Disturbances of pulmonary function in patients with fat embolism¹

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A number of theories have been advanced to explain the clinical syndrome of fat embolism, its diverse presentation, and in particular the unexplained rarity of the clinical syndrome as compared with the relatively common postmortem appearance of pulmonary fat embolism following trauma. Emphasis has recently been placed on the concurrent arterial hypoxaemia as a major factor contributing to the mortality of the condition (Sproule, Brady, and Gilbert, 1964; Greenbaum, Nunn, Prys-Roberts, Kelman, and Silk, 1965; Nunn, 1966; Collins, Gordon, Hudson, Irvin, Kelly, and Hardaway, 1968); Wertzberger and Peltier, 1968) but two conflicting theories of its causation have remained unresolved. The traditional view proposed by Gröndahl (1911) and supported by Armin and Grant (1951) and Sevvit (1962) maintains that the lethal effects are secondary to cerebral fat embolism rather than to embolization of fat in the lung capillaries. The opposite view holds that the arterial hypoxaemia is the predominant physiological disturbance, and that it results from deterioration in pulmonary function which arises directly from the embolization of fat in the lungs (Peltier, 1967). This view is also supported by Szabó (page 123). Previous reports have described desaturation of arterial blood in cases of fat embolism, but have provided little evidence of the causative mechanisms. This paper describes investigations of cardiopulmonary function made during 1965-66 in five patients in whom a clinical diagnosis of fat embolism was established. The patients were nursed in the Intensive Care Unit of the Leeds General Infirmary, and all observations made were incidental to the clinical management of the individual cases. A preliminary report has already been published (Greenbaum *et al*, 1965).

Case Reports

CASE 1

D.W., a man aged 21 years, was involved in a road traffic accident and sustained a compound fracture of the left tibia and fibula, and a closed comminuted fracture of the left femur. He was fully conscious on admission, and there was no evidence of head injury. Internal fixation of the fractures was performed under general anaesthesia, from which he made a full recovery. Thirty-six hours after admission his body temperature rose to 39° C and he became drowsy although rousable. Sixty hours after admission he developed a petechial rash over the neck, chest, and axillae, and had a right fundal haemorrhage. His left arm showed increased muscle tone. He was treated with antibiotics, sedation, and oxygen therapy by a Venturi mask. A few hours later he complained of colicky abdominal pain, and became increasingly agitated, with respiratory distress and rapid, shallow breathing. A tracheostomy was performed and artificial ventilation by intermittent positive pressure ventilation started. The inspired oxygen concentration was raised to more than 60% in order to maintain adequate arterial oxygen tensions (PaO₂). Consciousness deteriorated progressively, and subsequently he became intensely cyanosed unless he was ventilated with 100% oxygen.

On the tenth day, bowel sounds were absent and there was abdominal wall rigidity, so a laparotomy was performed which revealed bile-stained peritoneal fluid with much gas, a necrotic spleen with thrombosed vessels, and a large gastric perforation. A heavy growth of *Clostridium welchii* was cultured from the spleen, and he was treated with tetracycline and hydrocortisone. At this stage his pulmonary function was improving,

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but on the twelfth day he developed a left tension pneumothorax which was drained. A pericardial effusion was drained on the thirteenth day, but he died on the following day.

Cardiopulmonary function is shown in Table I.

Necropsy findings

Slight cerebral oedema, bilateral suppurative pneumonia and pulmonary collapse, pleural and pericardial effusions, ascites, and hepatic infarcts were found.

CASE 2

M.C., a man aged 18, sustained a closed fracture of the left femur and a compound fracture of the right tibia and fibula in a road traffic accident. Five days after admission he suddenly became incoordinated and drowsy, developed axillary petechiae, and a right fundal haemorrhage. His breathing was laboured at a rate of 40 per minute, and a chest radiograph showed the characteristic snowstorm opacities throughout both lung fields. He was given oxygen therapy by a Venturi mask with inspired O_2 concentrations up to 63%. Haemoglobin was found to be 6.9 g/100 ml, and he was transfused with blood and low molecular-weight dextran (Rheomacrodex). By the twelfth day he was clinically fully recovered. Cardiopulmonary function is detailed in Table II.

