References

- Carnegie, P. R. (1971). *Nature*, 229, 25.
 Caspary, E. A. (1971). *Nature New Biology*, 231, 24.
 Caspary, E. A., and Field, E. J. (1965). *Annals of the New York Academy of Science*, 122, 182.
 Caspary, E. A., and Field, E. J. (1971). *European Neurology*, 4, 257.
 Field, E. J. and Caspary, E. A. (1970). *Lancet*, 2, 1337.
 Field, E. J., and Caspary, E. A. (1971). *Journal of Clinical Pathology*, 24, 179.
 Field, E. J., Caspary, E. A., and Carnegie, P. R. (1971). *Nature*. In press.
 Field, E. J., Caspary, E. A., Hall, R., and Clark, F. (1970). *Lancet*, 1, 1144.
 Klein, G. (1970). *British Medical Journal*, 4, 418.
 Klein, G. (1967). In *Specific Tumour Antigens; Symposium*, ed. R. J. C. Harris, p. 364. Copenhagen, Munksgaard.
 Southam, C. M. (1967). *Progress in Experimental Tumour Research*, 9, 1.
 Westall, F. C., Robinson, A. B., Caccam, J., Jackson, J., and Eylar, E. H. (1971). *Nature*, 229, 22.

Fatal Fat Embolism following Replacement Arthroplasty for Transcervical Fractures of Femur

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Summary

Seven cases are reported of death in old people associated with transcervical fractures of the femur and occurring shortly after insertion of a Thompson prosthesis. They are compared with six fatalities following similar injury but not surgically treated and with three which followed internal fixation. Positive controls for massive fat embolism were selected from fatal cases of multiple and severe skeletal fractures due to road accidents.

It seems likely that patients undergoing this operation are peculiarly susceptible to lethal fat embolism. The clinical features, diagnosis, pathological aspects, and prevention of fat embolism are discussed.

Introduction

Fat embolism is a well-recognized complication of all major fractures. Wilson and Salisbury (1944) found a 5% mortality among 119 fractured long bones in battle casualties from this cause. Postmortem studies after traumatic deaths have shown a high incidence of severe fatal fat embolism—20% by Vance (1931) and 33% by Robb-Smith (1941). Sevitt (1966) reported that 90-100% of people dying after injury show varying degrees of pulmonary fat embolism.

As a clinical problem fat embolism has been mentioned only rarely after transcervical fractures in the elderly. A review of replacement arthroplasty, carried out under the auspices of the American Orthopaedic Association, makes no mention of the problem (Reynolds, 1958). Vanderwater (1961) reported the case of an elderly patient with a transcervical fracture of the femur who died under a general anaesthetic from this cause, but no details are given. Sporadic reports have recently appeared in the medical literature (Burgess, 1970; Gresham and Kuczyński, 1970; Harris, 1970; Hyland and Robins, 1970).

Clinical distinction between sequelae of fat or thrombotic embolization and old age is difficult: confusion, tachycardia, and faecal or urinary incontinence are common to both states. It is not sufficiently appreciated how often pulmonary embolization in the elderly produces psychiatric or neurological

symptoms and signs (Fred *et al.*, 1967). Petechiae, a diagnostic feature, appear relatively late and inconstantly in the diathesis.

A prospective seven-month study of all deaths (in our group of hospitals) associated with fractures of the femoral neck and elective hip operations was therefore arranged.

Patients, Materials, and Methods

During the period of study 110 patients were admitted with fractures of the upper end of the femur (Table I). All who died (16) in this time were brought to thorough necropsy. Sections for histological examination were taken as indicated, but in all cases included thick (10 μ) frozen preparations of lungs, kidney, and brain, which were stained with haematoxylin and eosin and Scharlach R. Seven (Table II) had undergone prosthetic replacement of the hip (Thompson's); three (Table III) had had internal fixation by nail-plate; and six, owing to their poor condition, had had no surgical procedures whatever (Table III).

