ticularly peak-expiratory-flow measurements at work, can be applied in any circumstances where occupational respiratory disease is a possibility. The increasing simplicity and decreasing cost of devices to measure peak expiratory flow put such techniques easily in the grasp of any doctor with a patient who may have occupational lung symptoms. More detailed study may later be necessary under controlled laboratory conditions, but the first necessity is to follow up clues in the history and, whenever possible, to pursue them at work. A large-scale investigation has shown a major problem with colophony fumes in an electronic factory. How many radio construction enthusiasts and one-man television repairers also suffer from colophony asthma? Since colophony is a derivative of pine resin, does colophony asthma come in the same group as the woodworker's asthma caused by dust from western red cedar, iroko, and other hardwoods? The immunological details of the colophony reaction need to be clarified. Drugs such as sodium cromoglycate and salbutamol are of temporary value in management, but prevention is much more important. Efficient exhaust ventilation is a first step, and a search for a safer flux will be a long-term objective.

Amniotic-fluid Embolism

OVER the fifty years from 1928 to 1977 maternal mortality fell in England and Wales from 4·4 per 1000 births to 0·13. Changes during the past twenty years may have been less striking, but the major pillars on the histograms (abortion, pulmonary thromboembolism, hæmorrhage, and toxæmia) have gradually been whittled down. In 1977 toxæmia, ectopic pregnancy, and pulmonary thromboembolism headed the list, but four other causes now vie for prominence because their rates are not decreasing: sepsis, cardiac disease, anæsthesia, and amniotic-fluid embolism. Of the major causes of maternal mortality, it is only of amniotic-fluid embolism that it can be said that "This cause of maternal death remains unpredictable and largely unpreventable".[1] MORGAN's review[2] reveals that of 272 reported cases 86% were fatal. In England and Wales the incidence of amniotic-fluid embolism is steady at approximately 1 case for every 80 000 deliveries (8 cases per year). Large American series give higher rates.[3,4] To have any impact on mortality from this disorder clinicians will ask the following questions: can amniotic-fluid embolism be recognised clinically and can the suspected diagnosis be confirmed in life; are the predisposing factors known; is the pathogenesis understood; how should the patient be managed; and is specific therapy available? Not all can yet be answered.

The clinical picture is not one that the witnessing obstetrician will forget: profound cardiovascular shock and respiratory difficulty with deep cyanosis, often accompanied by uterine atony and hæmorrhage, were the features described by STEINER and LUSHBAUGH in 1941.[5] Dyspnœa, cyanosis, collapse, hæmorrhage, and coma feature to varying degrees, although bleeding is noted in only half the cases and is not always confined to the uterus. 10% of cases may present with convulsions and 12% with hæmorrhage before collapse leads to coma.[2] The respiratory embarrassment begins as air hunger and the chest is clear at first. However, pulmonary œdema often develops subsequently. Bronchospasm is rare. A small number of patients have prodromal symptoms such as vomiting, shivering, or convulsions. A confident clinical diagnosis can usually be made, but amniotic-fluid embolism has been confused with eclampsia (in fitting patients), accidental hæmorrhage, uterine rupture, severe supine hypotension, acid aspiration syndrome, and pulmonary thromboembolism. If the patient survives, long-term ill-effects are rare. If not, then the pathologist can confirm the diagnosis by finding, in the pulmonary arterioles, epithelial squames from fetal skin, lanugo hair, fat from vernix caseosa, mucin presumed to be from the fetal gastrointestinal tract, and, occasionally, bile from meconium contamination of the amniotic fluid. STEINER and LUSHBAUGH[5] provided a clear clinicopathological correlation, and the post-mortem features are unique to patients with the clinical picture of amniotic-fluid embolism.[6] Detecting amniotic material in the lungs may require special stains, such as those for fat, alcian-green phloxin for squames, or Mowry's colloidal iron for acid mucopolysaccharide in mucus. In life, hypofibrinogenæmia, platelet consumption, depletion of factors V and VIII, and other features of disseminated intravascular coagulation provide strong supportive evidence of the diagnosis, but are not specific. Aspiration of blood from the right atrium via the mandatory central-venous-pressure (CVP) line will allow a positive diagnosis. In 1947 GROSS and BENZ[7] demonstrated an extra-flocculant layer on centrifuged blood collected immediately post mortem, and this finding has been applied to life.[8] The

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finding of fetal squames in maternal sputum cytology can be corroborative and lung scans may show evidence of perfusion defects compatible with embolism in patients surviving the initial insult.