CASE 3

R.L., a woman aged 53, was involved in a road traffic accident and was unconscious on admission. She sustained a closed fracture of the right tibia and fibula, and a compound fracture of the right femur. External reduction and fixation of the fractures was performed under general anaesthesia. On the second day after admission, having regained consciousness, she then became drowsy, and developed a petechial rash over the anterior and posterior chest walls. She had no respiratory distress, and her chest radiograph was clear. She made an uneventful recovery. Cardiopulmonary investigations are detailed in Table III.

CASE 4

F.W., a woman, aged 75, sustained a closed fracture of the right femoral shaft and a compound fracture of the right tibia and fibula in a road traffic accident. Internal fixation of the femoral fracture and closed reduction of the lower leg fractures were performed under general anaesthesia. She did not fully regain consciousness after this procedure, but remained drowsy and slowly responsive to painful stimuli. On the second day, a petechial rash developed over the upper chest, and in spite of hyperventilation she became cyanosed while breathing air. A tracheostomy was performed and she breathed humidified

Time (days)	Ventilation	$\dot{V}_E$ (l/min)	f (per min)	Hb (g per 100 ml)	FIO_2	PAO_2 (mm Hg)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	$\dot{V}O_2$ (ml/min) STPD	V_D/V_T (%)	$\dot{Q}_s/\dot{Q}_t$ (%)	Cardiac Output (l/min)
2	SV	33.0	50	12.0	0.21	108	37	27	520	56.0	55.0	—
3	SV	—	—	11.9	0.62	408	72	40	—	—	—	—
4	SV	—	—	10.8	0.35	216	34	32	—	—	—	—
5	IPPV	17.0	22	8.4	1.00	682	165	33	404	51.0	37.0	—
6	IPPV	12.0	20	9.7	1.00	675	229	34	260	50.0	39.0	9.10
8	IPPV	16.0	18	10.4	1.00	673	240	27	328	48.0	30.0	10.70
10	IPPV	17.0	17	12.0	0.81	535	225	33	—	34.0	18.0	—
11	IPPV ^a	—	—	14.3	0.76	512	85	28	—	—	—	—
12	IPPV	16.8	17	12.3	0.75	498	152	35	391	33.0	21.0	—

Table I Results of sequential investigations in case 1^a

^aRiley-Cournand analyses were performed with a physiological mouthpiece during spontaneous ventilation.

^bMeasurements before drainage of pneumothorax.

Time (days)	$\dot{V}_E$ (litres per minute)	f (per minute)	Hb (g/100 ml)	FIO_2	PAO_2 (mm Hg)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	$\dot{V}O_2$ (ml/min) STPD	V_D/V_T (%)	$\dot{Q}_s/\dot{Q}_t$ (%)	Cardiac Output (l/min)
6	16.2	30	6.9	0.21	108	40	30	390	48.0	55.0	—
7	—	—	—	0.63	420	110	28	—	—	—	—
8	—	—	—	0.49	350	127	31	—	—	—	—
9	17.0	24	10.9	0.21	104	65	33	498	37.0	21.0	—
13	10.2	17	10.9	0.21	106	79	30	374	23.0	15.6	13.8

Table II Results of Riley-Cournand analyses during spontaneous ventilation in case 2

The abbreviations set out below apply to Tables I-IV.

$\dot{V}_E$ = minute volume of ventilation; f = frequency of breathing; FIO_2 = fractional concentration O_2 inspired; PAO_2 = alveolar oxygen tension; PaO_2 = arterial PO_2 ; $PaCO_2$ = arterial PCO_2 ; $\dot{V}O_2$ = oxygen uptake; V_D/V_T = dead-space to tidal volume ratio; $\dot{Q}_s/\dot{Q}_t$ = pulmonary venous admixture; SV = spontaneous ventilation; IPPV = intermittent positive pressure ventilation.

oxygen-enriched air spontaneously, but with increasing respiratory distress. Intermittent positive pressure ventilation was instituted on the fourth day with 100% oxygen. She died on the fifth day.

