Corticosteroid-induced Bone Collapse

Three recent reviews provide an opportunity for reconsidering the not uncommon but still mysterious condition of bone collapse, variously termed ischaemic, avascular, or aseptic necrosis of bone. It was probably first described in 1888, when a vascular cause was suggested. Collapse of the femoral head which almost invariably progresses to destruction of the joint is the most frequent and dramatic form, though bones and joints elsewhere may be affected. Osteochondritis dissecans and spontaneous osteonecrosis of the knee may be variants. The changes preceding necrosis and collapse are probably gradual and there are its known. Nevertheless osteoporosis of the bone end, collapse of subchondral bone cysts, and ischaemia due to either vasculitis or embolism are the three most likely prodromal lesions.

Bone collapse in the femoral head always occurs in the upper anterior central area, where the weight bearing is greatest and the vascular supply most at risk. In the early stages the articular cartilage may be intact, but later it is irregular and disrupted and eventually it is ground into fragments. The collapsed bone appears to be chalky and acellular and separated from the trabecular bone by fibrous tissue. D. E. Fisher and W. H. Bickel indentified probable fat emboli in subchondral arteries in 12 out of 25 specimens—10 from patients receiving corticosteroids and two from alcoholics. Of their 446 patients with avascular necrosis affecting the femur, 75 took alcohol excessively and 72 had been receiving corticosteroids. An association of the disease with diabetes mellitus, liver disease, and Gaucher's disease is further evidence for an underlying alteration in fat metabolism resulting in fat embolism as a pathogenic factor.

Ischaemia produced by decompression disease and sickle cell anaemia are also complicated by bone collapse. R. Lagier has found microfractures in the very early stages of osteoporosis leading to interruption of the blood flow in the smallest blood vessels of the porotic bone, and P. Rinkler and A. H. Huggler have confirmed that the circulation is impaired at capillary level in some type of bone collapse. Thus osteoporosis, either by predisposing to recurrent microfractures or by leading to collapse of bone ends, might produce collapse in normal people. That collapse can occur without radiologically visible osteoporosis is well recognized, and may be due to the wide variation in compressibility of cancellous bone. The joint generates considerable pressures during normal use, and these are transmitted in full to the bone end since cartilage is a poor energy absorber. The underlying marrow is replaced by fat, which is less compressible than blood and marrow, and thus the resilience of the cortex to recurrent compression is reduced.

Collapsing subchondral bone cysts, common in both rheumatoid arthritis and osteoarthrosis, could easily produce the clinical picture of bone necrosis. The hypothesis that the Charcot-like joints found in rheumatoid arthritis might be the result of the accompanying neuropathy seems to have been disproved.

Most of Fisher and Bickel's 72 patients who had been receiving corticosteroids developed bilateral hip disease. The feature common to all cases was not the disorder for which they were being treated but a prolonged dosage of corticosteroids in greater than physiological requirements. There seems little doubt that corticosteroids can produce or exacerbate bone necrosis. Several factors, such as fatty liver change resulting in fat emboli, altered bone mechanics, and vasculitis, may account for this, though evidence pointing to corticosteroid-induced vasculitis becomes less convincing. The femoral head is most often affected owing to the stresses it bears. The increased incidence with age is due to reduced subchondral resilience, and in some people this may be predetermined. In other cases fatty embolism may be the cause.

Corticosteroids probably exacerbate one or more of the secondary mechanisms. Because various associations have been demonstrated in connexion with bone collapse the term "idiopathic" should be abandoned, and, since the evidence for ischaemia is poor and may not apply in all cases, "ischaemic" and "avascular" should not be used either. "Aseptic" and "necrotic" are pathological descriptions. A non-committal but not wholly accurate term would be "cortical bone collapse."

4 Konig, F., Deutsche Zeitschrift fur Chirurgie, 1888, 27, 90.
Donors for Organ Grafting

A shortage of donor organs still results in many unnecessary deaths from kidney disease and seriously curtails progress in heart and liver transplantations. Despite improvement in methods of preservation, organs tend to deteriorate with current methods of storage.