TABLE I—Treatment of Femoral Neck Fractures admitted during the Period of Study

Treatment	Fractures	
	Intertrochanteric	Transcervical
Nail-plate fixation	45 (3)	5
Thompson	—	32 (7)
Smith Petersen nail, Moore's pin ..	—	8*
Non-operative	11 (3)	9 (3)
Total	56 (6)	54 (10)

Numbers in parentheses are of deaths during period in hospital.

*Two patients had Thompson's arthroplasty later.

TABLE III—Clinicopathological Features of Deaths following Conservative and Internal-fixation Procedures

Case No.	Sex	Age	Survival after Fracture	Cause of Death	Site of Fracture	Treatment
8	F.	83	2 days	Myocardial ischaemia	Pertrochanteric	Non-operative
9	"	85	5 "	Bronchopneumonia	Pertrochanteric	"
10	"	86	1 "	"	Transcervical	"
11	"	86	1 "	"	Transcervical	"
12	"	76	6 "	Acute left ventricular failure with myocardial fibrosis	Transcervical	"
13	M.	79	12 "	Bronchopneumonia	Pertrochanteric	"
14	F.	86	5 "	Acute heart failure, with hypertensive disease	Pertrochanteric	Nail-plate
15	"	65	5 "	Pulmonary embolus, Bronchopneumonia	"	"
16	"	74	11 "	Pulmonary embolus. Deep-vein thrombosis	"	"

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TABLE II—Clinicopathological Features of Deaths following the use of Thompson's Prosthesis

Case No.	Sex	Age	Physique	Survival	Mode of Death	Cause of Death	Associated Abnormalities
1	F.	82	Thin	9 hours	Postop. confusion, syncope	Fat embolism	Ovarian cyst.
2	"	92	Thin	*Intraoperative	Fall of B.P. under G.A. Cardiac arrest	Fat embolism	Pituitary adenoma
3	"	83	Obese	14 hours	Postop. confusion, progressive drowsiness, syncope	Fat embolism	Atherosclerosis
4	"	72	Stout	†Intraoperative	Fall of B.P. under G.A. Cardiac arrest	Fat embolism	Osteoporosis. Chronic bronchitis.
5	"	81	Stout	34 hours	‡Fat embolic syndrome	Fat embolism	Myocardial fibrosis
6	"	67	Obese	10 days	Sudden syncope	Pulmonary thromboembolism	Coronary atherosclerosis, Cholelithiasis
7	"	83	Thin	20 days	Progressive confusion for 4 days. Syncope	Bronchopneumonia	Nodular colloid goitre. Uterine fibromyomata. Atherosclerosis
							Deep-vein thrombosis. Mild atherosclerosis
							Inhalation of vomit. Atherosclerosis

*During closure of wound.

†Immediately after insertion of prosthesis.

‡The clinical features were: postoperatively, progressive confusion, breathlessness and cyanosis, with onset of urinary incontinence at 24 hours, hyperpyrexia (105°F; 40.6°C) at 30 hours, and sudden death at 34 hours.

Five randomly selected road traffic accident casualties with multiple major fractures (three dying primarily of fat embolism) were examined postmortem in a similar manner and used as control samples of massive fat embolism.

All surgical operations were performed in a standard manner and anaesthetic procedures were similar. In general patients with transcervical fractures were treated by replacement arthroplasty if over 65 years of age and by internal fixation if the patient was under 65 or the fracture was not displaced. The technique used has been the insertion of a Thompson (titanium) prosthesis through an anterolateral approach with methylmethacrylate cement to imbed the implant. In this time no deaths followed Charnley or McKee-Farrar types of total hip replacement.

Clinicopathological findings

The seven deaths in Table II represent 21.9% of all Thompson procedures during the study period. In five of these unequivocal histological evidence was found of massive fat embolism (see Fig.). All five formed an "early death" group, which survived less than 36 hours (two died on the operating table); none of these showed any other acceptable cause of death, though conditions carrying various degrees of morbidity were associated, nor did any slides show the presence of foreign particulate matter suggesting embolized cement. The other two died much later, and showed no signs of embolic fat. In one, however (Case 7), fat embolism had been suspected on the second postoperative day, when urine and sputum examined at the time did show fat globules, but this kind of investigation is notoriously unreliable.