Necropsy findings

Numerous petechial haemorrhages were found throughout the white and grey matter of the brain. The lungs were brawny and showed multiple small abscesses. Histology confirmed both pulmonary and cerebral embolization of fat.

Cardiopulmonary investigations are also detailed in Table III.

CASE 5

C.L., a man aged 28, a heavily pigmented Negro weighing over 100 kg, was crushed and trapped by a large falling concrete slab. His left arm was virtually severed from the body at the shoulder, and he sustained a fractured skull and fractured pelvis. Under general anaesthesia, a transglenoid amputation of the left arm was performed, the compound skull fracture was explored, and corneal lacerations were repaired. Five litres of blood were transfused together with 250 m-equiv of sodium bicarbonate. He recovered consciousness, and although drowsy, was cooperative and responded to questioning. He had a left hemiplegia, and there was paradoxical movement of the left side of the chest, but no evidence of chest injury. Cardiopulmonary investigations at this stage showed normal dead-space/tidal volume ratios and moderate impairment of oxygenation

with characteristic features associated with injury. Subsequent studies demonstrated increased dead-space/tidal volume ratios (see Table IV and results) which induced suspicion of a fat embolism. Because of his deeply pigmented skin, it was impossible to ascertain the existence of petechiae, but there were conjunctival petechiae, and fat globules were seen on microscopy of the serum. He was breathing rapidly (38 per minute) and was maintaining a high minute volume by spontaneous ventilation. His inspired oxygen concentration was raised to and maintained at 30% by a Venturi mask. He made a progressive and uneventful recovery. Details of the cardiopulmonary investigations are shown in Table IV.

Methods of Cardiopulmonary Investigation

The investigations carried out on these patients followed the principles described by Nunn (1969) and were based on the classical methods of Riley, Cournand, and Donald (1951). These methods of analysis of the distribution of ventilation and perfusion allow a distinction to be made between disturbances of alveolar perfusion and those of alveolar ventilation. The former may occur following the pulmonary embolization of blood thrombi (Stein, Forkner, Robin, and Wessler, 1961), fat or air (Severinghaus and Stupfel, 1957), or a severe reduction in total pulmonary perfusion as a result of reduced cardiac output during haemorrhagic shock (Freeman and Nunn,

Case No.	Time (days)	$\dot{V}_E$ (litres per minute)	f (per minute)	Hb (g/100 ml)	FIO_2	PAO_2 (mm Hg)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	$\dot{V}O_2$ (ml/min) STPD	V_D/V_T (%)	$\dot{Q}_s/\dot{Q}_t$ (%)	Cardiac Output (l/min) (dye)
3	2	6.0	18	16.6	1.00	676	560	39	—	39.6	6.7	—
4	2	10.0	22	11.0	0.21	118	36	24	228	41.0	41.3	5.08
	2	—	—	11.0	1.00	687	90	30	228	—	27.7	—
	3	—	—	—	0.48	306	53	25	—	—	—	—
	4	8.7	26	10.7	1.00	680	80	39	—	61.0	30.4	3.92

Table III Results of Riley-Cournand analyses in cases 3 and 4 during spontaneous ventilation

Time (days)	$\dot{V}_E$ (litres per minute)	f (per minute)	Hb (g/100 ml)	FIO_2	PAO_2 (mm Hg)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	V_D/V_T (%)	$\dot{Q}_s/\dot{Q}_t$ (%)
1	10.9	26	11.4	1.00	661	425	36	41.5	12.0
2 ¹	13.2	38	11.2	1.00	661	271	42	54.5	20.0
3	12.5	37	11.9	1.00	653	348	45	57.0	16.1
4	14.2	38	10.4	0.98	662	329	39	49.5	17.5
7	15.6	37	10.3	0.95	671	320	32	37.2	18.0

Table IV Details of Riley-Cournand analyses in case 5 during spontaneous ventilation through a physiological mouthpiece

¹Clinical diagnosis of fat embolism established.

