ASEPTIC NECROSIS OF BONE

edited by **J. K. Davidson**

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Preface

Aseptic bone necrosis presents many problems in diagnosis, prevention and management. It is a frequent complication of fracture of the neck of the femur which is a major cause of disability in the elderly and a serious hazard to divers and others working under compressed air; it is encountered in many patients who are receiving large doses of steroids, either for treatment or to suppress the rejection of an organ transplant. These and a number of other diseases, in some of which the cause of the bone necrosis is obscure, are described herein by experts in their various fields.

Unfortunately, there are no early clinical signs of bone death and symptoms only appear when collapse of necrotic bone occurs, which may be months after the ischaemic episode. Increase in bone density is often regarded as a reliable radiographic sign, but it is not present in the early stages and again some time may elapse before it is apparent. Even then it may be difficult to distinguish between the relative increase in bone density, which is a sign of necrosis, and the absolute increase in bone density, which indicates an attempt at repair. Furthermore, the same radiographic picture may be produced by different morphological changes and the events which have brought about these changes are open to different interpretation. One of the most puzzling and as yet unexplained facets of bone necrosis are the factors responsible for the arrest of revascularisation of a necrotic segment of bone in the absence of any obvious barrier such as an ununited fracture.

These and many other features of bone necrosis are discussed in some detail in this book; answers will not be found to all the fascinating problems but it should produce an awareness of the many questions that remain unanswered and stimulate co-operation between clinicians, radiologists and pathologists in finding solutions to some of the problems associated with a group of diseases which are of increasing clinical importance.

June, 1975

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Explanation of terms

Differing words are used in the text and for clarification these are defined below:

Aseptic necrosis of bone
This means that a segment of bone has lost its blood supply and died. Similar terms are osteonecrosis, infarction, or avascular necrosis of bone. The term aseptic means that osteomyelitis is not present.

Increased density
This implies that an area of bone is more dense than the surrounding structure. Similar terms are increased radiodensity, radiodensity, or sclerosis.

Decreased density
The opposite applies in that the area of bone is less dense than the surrounding structure. Similar terms would be increased radiotranslucency, rarefaction, porosis, translucency or radiolucency.

Erosion
A circumscribed area of bone resorption from whatever the cause.

Periosteal reaction
A descriptive term to indicate the abnormality adjacent to the cortex suggesting periosteal new bone. The radiographic abnormality is basically the same whether the result of inflammation, haematoma or neoplasm.

Contents

CHAPTER 1

Aseptic necrosis of bone - an introduction

John K. DAVIDSON

Aseptic necrosis of bone may arise in a variety of different clinical circumstances. The most noteable of these are trauma; the interesting, spontaneous or drug-induced group; the haemoglobinopathies and dysbaric diseases. Each of these is considered in a separate chapter and we are fortunate in having an expert to provide an authoritative account of aseptic necrosis of bone in each of these situations.

The condition is becoming increasingly common. Patients may consult their clinicians or general practitioners with a painful arthritis and the subsequent history reveals therapy involving large doses of steroids, past trauma, or even exposure to a hyperbaric environment such as tunnel working or diving, so giving a clue to a probable osteonecrosis. Osteonecrosis is of particular importance to radiologists, pathologists, and orthopaedic surgeons and it is hoped that those who are involved in the diagnosis or management of this type of case will find here information which is of value. It is intended that each chapter provides a comprehensive account so inevitably there is some overlap.

Clearly it is essential to appreciate the underlying pathology of the condition and it is fitting that the opening chapter (Chapter 2) should be contributed by an acknowledged expert of bone pathology who has done so much valuable work in osteonecrosis. Many will find information of interest and value in this chapter, each aspect of osteonecrosis is considered, thus providing a complete account. Inevitably there is some overlap but the comprehensive form will be of considerable value to pathologists. There are many gaps in our knowledge and understanding of osteonecrosis and it is through pathological study of early lesions, before radiological changes are evident, that our understanding of its pathogenesis will be improved.

Trauma is the commonest cause of osteonecrosis (Chapter 3) and the most frequent site is the femoral head following a fracture of the femoral neck. Orthopaedic management now includes internal fixation and early mobilisation. Consequently, the earliest radiological features may not be a relative increase in density but an absolute increase in radiographic bone density resulting from revascularisation with laying down of new bone. Post-traumatic osteonecrosis may also develop in the proximal pole of the carpal scaphoid and in the body of the talus and there is an interesting account of osteonecrosis

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in these sites. This chapter includes a description of the blood supply in the femoral head, scaphoid and talus.

