BIOCHEMICAL DISTURBANCES ASSOCIATED WITH TOTAL HIP REPLACEMENT

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A prospective study on 227 patients undergoing arthroplasty of the hip was carried out with reference to the effects on the cardiovascular and respiratory systems. Investigations revealed that the placing of acrylic bone cement and the prosthesis in the femoral shaft produced clinical and biochemical disturbances which were consistent with pulmonary microembolism. A fall in arterial oxygen tension during the procedure and hypoxaemia extending into the postoperative period with elevation of serum lipase and a fall in triglycerides supported the idea that embolisation with marrow fat occurred. The method of venting (by catheter or proximal hole) did not influence the biochemical disturbances. The implications of these findings are discussed.

The use of acrylic bone cement in arthroplasty of the hip has resulted in many reports in the literature of cardiovascular and pulmonary reactions, particularly after impaction of the femoral component of the prosthesis. These reactions include cardiac irregularities, arterial hypotension and arterial hypoxaemia. Pulmonary fat emboli (Dandy 1971; Sevvit 1972), absorption of acrylic monomers (Ling and James 1971), pulmonary microembolism (Modig *et al.* 1975), and neurogenic reflexes (Pelling and Butterworth 1973) have all been incriminated in the production of these complications.

Cardiac irregularities. Cohen and Smith (1971) reported a case of bradycardia occurring a few minutes after insertion of an Austin Moore prosthesis into bone cement. Thomas, Sutherland and Waterhouse (1971) described four patients who exhibited extrasystoles, but considered these to be due to profound hypotension rather than to a toxic effect of the methacrylate on the myocardium. Charnley (1970) reported four cases of cardiac arrest in 3700 total hip replacements. Reports from many centres (Kallos 1975) suggest that cardiac arrest is commoner during replacement arthroplasty in transcervical fractures of the femur but this may well be a reflection of the age and poor physical condition of patients with this type of disorder.

Hypotension. Studies such as those of Thomas *et al.* (1971), which were carried out using intra-arterial cannulation, showed that a fall in arterial blood pressure was almost invariable, but was often of such a transitory nature that it might well be missed by conventional sphygmomanometry. These workers showed that patients with higher blood pressures before operation had a greater fall in arterial pressure during impaction of

the prosthesis into the femur. Harris (1970) reported transitory hypotension in the majority of 200 patients undergoing this type of operative procedure.

Animal experiments have indicated that neurogenic reflexes following a rise in intramedullary pressure (Pelling and Butterworth 1973), and peripheral vasodilatation caused directly by entry of monomeric methylmethacrylate into the circulation (Peebles *et al.* 1972) both play a part in causing hypotension.

Hypoxaemia. Modig *et al.* (1975) presented results of blood gas analyses on thirteen patients undergoing total hip replacement. They found a small but significant drop in arterial oxygen tension (P_{a,O_2}) after insertion of the acetabular component. This returned rapidly to normal and was followed by a more marked depression of P_{a,O_2} after insertion of cement and the prosthesis into the femoral canal. Similar changes have been noted by Park *et al.* (1973).

Pulmonary microembolism. Modig *et al.* (1975) found a significant correlation between the release of tissue thromboplastic products into the pulmonary circulation and circulatory and respiratory disturbances. The thromboplastic products were considered to have resulted from the aggregation of platelets and fibrin. Dandy (1971) reported two fatal cases of fat embolism and Sevvit (1972) had an 8 per cent incidence in his series of subcapital fractures where cement was used to stabilise the prosthesis. Jones (1975) emphasised the importance of adequate venting of the femoral canal to facilitate escape of marrow contents, since the intramedullary pressure has been shown to increase with the insertion of the cement and the femoral component (Kallos *et al.* 1974).

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METHODS

A prospective study was carried out on 227 patients undergoing total hip replacement under general anaesthesia. Operations were either the Howse or the modified Charnley arthroplasty, using the posterolateral approach and without removal of the greater trochanter. All operations were carried out with the patient in the lateral position. Details of the clinical management of these patients are reported elsewhere (Alexander and Barron 1978). All patients were intubated and divided into two groups depending on whether

Fig. 1

Comparison of triglyceride levels in patients undergoing arthroplasty of the hip with those of controls.

respiration was spontaneous, breathing nitrous oxide and halothane with 33 per cent oxygen from a Magill circuit, or controlled, after curarisation, using a mechanical ventilator (Manley) with nitrous oxide, 0.5 per cent halothane and 33 per cent oxygen. Venting of the femoral shaft was carried out either by plastic catheter or by making a hole with a power drill in the distal part of the uppermost third of the femoral shaft. All patients were monitored electrocardiographically and blood pressure readings were obtained using standard sphygmomanometry.