1963). Disturbances of alveolar ventilation may be general or regional, the former being the result of alveolar hypoventilation, whereas regional disturbances may arise from lobar or segmental atelectasis, pneumothorax, or when a significant population of alveoli cannot take part in gas exchange because their lumina are filled or occluded by fluid (eg, pulmonary oedema), blood, fibrin, or fat or its degradation products.

During spontaneous ventilation, patients breathed either air or 100% oxygen through a non-return valve connected to a tracheostomy or to a physiological mouthpiece. Intermittent positive pressure ventilation was maintained either with air, oxygen-enriched air, or 100% oxygen delivered by a constant volume ventilator (Cape Engineering Co. Ltd, Warwick) using deliberately high tidal volumes (800-1,100 ml) at a slow rate (8-10 per minute). Expired gas was collected in plastic Douglas bags over two-minute periods and the volume collected was measured with a dry gas meter. Concentrations of oxygen in the inspired and expired gas mixtures were analysed with a Servomex DCL 101 paramagnetic oxygen analyzer. Expired concentration of carbon dioxide was analysed with a Lloyd-Haldane apparatus. Samples of arterial and mixed venous blood were simultaneously collected from catheters placed respectively in the brachial artery, or floated from an arm vein into either right ventricle or pulmonary artery. These blood samples were immediately analysed at 37°C for pH by capillary microelectrode, and for PCO₂ by the interpolation technique using Radiometer equipment (Kelman, Coleman, and Nunn, 1966). PO₂ was measured with a Beckman macrocathode polarograph. Oxygen content was measured by the polarographic method described by Linden, Ledsome, and Norman (1965). In cases 1 and 2, cardiac output was estimated by the Fick method, whereas in case 4 it was measured by the indicator dilution technique using indocyanine green dye. Alveolar oxygen tension was derived from the formula proposed by Nunn (1963) or from a simplified form of the alveolar air equation when patients were breathing 100% oxygen: $PAO_2 = PIO_2 - PaCO_2 - PH_2O$. Estimates of the alveolar-arterial PO₂ difference ($PAO_2 - PaO_2$), percentage pulmonary venous admixture (Q_s/Q_t), dead-space/tidal volume ratio (V_d/V_t), oxygen uptake ($\dot{V}O_2$), and arteriovenous oxygen content difference ($CaO_2 - C\bar{v}O_2$) were made using conventional formulae (Nunn, 1969).¹ The detailed methodology used in this study has been described

elsewhere (Kelman and Prys-Roberts, 1967). Riley analyses were usually performed daily.

Results

The results of the studies in individual patients are detailed in Tables I-IV. In all the patients, a raised V_d/V_t was found either at the initial study or on the second occasion (case 5), but tended to fall towards normal values (25-35%) within the first three to six days. Venous admixture remained high for much longer periods, even in those patients who recovered.

CASE 1

During spontaneous ventilation in the early stages, this patient had a high oxygen uptake (520 ml/min, approximately 200% of the predicted basal oxygen uptake for a man of his age and size), a very high V_d/V_t (56%) associated with marked hyperventilation ($\dot{V}E$: 33 litres/min, f = 50 per minute), and was markedly hypoxaemic when breathing air (PaO_2 : 37 mm Hg, SaO_2 : 68%) as a result of a severe degree of pulmonary venous admixture (Q_s/Q_t : 55%). Subsequent measurements under intermittent positive pressure ventilation with 100% oxygen showed that between the fifth and the tenth day his V_d/V_t fell from 51 to 34%, implying an improvement in the overall and regional perfusion of the lungs. Although the pulmonary venous admixture also improved at the same time the values did not approach normality and indicated a marked degree of ventilatory disturbance, even at a time when V_d/V_t was within the normal range. Oxygen uptake also decreased but still remained high when compared with normal values for patients on artificial ventilation. Despite the improvements he still needed 76% inspired O₂ to maintain a 'normal' PaO_2 of 85 mm Hg on the eleventh day. Estimations of airway mechanics on the tenth day yielded evidence of marked reduction of pulmonary compliance (29 ml/cm H₂O) but normal values for airway resistance (0.025 cm H₂O/ml at a flow of 865 ml O₂/sec). On the sixth and eighth days, cardiac output was raised to approximately 200% of the predicted resting levels, but was in proportion to the increased oxygen uptake, yielding subnormal values of $CaO_2 - C\bar{v}O_2$ (2.9-3.1 ml/100 ml