R. B. Gripp and colleagues,1 from Stamford, California, maintain that the only suitable donor of a heart is a patient “neurologically dead, but otherwise physically intact.” These workers have by far the largest experience of heart transplantation in man and also their results are best. They report on an evaluation of cardiac function in 22 neurologically dead patients in whom irrevocable loss of cortical function had been diagnosed by neurologists or neurosurgeons before referral as possible heart donors. In half the cases the family of the prospective donor had first suggested organ donation. In the remainder the suggestion was made by the patient’s doctor, and consent was obtained from the next of kin.

The cause of cerebral death in the 22 patients was either intracranial haemorrhage, blunt trauma to the head, gunshot wound of the head, or brain tumour. The average time between hospital admission and certification of cerebral death was 61 hours, and from certification to removal of the heart 6 hours and 20 minutes. Cerebral death was certified by an independent transplantation committee of neurosurgeons and neurologists of Stamford University Medical Center. The cerebrospinal fluid, vestibular caloric stimulation, and electroencephalography at maximum gains were studied in addition to a complete neurological examination, and a five minute test for apnoea was made at a normal arterial Pco₂. The criteria for cerebral death were those of the Harvard Committee,2 in each case the three committee members were unanimous that there was irretrievable loss of brain function and that no further investigation or therapy was indicated.

Next the transplantation team studied the cardiac function of the prospective donors. Only when physical examination, chest radiography, and electrocardiography did not provide enough information was cardiac catheterization or angiography performed. Intravenous and arterial pressures and arterial blood gases were monitored; the blood, urine, and swabbings from the trachea were cultured; and prophylactic antibiotics given. Mechanical ventilation was continued together with intravenous fluids and vasopressor and antidiuretic drugs as required. The operation of heart transplantation was performed simultaneously in two adjacent rooms. The donor was given heparin systemically and the heart was isolated while still beating and removed for transplantation. Twenty-one of the 22 patients were used as donors. Their average age was 30 years.

In many parts of the U.S.A. and in continental Europe death may be certified on the death of the brain when the circulation is intact and all organs apart from the brain viable. Apparently the public can accept cerebral death as enough to permit organ removal, since in half the Stamford cases donation was suggested by the relatives. In Britain the criteria for stopping resuscitation are similar to those used in Stamford for establishing cerebral death, but British workers believe that the circulation should cease after stopping resuscitation before organs are removed. Thus the diagnosis of cerebral death is proved beyond even the remotest chance of mistake. Organs from such patients are generally satisfactory for transplantation—even the liver. Probably neither British medical nor public opinion on the management of potential donors for organ grafting will change quickly. Indeed, there is no need for any change in the traditional ways of caring for the dying or in the criteria for diagnosing death. There is, however, an urgent need for more organs, and these might be available if the medical profession and public were more aware of the lives that could be saved by donations from the dead—the lives, for example, of young patients with terminal kidney disease.


Herpes Encephalitis

The cause of encephalitis lethargica was at one time mistakenly ascribed to Herpesvirus hominis, which is perhaps the most ubiquitous virus infecting man. The anticlimax which followed this discredited theory then produced an atmosphere in which it became impossible for almost half a century to attribute any nervous diseases of man to the herpesvirus. Renewed interest in its neurotropic properties was awakened with the reports that it could be recovered from cases of acute encephalitis.

J. G. Greenfield1 and L. van Bogaert and his colleagues2 provided the histological descriptions of a distinctive form of acute necrotizing encephalitis with intranuclear inclusions of herpetic type in neurones and oligodendrocytes.3 They did no more than suggest that herpesvirus might be one of many causes of the disease, a view recently re-emphasized by others.4 But with few exceptions⁵ there is now overwhelming evidence to confirm that most, if not all, cases of acute necrotizing encephalitis are of herpetic origin. The virus can also perhaps cause milder disease of the central nervous system, leading to psychiatric disorders.⁶

Herpes encephalitis is probably the commonest form of sporadic fatal encephalitis⁸ and has a peak incidence in two distinct age groups—the newborn and young adults⁴—though it may occur at any age. In newborn babies the disease often appears as a multi-organ infection in a highly

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12 James, C. C. M., Lancet, 1945, 2, 6.