Predisposing factors do not seem to be specific. The older multiparous patient who is at term or just beyond it seems most at risk. The notion that large babies and obstructed labour increase the risk is not supported by the figures, but tumultuous or tetanic contractions are common (28% in MORGAN's analysis[2]) and labour is often rapid. Oxytocin use was noted in 22% of cases. Amniotic-fluid embolism usually occurs during delivery. 3 probable cases have been described in the mid-trimester, 2 during evacuation for missed abortion and 1 spontaneously in a threatened abortion.[9-11]

Despite STEINER and LUSHBAUGH's experiments producing shock, cyanosis, pulmonary œdema, and death in dogs and rabbits by injecting human amniotic fluid, the pathogenesis of the clinical syndrome remains unsolved. Amniotic fluid probably enters uterine veins through tears in fetal membranes above the presenting part and then finds its way into the maternal circulation via lacerations of the lower segment and cervix (SMIBERT[12] demonstrated disruption of the birth canal in 70% of his series) or by shelving under the placental margin to enter maternal venous sinuses (premature placental separation was noted in 45% of cases just before collapse in the series reported by PETERSON and TAYLOR[13]). The mechanism whereby, with the fetal presenting part wedged in the pelvis, excessive contractions drive liquor into the maternal circulation is plausible, but it is noted in only a minority of cases. The clinical syndrome is associated with amniotic-fluid transport to the lungs, but three controversial observations await explanation. Animal experiments incriminate particles in the amniotic fluid as the cause of cyanosis, respiratory difficulty, and shock, yet mucin is the most common agent identified in pulmonary vessels post mortem. Mucin is presumed to arise from the fetal gastrointestinal tract, though meconium staining of liquor is not the rule; mucin can hardly be incriminated in mid-trimester cases and nor can fetal squames. ADAMSON et al.[14], critical of much of the experimental work, injected late-pregnancy autologous amniotic fluid into pregnant rhesus monkeys; cardiovascular performance, acid-base studies, oxygenation of mother or fetus, and fibrinogen concentration did not change and there were no long-term effects. They concluded that amniotic-fluid embolism was a misnomer. Although COURTNEY and ALLINGTON[15] showed that amniotic fluid contains a factor-X-activating property, other workers[16] reported that this activity is insufficient in chorioamniotic fluid to cause significant intravascular coagulation in the event of an amniotic fluid infusion, so the strong thromboplastic activity noted in this syndrome remains to be explained.

Our limited knowledge of the pathophysiology of this condition dictates attitudes to prevention, treatment, and further research. The traditional view is that the acute cardiorespiratory effects result from the combined action of partial mechanical occlusion and pulmonary arteriolar vasospasm leading to acute cor pulmonale. Systemic vasodilation and, possibly, a direct or reflex myocardial inhibition causes marked hypotension and perhaps contributes to pulmonary œdema. The coagulation defect is a consequence of disseminated intravascular coagulation usually associated with uterine hæmorrhage. One possibility warranting research is the role of prostanoids. Prostaglandins in amniotic fluid increase during labour[17,18] and unstable products of the prostaglandin-synthetase enzyme complex may convert to thromboxanes, prostaglandins or prostacyelin, all with known effects on uterine relaxation/contraction, vasodilation/vasoconstriction, and platelet aggregation/disaggregation. Many of the clinical features of amniotic-fluid embolism could be explained by various prostanoid actions, and the work of KITZMILLER and LUCAS,[19] who found that $PGF_{2\alpha}$ and liquor from labouring women produce a similar picture of hypotension and raised central venous pressure in cats, is encouraging.

The few reports on survivors provide no clear reasons for survival, other than reduced severity of the condition, and this, with our poor understanding of the pathogenesis, means that no specific treatment is known. The first priority is the cardiopulmonary derangement. Early intubation and positive-pressure respiration are required. An intravenous line is essential, but a CVP line is also mandatory to guide fluid requirements and allow access to right atrial blood for accurate diagnosis. If the CVP remains very high, rotating tourniquets and possibly venesection should be considered. The value of digoxin, diuretics, antispasmodics, vasodilators, low-molecular-weight dextran, and hydrocortisone is unclear. However, isoproterenol reverses the changes of experimental amniotic-fluid embolism in the sheep model[20] and this drug has a positive inotropic effect on the myocardium. Atropine could counter cardiac depression from excessive vagal tone and the coronary and pulmonary