CASE 2

This patient initially showed essentially the same pattern as case 1 of raised oxygen uptake (390-498 ml/min STPD), raised V_d/V_t (46-48%) and markedly raised venous admixture (55%). By the time that he had clinically recovered, his V_d/V_t had returned to normal, although the venous admixture was still abnormally high

¹Normal values for healthy young subjects.

V_d/V_t : 25-35%. The value increases with age, and particularly in lung diseases which cause ventilation/perfusion disturbances. Tracheostomy reduces V_d/V_t to between 15 and 30% in the same group of subjects.

Q_s/Q_t : 2-8% when breathing air; 2-6% when breathing 100% O₂. Q_s/Q_t also increases with age.

$CaO_2 - C\bar{v}O_2$: 3.5-5.0 ml/100 ml

$PAO_2 - PaO_2$: 5-20 mm Hg breathing air; 20-80 mm Hg when breathing 100% O₂.

(15%). Despite spontaneous hyperventilation (PaCO_2 : 30 mm Hg, $\dot{V}_E$: 16 litres/minute), this patient was also severely hypoxaemic when breathing air (PaO_2 : 40 mm Hg; SaO_2 : 72%).

CASE 3

This patient showed remarkably little evidence of pulmonary dysfunction when breathing 100% oxygen, and her V_D/V_T and $\dot{Q}_s/\dot{Q}_t$ values were within normal limits for a woman of her age.

CASE 4

This patient was severely hypoxaemic when breathing air (PaO_2 : 36.5 mm Hg; SaO_2 : 67%) and had a grossly elevated V_D/V_T (60%) and $\dot{Q}_s/\dot{Q}_t$ (30-40%) up to the time of death. Her cardiac output and oxygen uptake values were within normal limits.

CASE 5

The findings in this patient were unique, in that a set of measurements made on the first day of admission showed essentially normal gas exchange, whereas the diagnosis of fat embolism was first suspected as a result of the marked elevation in V_D/V_T found on the second day, together with increased $\dot{Q}_s/\dot{Q}_t$, and subsequently confirmed by the stigmata of systemic fat embolism. Although the V_D/V_T in this patient returned rapidly to normal, the venous admixture remained raised beyond the sixth day. Although this patient was not allowed to become hypoxaemic, it is difficult to interpret the central nervous disturbances in view of his preexisting head injury.

Discussion

It has been suggested that pulmonary fat embolism alone is insufficient to cause disturbances of gas exchange in previously healthy subjects (Szabó, Jankovics, and Farkas, 1969) or to account for the clinical syndrome and the mortality arising from it (Sevitt, 1962). With the exception of case 3, the most striking feature of the measurements of pulmonary gas exchange described in this paper was the severe disturbance of ventilation/perfusion relationships, in each case causing marked desaturation of arterial blood to a degree similar to that described by previous authors (Sproule *et al*, 1964; Collins *et al*, 1968; Wertzberger and Peltier, 1968; Szabó *et al*, 1969).