Arterial blood samples were taken in heparinised syringes before anaesthesia and just before and immediately after insertion of the cement and prosthesis into the femoral shaft. Further samples were taken at thirty minutes after the end of the operation and in forty patients daily or on alternate days up to the fifth day. The arterial samples were analysed immediately using a Corning-Eel 165 blood-gas analyser. Venous samples of 10 millilitres of clotted blood were taken before operation, at four hours, twenty-four hours and on the fourth day after operation. These samples were centrifuged and the serum deep-frozen until sufficient numbers were available to carry out batch analysis for triglyceride and lipase content.

Estimates of the amount of marrow produced by the two alternative methods of venting were made by weighing swabs. In the cases where a hole in the femoral shaft was used, the swab was held near the hole by an assistant and reweighed after insertion of the cement and the prosthesis. The hole was made using a 4 millimetre (5/32 inch) drill. Where venting was carried out by catheter a 16-gauge plastic tube was employed and the contents plus surplus were collected on a swab which was then reweighed.

Triglycerides. Neutral fats were assayed enzymatically by way of their triglycerol content according to the methods described by Eggstein and Kreutz (1966) and by Schmidt and von Dahl (1968). Estimations were carried out on twenty patients having non-orthopaedic operations, each lasting about one hour and with a comparable amount

of muscle mass involvement. These comprised cholecystectomies, gastrectomies and hysterectomies and the results obtained are shown as controls in Figure 1.

Lipase. Estimations were carried out, using kit supplied by Sigma, by the method described by Tietz and Fiereck (1966) based on the hydrolysis of triglycerides in olive oil into fatty acid, diglycerides and glycerol; the quantity of fatty acids formed was a measure of lipase present in the sample. Control figures were produced by carrying out estimations on the control samples used in the triglyceride study (Fig. 2). In twenty-five patients samples of sputum and twenty-four hour specimens of urine were examined for the presence of fat globules but, as all proved negative, this study was not pursued.

RESULTS

The marrow venting study. Three times as much intramedullary fluid was vented by 16-gauge catheter (15.32 grams) as by the 4 millimetre drill hole (5.16 grams). Analysis showed that approximately 50 per cent of this fluid was fat. More fat may therefore remain available for embolisation when the drill hole method is employed.

Triglycerides. In sixty-one patients out of seventy there was a marked fall in triglyceride in the arterial blood samples; by contrast, in fourteen out of twenty controls it remained unchanged or showed a slight rise. Serial examinations revealed that a return to the preoperative level did not usually take place until the fourth day after operation (or later) in patients having hip replacements (Fig. 1).

Lipase. Comparison of the preoperative and four-hour levels (Fig. 2) shows that the lipase content was elevated in the latter. It was more than doubled in 40 per cent of

Fig. 2

Comparison of lipase levels in arthroplasty patients with those of controls.

arthroplasty patients whereas in the controls 70 per cent showed a fall or no change. Lipase levels had usually reverted to normal by the end of the first day after operation.

Cardiovascular effects. Although all patients were monitored electrocardiographically we were unable to demonstrate any dysrhythmias that we could attribute to the insertion of cement. Patients with pre-existing

dysrhythmias were not uncommon and there was no evidence that the procedure produced any alteration in their cardiac condition.

Measurement of arterial pressure by conventional means showed many incidents of hypotension and, although these were usually of short duration, a few were rather alarmingly profound and required active treatment. Modig *et al.* (1973) measured the cardiac output in one such case and found that there was no diminution, suggesting that the cause was peripheral rather than central.

hypoxaemia. In 227 patients (Table I) in whom oxygen tensions before and after insertion of the prosthesis were subjected to statistical analysis using Student's *t* test, there was a significant fall in P_{a,O_2} ($P < 0.001$). The mean fall was 10.7 millimetres of mercury (1.54 kilopascals). In a small number of patients oxygen tensions below 52.5 mmHg (7 kPa) were recorded, the lowest being 45 mmHg (6 kPa). The fall in P_{a,O_2} was selective in that it was not accompanied by hypercarbia and there was little alteration in pH, total carbon dioxide or base excess. Table I also shows a significant fall in P_{a,O_2} ($P < 0.001$)

