying cardiovascular or respiratory disease to account for her acute collapse and pulmonary oedema. A full examination was made and no such cause was found. The patient was dismissed home, well, with her baby, on the 12th day after operation.

DISCUSSION

The definitive diagnosis of amniotic fluid embolism can be made only after death by examination of the lungs or of blood from the right side of the heart to show the presence of squames derived from amniotic fluid. Fortunately, such evidence was not available in this case. In the absence of heart disease there is only one other condition which might have been responsible for the symptoms—Mendelson's syndrome due to inhaled vomit. This seems unlikely, as the patient was fully prepared for anaesthesia, was not in labour, and at no time was there any evidence of regurgitation, though silent regurgitation cannot be excluded. Also the pulmonary signs appeared during the operation, whereas in Mendelson's syndrome there is usually a latent period.

This patient showed the clinical features of acute respiratory distress, cyanosis, and cardiovascular collapse in association with childbirth which were presented by Steiner and Lushbaugh (1941) in their classic paper on amniotic fluid embolism.

Defibrination, probably due to intravascular clotting in the lungs, is said to occur in 40% of cases of amniotic fluid embolism (Aguillon *et al.*, 1962). Russell and Jones (1965) point out that very few acute cases have been studied completely for various clotting defects. In the present case detailed information is available (see Table I). Weak fibrinolysis was observed in two specimens, one taken immediately after opera-

tion and the other one hour later, but there was no fibrinolysis in a specimen taken six hours after operation. There was no detectable destruction of circulating fibrinogen or of factor V, nor was there evidence of the production of an anticoagulant due to fibrinogen breakdown products. The platelet count was normal throughout. This fibrinolysis was interpreted as being probably helpful in the resolution of intravascular emboli and it was not severe enough to cause a haemorrhagic state. From these considerations it was strongly felt that treatment with epsilon-amino-caproic acid should be withheld.

We believe that this is the first case of its kind in which arterial oxygen tension has been measured. The severity of hypoxia was indicated by the fact that three hours after operation cyanosis was still present despite I.P.P.V. with 100% oxygen, and the P_{aO_2} was only 38 mm. Hg. Five hours after operation, when the patient was conscious and responding to questions, the P_{aO_2} was 45 mm. Hg. It was eight hours after operation before a normal value (of 115 mm. Hg) was recorded—the patient being still on I.P.P.V. with 100% oxygen.

The reasons for our treatment were as follows: (1) I.P.P.V. with 100% oxygen was used as the most efficient means of producing oxygenation; (2) tracheal aspiration removed a considerable amount of fluid from the lungs; (3) aminophylline was given to dilate the bronchi and reduce pulmonary vasospasm; (4) low-molecular-weight dextran (Rheomacrodex) was given in the hope of increasing pulmonary blood flow; (5) sodium bicarbonate was given to correct the metabolic acidosis which was demonstrated; (6) hydrocortisone was given for the rather vague reason of protecting the patient in a situation of severe stress; (7) frusemide (Lasix) was given to produce diuresis and thus to reduce pulmonary oedema; and (8) digoxin was given to strengthen the myocardium, reduce the pulse rate, and also for its diuretic effect.

The detailed management of the case would have been impossible without the biochemical and haematological tests.

An association with a large general hospital and co-operation with a specialized department on anaesthetics enable a complex case like this to be treated in a manner quite outside the scope of a maternity unit which is isolated from other facilities.

Our thanks are due to Professor Ian Donald for permission to publish this case. We are also grateful to Dr. M. L. N. Willoughby, consultant haematologist to the Queen Mother's Hospital; to Dr. I. McA. Ledingham and Dr. Simon Tindal, who made the P_{aO_2} measurements; and to Dr. Donald D. Moir, who helped with the preparation of this paper.

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