Numerous elongated fat emboli in pulmonary capillaries. (Sudan III/IV. 83.)

None of the fatalities following internal fixation or conservative treatment showed a significant amount of fat in their lungs, kidneys, or brain—that is, under $\times 100$ magnification one or at most two capillaries were seen to contain fat, in globular rather than "sausage" form.

No evidence was found of platelet aggregation or thrombus formation in vessels of the lungs containing embolized fat, though increased numbers of megakaryocytes were seen in three of the road traffic victims. This last, of course, is not unusual.

In six instances the possibility of fat embolism was not even mooted. Only one patient (Case 5) showed a diathesis which could be said to characterize the fat embolism syndrome: she was, probably not coincidentally, the longest survivor; this would support the hypothesis that the syndrome develops after release of fat from the pulmonary circulation. However, at no time were petechiae present.

Discussion

The above data suggest that neither internal fixation nor the fracture itself is the likely cause of serious fat embolism. The comparison is valid, especially with the untreated group, which was, coincidentally, well matched for age (Table IV) and sex. In striking contrast, a review of 28 consecutive "cold" hip operations performed during this time (6 Charnley, 21 McKee-Farrar, and 1 Osborne-Ball procedures) showed a low morbidity and no mortality.

TABLE IV—Comparison of Ages of the Groups Examined

	Group 1 Trial	Group 2 Unoperable	Group 3 Int. Fixation	Group 4 "Cold" (Charnley, etc.)
Mean age	80	82	75	64.5
S.D.	8.16	4.13	10.54	6.62
P*	—	0.50	0.40	0.001

*Compared against "Trial" group.

It is of interest that neither Charnley (1970a, 1970b) nor G. K. McKee (personal communication, 1970) themselves have noted fat embolism or have had a death from that cause. Arden (1970) reported two cases of fat embolism, one fatal, after total knee-replacement arthroplasty using cement, but there does not seem to be any other record of problems in the "cold" case. The other major difference in our series was that the mean age of candidates for a Thompson prosthesis was 15.5 years higher than that of the "cold" group.

Methylmethacrylic cement is probably not responsible. In the first place, it is used in the McKee-Farrar procedure in much the same fashion as with Thompson's prosthesis. Secondly, methylmethacrylic cement has been used in orthopaedic surgery for 19 years and has not been noted to cause general

toxic problems in clinical use. High doses—for example, 125 mg/100 ml—of the monomer given intravenously to dogs cause death; this corresponds to 6.25 g in man. The only noted effect in man seen in total hip replacement operations has been a transient drop in blood pressure three minutes after the cement had been used in two-thirds of the patients; this is also seen in other arthroplasties, and occurs more often after the acetabular (rather than the femoral) component has been cemented into place. This suggests that the pressure of forcing the cement into the femoral cavity may be the fault, rather than the cement itself.

Reaming of the medullary cavity is a feature of all commonly used operations for replacement of the femoral head. It is interesting to note that the mortality in, for instance, Moore's prosthesis (Hunter, 1969) is remarkably similar to that in our series; these deaths may also be related to the incidence of unrecognized fat embolism.

The pressure created by ramming cement into the femur must be considerable in clinical practice, particularly if no vent is provided to allow blood and marrow to escape; but no pressure measurements seem to have been carried out in vivo without venting, partly on eminently reasonable ethical grounds. D. W. Parsons (personal communication, 1970) finds in vitro that almost any pressure can be obtained, according to the time of measurement and the degree of packing; even fixed specimens of femur, when packed without a vent, show marked subperiosteal oozing of fluid and fat; this is also seen during the insertion of the Thompson stem, as the vent becomes no longer functional. Embolic fat (originating partly in marrow fat cells, as was nicely shown by Hillman and LeQuire (1968)) is probably injected into the circulation by this mechanism.

The absence of deaths with McKee-Farrar prostheses may be explained partly by the age difference. At least two patients (Cases 2 and 4) and possibly two others (Cases 1 and 3) may have died of vasovagal shock, rather than an oxygen diffusion block; it is possible that the younger McKee cases withstand the insult more effectively.