Table I. Mean values for P_{a,O_2} before and after insertion of the femoral prosthesis

Type of case	Number of patients	Before insertion kPa (S.D.)	After insertion kPa (S.D.)	Fall in P_{a,O_2} kPa	<i>t</i> test
All cases	227	15.23 (4.26)	13.69 (4.18)	1.54	$P < 0.001$
Catheter venting	177	15.47 (4.32)	13.88 (4.33)	1.59	$P < 0.001$
Hole venting	50	14.44 (3.99)	12.97 (3.57)	1.47	$P < 0.1$

Conversion: kPa $\times$ 7.5 = mmHg

Table II. Mean values for P_{a,O_2} before and at 24 or 48 hours after operation

Type of case	Number of patients	Before operation kPa (S.D.)	24 or 48 hours after operation kPa (S.D.)	Fall in P_{a,O_2} kPa	<i>t</i> test
All cases	40	10.43 (2.30)	8.57 (1.55)	1.86	$P < 0.001$
Catheter venting	23	10.82 (2.33)	8.85 (1.77)	1.97	$P < 0.01$
Hole venting	17	9.80 (2.20)	8.07 (1.07)	1.73	$P < 0.02$

Conversion: kPa $\times$ 7.5 = mmHg

Pelling and Butterworth (1973), on the basis of animal experiments, have suggested that more than one mechanism may be involved in the production of hypotension.

Haemoglobin. Every patient received 500 millilitres of Dextran 70 followed by stored blood in quantities thought sufficient to replace the losses during and after operation. Each patient also received a further 500 millilitres Dextran 70 on the first and second day after operation in an attempt to reduce the incidence of deep venous thrombosis (Browse 1977). Almost all patients showed a considerable fall in haemoglobin on the third day as compared with the level before operation.

Respiratory effects. Immediately after the insertion of the methacrylate and the prosthesis into the shaft of the femur, there was a high incidence of relative arterial

when catheter venting is used. The mean fall with hole venting was less, and the figures are not significant at the 0.05 level. Table II indicates that there was a significantly ($P < 0.001$) lower P_{a,O_2} in the first forty-eight hours after operation as compared to those before, the fall averaging 14 mmHg (1.86 kPa). Remarkably low levels were recorded in a few patients, the lowest being 46 mmHg (6.1 kPa). Oxygen tensions before operation in some elderly patients could be as low as 60 mmHg (8 kPa).

Patients were divided into groups depending on sex, type of ventilation and method of venting. There was no statistically significant evidence to suggest that any of these factors were advantageous in preventing substantial falls in P_{a,O_2} during insertion of the prosthesis, although some of the groups were small. We have not

been able to substantiate the claim of Jones (1975) that catheter venting is beneficial as judged by arterial oxygen tensions.

The samples taken at thirty minutes after operation demonstrated that many patients were hypoxic at this time, and this was particularly evident in those who had received analgesics before blood was taken.

DISCUSSION

A diagrammatic representation of the above findings is presented in Figure 3 and it can be seen that a definite series of changes occurs after the insertion of the bone cement and the prosthesis into the marrow cavity of the femur.

The marrow cavity is essentially a low-pressure chamber equipped with thin-walled vessels (Brookes 1971). These are not normally required to withstand pressures greater than about four torr (0.5 kPa) according to Kallos (1975). The fat content of this cavity has been shown by Lehman and Moore (1927) to be 60 to 70 millilitres and some of this is extruded during the reaming. If venting is carried out by catheter a further 15 millilitres is released whereas venting by drill hole produces a mere 5 millilitres. In either case some marrow and air is retained and is therefore available for intravasation of these thin-walled blood vessels if the intramedullary pressure rises. Studies of these pressures by Kallos *et al.* (1974) and other workers have demonstrated pressures of several hundred torr and have shown that even with effective venting, pressures are still well above those which cause intravasation of marrow contents leading to pulmonary microembolism. Experimental work by Breed (1974) has shown that it is the rise in pressure which is the important factor and not the nature of the inserted substance; inert materials such as bone-wax, plasticine or chewing gum are equally effective in producing demonstrable marrow and fat emboli in the lungs. Breed suggests that methylmethacrylate monomer does not contribute to the embolisation.