The changes in V_D/V_T found in the early stages of the syndrome, and which decreased steadily towards normal values over a period of days, are compatible with a significant obstruction to pulmonary perfusion, either on a regional or a

diffuse basis. Indeed it would have been surprising if such changes had not been found, since they could have been predicted from a knowledge of the proportion of pulmonary capillaries occluded by fat at any one time. Similar changes in V_D/V_T have been found in other pulmonary embolic conditions, the effect being attributed to an increase in the alveolar component of the total dead space. The migration of peripheral thrombi into the pulmonary circulation has been shown to cause increased alveolar dead space both in dogs (Stein *et al*, 1961) and in man (Prys-Roberts, unpublished observations); air embolism causes a similar effect (Severinghaus and Stupfel, 1957). Impaired perfusion of the pulmonary capillaries due to reduced cardiac output may occur either during haemorrhagic shock (Gerst, Rattenborg, and Holaday, 1959; Freeman and Nunn, 1963) and during deliberate hypotension (Eckenhoff, Enderby, Larson, Edridge, and Judevine, 1963). It is of course important to exclude these other causes before attributing the measured changes in V_D/V_T to the embolization of fat, but in none of our patients was there any evidence of such changes; indeed the cardiac output estimations yielded values which were higher than normal. Similar findings were described by Sproule *et al* (1964). Increased alveolar dead space implies a wastage of ventilatory volume and a gross inefficiency of carbon dioxide elimination (Enghoff, 1938); thus, in order to maintain normal arterial carbon dioxide tensions, the patient has to increase his minute volume, particularly when carbon dioxide production is increased in parallel with the raised oxygen consumption. Other mechanisms clearly play some part in the generation of the tachypnoea, which is a characteristic feature of pulmonary embolism with either fat, air, or thrombi (Binger, Brown, and Branch, 1924), and the alveolar hyperventilation which maintains subnormal levels of arterial PCO_2 . Only in case 5 was there evidence of raised arterial PCO_2 during spontaneous ventilation, at a time when the V_D/V_T was increased to almost double the normal range. It is probable that hypoxaemia, even of a mild nature, contributes to the excessive ventilatory drive.

Pulmonary fat embolism differs from the other forms of embolism in a number of ways, in particular in its gradual onset and progressive elution through the pulmonary circulation into the systemic capillary bed. The gradual onset of symptoms may be accounted for by the diffuse spatial distribution of emboli in lung capillaries (Szabó, Jankovics, Magyar, Szabó, and Szepe-shazy, 1967) and to some extent by the time scale of embolism and disappearance of fat from the pulmonary capillaries (Szabó *et al*, 1967). The latter factor is emphasized by the progressive improvement in V_D/V_T with time in our patients.

Arterial hypoxaemia is now widely recognized as a major feature of the clinical syndrome of fat embolism. In severe cases, the marked desatura-

tion of arterial blood is clinically obvious from the cyanosis, and yet arterial saturation levels provide only coarse indications of the severity of disturbance of pulmonary gas exchange. In patients breathing air, a fall in PaO_2 from 90 to 60 mm Hg represents a significant deterioration of gas exchange, but is equivalent to a reduction of arterial O_2 saturation of only 7%, a change which may not be clinically recognized except under ideal lighting conditions. Changes in the alveolar-arterial PO_2 difference estimated at two different levels (breathing air or 100% oxygen) give a much more sensitive index of the proportion of the cardiac output which is effectively perfusing alveoli which are either seriously under-ventilated or frankly collapsed (Nunn, 1966). In this study, the levels of pulmonary venous admixture found which were equivalent to collapse of between 30 and 50% of the lung cannot necessarily be attributed to the effects of vascular occlusion (Kovacs, Hill, Abert, Blesovsky, and Gerbode, 1966). Clearly a different mechanism must be implicated in order to explain the difference in the time course of the changes in V_D/V_T and those of pulmonary venous admixture. The hypothesis advanced by Szabó, Magyar, and Jankovics (1968) attributes the arterial desaturation following pulmonary fat embolism to inflammatory reaction and exudation into the alveoli as a result of free fatty acids released from the embolized neutral fat. This hypothesis is doubly attractive in that Szabó and his colleagues demonstrated that these inflammatory reactions occurred immediately after infusion of free fatty acids but only gradually after infusion of neutral fats, thus confirming the earlier studies of Peltier (1956) and de Ruiter (1966) on the pulmonary toxicity of oleic acid. De Ruiter's findings of bloodstained, frothy nasal discharge and post-mortem evidence of haemorrhagic alveolar exudates and heavy, oedematous lungs are characteristic of the clinical syndrome, and are fully compatible with both the clinical findings and the disturbances of gas exchange found in our patients.