The patient seems to be at risk principally in the first 48 hours; presumably by the end of that period the fat has been absorbed and finely dispersed in the survivors. Alternatively, it may be that in different patients fat is released into the circulation at varying rates, allowing tolerable degrees of embolization in some cases and causing lethal episodes in others.

During this "early" period, however, clinical diagnosis is impossible or at best difficult; blood gas studies are recommended by Ross (1970) but would be of no value in cases where death is sudden during anaesthesia. Treatment, again, is in such cases too late by definition; anyway, the use of heparin or alcohol is no longer held in repute, while the more strongly-recommended positive-pressure ventilation with oxygen was, in fact, actually in use (as part of the anaesthetic procedure) in the two intraoperative deaths. Treatment is more useful in young people well able to survive the initial attack. Prevention must be instigated by choice. The value of drugs such as heparin given prophylactically is yet to be assessed. Venting

as a routine procedure might reduce susceptibility to fat embolism.

In many series the mortality rate following replacement arthroplasty has been greater than that of internal fixation (Addison, 1959; Garcia *et al.*, 1961; Boyd and Salvatore, 1964; Hunter, 1969). In the past this increased mortality has been accepted in order to avoid the morbidity and subsequent deaths which arise from avascular necrosis, non-union, and their treatment. Hunter (1969), however, showed that the mortality from a secondary prosthetic replacement procedure is low: 90% of patients are alive six months later. It is difficult to explain this difference but reasonable to reconsider the role of femoral head replacement in acute fractures of the elderly.

Conclusion

The use of Thompson's replacement arthroplasty with methyl-methacrylic cement is associated with a high risk of fatal fat embolism in the immediate postoperative period; this may be due partly to the age of the patient and in part to the technique used.

Search for fat embolism should be more often performed in investigation of death following orthopaedic procedures, especially those involving compression of marrow spaces; clinical evidence tends to obscure and be obscured. That fat embolism occurs more often than it is recognized can be inferred from the close similarity between the death rates in our series and those of other authors.

It is suggested that internal fixation may be preferable in the treatment of acute fractures of the femoral neck, unless and until acceptable prophylactic measures can be devised.

References

- Addison, J. (1959). *Proceedings of the Royal Society of Medicine*, 52, 908.
- Arden, G. P. (1970). British Orthopaedic Association Meeting, September.
- Boyd, H. B., and Salvatore, J. E. (1964). *Journal of Bone and Joint Surgery*, 46A, 1066.
- Burgess, D. M. (1970). *British Medical Journal*, 3, 588.
- Charnley, J. (1970a). *Acrylic Cement in Orthopaedic Surgery*. Edinburgh, Livingstone.
- Charnley, J. (1970b). British Orthopaedic Association Meeting, September.
- Fred, H. L., Willerson, J. T., and Alexander, J. K. (1967). *Archives of Internal Medicine*, 120, 33.
- Garcia, A., Neer, C. S., and Ambrose, G. B. (1961). *Journal of Trauma*, 1, 128.
- Gresham, G. A., and Kuczyński, A. (1970). *British Medical Journal*, 3, 465.
- Harris, N. H. (1970). *British Medical Journal*, 3, 523.
- Hillman, J. W., and LeQuire, V. S. (1968). *Surgical Forum*, 19, 465.
- Hunter, G. A. (1969). *British Journal of Surgery*, 56, 229.
- Hyland, J., and Robins, R. H. C. (1970). *British Medical Journal*, 4, 176.
- Reynolds, F. C. (1958). *Journal of Bone and Joint Surgery*, 40A, 877.
- Robb-Smith, A. H. T. (1941). *Lancet*, 1, 135.
- Ross, A. P. J. (1970). *Annals of the Royal College of Surgeons of England*, 46, 159.
- Sevitt, S. (1966). *Lancet*, 2, 1203.
- Vance, B. M. (1931). *Archives of Surgery*, 23, 426.
- Vanderwater, S. L. (1961). *Journal of Bone and Joint Surgery*, 43B, 863.
- Wilson, J. V., and Salisbury, C. V. (1944). *British Journal of Surgery*, 31, 384.