There is considerable clinical evidence that embolism with fat globules and with platelet and fibrin aggregates occurs. Jones (1975) reported that he and his colleagues were able to detect turbulence in the right heart with an oesophageal stethoscope after insertion of the femoral component. Daniel, Coventry and Miller (1972) reported a 12.4 per cent incidence of discoid atelectasis seen in radiographs taken after operation. Modig *et al.* (1975) showed the presence of fat globules, bone marrow cells, platelets and fibrin in pulmonary arterial blood. Kelly, Dodi and Eiseman (1972) detected these ultrasonically in the right heart and lungs. Whitenack and Hausberger (1971) injected fat labelled with ^{131}I -triolein into the marrow cavity and, when they raised the intramedullary pressure, were able to detect 23 per cent of the labelled fat in the lungs within five hours. Herndon, Riseborough and Fischer (1971) have

described the sequence of events following the release of emboli into the intramedullary vessels: these emboli are carried to the right heart, and from thence to the lungs via the pulmonary artery, where they block the smaller arterioles and capillaries, become coated with platelets and are then hydrolysed by lipase into free fatty acids. These acids are toxic to the lung parenchyma and cause disruption of the alveolar-capillary membranes and curtailment of surfactant activity producing oedema,

Fig. 3

Diagrammatic representation of changes after insertion of the femoral component with methacrylate cement (at arrow).

haemorrhage and alveolar collapse. In addition, they produce a mechanical blockage of capillaries leading to a diffusion block and increased arteriovenous shunting. These workers stress that the most important laboratory test is the measurement of arterial blood gases and this statement is reinforced by Peltier (1969) and Wright (1970).

The aggregation of platelets is also responsible for the release of serotonin, histamine and adenine nucleotides (Swedenborg 1971) which upset haemodynamics and may cause hypotension. Furthermore, sudden

increase in pulmonary vascular resistance with a transient reduction in venous return to the left atrium could be a contributory factor to disturbances in cardiac and pulmonary performance.

Tronzo, Kallos and Wyche (1974) have shown that a distal vent in the supracondylar area of the femur through a separate incision completely prevents the rise in intramedullary pressure and suggested that this may be good prophylaxis against embolisation. Their numbers were small (twelve patients), however, and our surgeons do not consider this to be a practical proposition during routine arthroplasties.

Arterial hypoxaemia. Kallos (1975), in a study on twenty-four patients undergoing Charnley total hip replacement, demonstrated a large decrease in arterial oxygen tension shortly after the insertion of bone cement and the prosthesis into the femur. This has also been reported by Modig *et al.* (1973) and Park *et al.* (1973); these findings are confirmed in the present study. Our investigations were extended into the postoperative period and it was noted that the Pa_{O_2} did not return to the pre-anaesthetic level until the fourth day or later. The methods we employed have not been sufficiently sophisticated to exclude other causes of postoperative hypoxaemia, such as the metabolic effects of anaesthesia, the respiratory depressive effect of analgesics, pulmonary microembolism from transfusion of stored blood and the effects of age, smoking habits and body build (Gillies *et al.* 1977). Nevertheless, it is of interest that the duration of relative hypoxia has been fairly consistent and that the other biochemical changes have taken a similar time to revert to normal. Our studies have revealed a clinical picture of hypotension, relative hypoxaemia, and anaemia, accompanied by a fall in triglycerides and a rise in lipase which is consistent

with pulmonary fat embolisation. We consider that this, in conjunction with hypovolaemia and altered cardiovascular haemodynamics, may threaten the lives of some patients. We have not been able to show that either method of venting, as performed by our surgeons, has influenced the biochemical disturbances.

Implications

The bilateral procedure has not been carried out for several years, as it was agreed that patients were much more upset than we would have expected. We believe that the two episodes of pulmonary microembolism were contributory factors to their poor condition after operation.

It has been shown by McNamara *et al.* (1972) and others that a failure to use microfilters in blood transfusion sets results in microembolic pulmonary disease, and if this factor is added to that produced by the cement and the prosthesis pulmonary failure could ensue.

Patients with pre-existing respiratory disease should be carefully assessed for this type of operation in the light of the above findings.

All patients would benefit from the addition of oxygen to the inspired air in the first two days after operation.

Other joint replacements

Similar studies to those outlined above have been carried out on ten knee replacements and one ankle replacement. Arterial samples showed a marked fall in Pa_{O_2} after release of the tourniquet at the conclusion of the operations. The results obtained so far have been even more dramatic than those in the hip arthroplasty series.

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