Patients with preexisting or coexisting pulmonary pathology might be expected to be predisposed towards a more severe manifestation of fat embolism in terms of arterial hypoxaemia and its secondary effects. Szabó *et al* (1969) have shown that a preexisting pneumothorax increases the mortality of experimental fat embolism, decreases the lethal dose of neutral fat, and causes severe desaturation of arterial blood. Such a combination could occur after combined chest and long bone injuries sustained in road traffic accidents. The converse effect, the occurrence of a pneumothorax during the recovery from fat embolism, was seen in case 1 on the eleventh day after admission and caused a sudden worsening of his pulmonary venous admixture. Drainage of his pneumothorax caused a partial resolution only of the changes in arterial PO_2 . Concurrent infection

of the lung is more likely to occur in patients with preexisting fat embolism, since the pulmonary exudate is an ideal culture medium for pathogenic bacteria. Both the patients in our series who died showed multiple areas of suppurative pneumonia and abscess formation.

The role of hypoxaemia in the causation of the central nervous disturbances associated with cerebral fat embolism cannot be ascertained from the results of our studies, but the full and rapid neurological recovery made by patients in this and other series does not compare with the end results in patients who have suffered a period of severe hypoxia. Conversely, it is difficult to provide an explanation of the disturbances in pulmonary gas exchange on a neurological basis. It therefore seems probable that the clinical syndrome can be attributed to the combination of the neurological effects of cerebral fat embolism and the biphasic disturbances of gas exchange arising from the initial embolization of fat in the pulmonary capillaries. To what extent either predominates is dependent on a number of other factors, most of which weigh heavily in favour of augmenting the pulmonary disturbances.

Summary

Investigations of pulmonary gas exchange have been carried out in five patients in whom a clinical diagnosis of fat embolism was established. Raised dead space/tidal volume ratios (48-60%) during the early stages of the condition indicated the degree of pulmonary vascular occlusion and reduced perfusion of alveoli, and the improvement of this index with time was compatible with the progressive disappearance of fat from the pulmonary circulation. Increased pulmonary venous admixture (20-55%) was responsible for the marked desaturation of arterial blood in patients breathing air, and was present shortly after embolism but did not decrease to normal levels in parallel with the improvement in pulmonary perfusion. This biphasic response may be interpreted as evidence of residual alveolar damage arising from the initial embolization of fat in the pulmonary capillaries.

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Discussion: Fat embolism

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Dr A. J. Watson has commented on the presence of petechial haemorrhages in the white matter of the brain in systemic fat embolism. His description seems to be accepted by most pathologists as typical of the naked-eye appearances in such cases. An example recently encountered in the Institute appears therefore to be of particular interest. This was a 33-year old woman who died of fulminating systemic fat embolism 29 hours after a road traffic accident in which one femur was fractured. At necropsy the brain was pale and rather swollen but, on section, there were no apparent focal naked-eye abnormalities in either the gray or white matter. The examination of large celloidin sections, however, disclosed innumerable foci of neuronal necrosis which, although predominant in the cerebral and cerebellar cortex, were also present in the basal ganglia and white matter (Fig.). I would

Fig. Occipital lobe: there are numerous randomly distributed foci of ischaemia in the cortex and at the corticomedullary junction. Similar but fewer lesions are seen in the white matter. Cresyl violet $\times 3$.

like to know how unusual the distribution of the pathological changes in this case is and whether lesions in the gray matter, if they have not been associated with petechiae, have been insufficiently recognized in the past.