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vasoconstriction. In rabbit experiments[21] the industrial surfactant 'Pluronic F-68' prevented and reversed shock from amniotic-fluid injection by preventing aggregation of platelets around particulate debris in the pulmonary circulation. Surfactants have not been tried clinically, but other methods of reversing platelet aggregation might usefully be studied. The coagulation disturbance has traditionally been treated by replacement of fibrinogen and fresh blood. Lately, heparin has been advocated. Early reports[8,10,11,22] suggest that heparin 5000–10 000 units intravenously before fibrinogen replacement may stop the enhanced fibrinolytic action which stems from simply providing fibrinogen fuel for the fire. The theoretical danger of ε-aminocaproic acid is the potential for widespread spontaneous thromboses. Oxytocin infusion should be stopped and the uterus should be evacuated when the patient's general condition is controlled. Sometimes uterine packing is required. Up to 40% of babies may be born alive since most of the cases occur in the late first and second stages of labour, and post mortem cæsarean section can produce live babies.[13]

ANAESTHESIA IN THE HYPERTENSIVE PATIENT

ANÆSTHETISTS find it difficult to win in the management of the hypertensive patient. If the patient has untreated severe hypertension, the induction of anæsthesia will often precipitate a sharp fall of blood-pressure which can have serious consequences because the circulation has become adapted to the increased tension. If the patient has been treated with antihypertensive agents for a long time, the blood-pressure will be nearer normal and the fall in tension associated with anæsthesia will be proportionately less and better tolerated, but the potent antihypertensive agents can interact with the anæsthetic drugs and produce severe hypotension and other unwanted effects such as serious bradycardia. If the anæsthetist asks for the antihypertensive drugs to be withdrawn, this must be done 10–14 days preoperatively to be effective, and during this period symptoms of hypertension, and even severe complications such as a stroke, may develop.

What is the anæsthetist to do for the best? The recent trend has been to keep patients on their routine doses of antihypertensive drugs and to anticipate circulatory problems by careful monitoring during anæsthesia. It is interesting, therefore, that Goldman and Caldera[23] now conclude, from a large prospective study of the risks of anæsthesia in hypertensive patients, that effective intraoperative management may be more important than preoperative control of hypertension. They were unable to identify significant differences between the mean lowest systolic pressures during anæsthesia in well-controlled, poorly controlled, and untreated hypertensive patients. Moreover, there were no differences in the proportions of patients who needed remedial measures such as adrenergic agents or fluid challenges in these three groups. Multivariate analysis showed that there were no correlations between preoperative systolic and diastolic blood-pressures and any of the following in the perioperative period: blood-pressure lability, cardiac arrhythmias, cardiac ischæmia, cardiac failure, and postoperative renal failure.

If Goldman and Caldera are right there is little justification for the last-minute postponement of routine surgery on patients who are found during preoperative assessment by the anaesthetist to be at risk directly from hypertension or indirectly from their antihypertensive medication. Whilst the need for postponement could largely be resolved by earlier communication with the anæsthetist, further studies are required to formulate the best way of actually managing the surgical patient when he is known to be hypertensive.

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THE GLOMERULUS

FIRST identified by Malpighi some two centuries ago, the renal glomerulus sits like a pinhead at one end of a long, thin tubule. Some species can do without this inconspicuous structure and many people must wonder why it so preoccupies nephrologists. But at a colloquium organised in June by Gabriel Richet at the Tenon Hospital, Paris, its complexity and importance were very obvious. The first part was concerned with the pathophysiology of glomerular filtration, the second with the nature of the control mechanisms which reside within the glomerulus itself. B. Aeikens (Hanover) gave a lucid account of the five-lobular structure of the rat glomerular tuft, emphasising the profuse anastomoses between lobules at the centre of the glomerulus. Filtration takes place principally at the glomerular basement membrane (GBM), and from embryological studies this membrane seems to be derived both from capillary endothelial cells and from visceral (as opposed to capsular) epithelial cells. Clearly, both categories of cell should be taken into account when attempts are made to explain the GBM lesions which characterise so many forms of nephritis.

The great debate about which part of the capillary wall plays the most important role in the control of permeability to macromolecules continued with a paper by J. Bariety[1] (Paris) recording the use of antiperoxidase antibodies as ultrastructural tracers. This technique allows the investigator, in effect, to display electronmicroscopically the point in the glomerular capillary wall at which injected IgG antibodies are arrested. Bariety's claim that in the normal rat the main barrier lies in the lamina densa of the GBM excited considerable controversy. His emphasis on the role of the GBM was

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