Dysbaric osteonecrosis (Chapter 4) is a much less common condition and is a late complication of exposure to a hyperbaric environment, whether in tunnel working or diving. It is a major hazard to compressed-air workers and an increasing hazard to divers. The earliest changes of aseptic necrosis may be detected radiologically about six months after exposure to a hyperbaric environment. Orthopaedic management is unsatisfactory and prevention is of major importance. Any attempt to reduce the incidence of this distressing condition must involve regular skeletal X-ray surveys of those at risk and correlation with the occupational history. The radiographs must be of high quality. Difficulties arise in distinguishing the earliest changes of osteonecrosis from variation of the normal bone architecture and this chapter includes many illustrations which will be of value to those involved in this type of work.

The cause of spontaneous aseptic necrosis of bone has been the subject of many reports and much speculation. There are a large number of contributory factors such as irradiation, thermal damage, haemophilia, Gaucher's disease and many associated features such as alcoholism, pancreatitis, gout, diabetes mellitus and systemic lupus erythaematosus. Probably one of the most interesting associations is between osteonecrosis and therapy involving large doses of steroids over a prolonged period. Patients requiring immunosuppressive therapy with steroids following renal transplantation form a specific group where the incidence has been found to be as high as 50%. Chapter 5 includes an account of these various factors.

Bone changes are frequently associated with the haemoglobinopathies and aseptic necrosis of bone is a common feature. Sickling of red blood cells may result from slow circulation and high oxygen utilisation in the marrow sinusoids of bone leading to thrombosis – followed by infarction and necrosis. These infarcts tend to be infected by typhoid/paratyphoid diseases leading to salmonella osteitis. The radiological features of osteonecrosis in the head of the humerus or the head of the femur in the Hb SC group are virtually identical to osteonecrosis from other causes. There are many other radiological features resulting from marrow hyperplasia, impaired growth and salmonella osteitis. These are well illustrated in Chapter 6, which includes an account of the disorders of haemoglobin and their distribution in the world.

In osteochondrosis (Chapter 7) the association with aseptic necrosis of bone is not clear. For example, when the vertebral body is involved (Calve's disease) histiocytosis is believed to be an associated factor. Osteochondrosis of the hip (Perthes' disease) is the most common form and the radiological changes are well illustrated and described. Osteochondrosis dissecans is a relatively common group involving the medial femoral condyle, the capitulum of the humerus and the talus. Trauma is thought to be an aetiological factor but very often there is no overt history and aseptic necrosis of bone may involve the epiphysis. The term osteochondritis has been widely used and its implication is clearly understood. However, there is no inflammation and the suffix 'itis' should be avoided. Almost every bone has been involved and there is an equal number of eponyms.

CHAPTER 2

Pathology of aseptic bone necrosis

Mary CATTO

2.1 Histological recognition of bone necrosis

It has long been accepted that empty osteocyte lacunae indicate death of bone. This statement requires the qualification that the bone should be fresh, rapidly fixed and the sections of good technical quality since artefactual loss of staining of osteocyte nuclei may result from slow tissue fixation while nuclei sometimes persist in sequestra and variously treated and stored bone allografts (Tucker, 1953; Frost, 1960a; Ray, 1964).

There is experimental evidence to suggest that ischaemia of more than 6–12 h duration produces bone death (Woodhouse, 1962; Henard and Calandruccio, 1970) though this conflicts with the reported capacity of osteocytes to incorporate radioactive amino acids and glucose for 48 h after the blood supply is cut off (Kenzora et al., 1969). While early morphological changes in osteocytes in animal material have been demonstrated by special techniques (Enneking, 1964; Rösingh and James, 1969) assessment of nuclear changes such as pyknosis in human biopsies without control material may be difficult, especially if they are from a fracture site. Loss of osteocytes in conventionally prepared histological sections often does not become apparent for a few days and is not complete for two to four weeks after the onset of ischaemia (Bonfiglio, 1964; Catto, 1965a). This observation in human material has been confirmed in animals following experimental bone infarction (Bonfiglio, 1954; Young, 1966). It thus appears that irreversible changes may occur in bone cells within hours of ischaemia, but the certain histological recognition of bone death may be delayed (Catto, 1965a).

The earliest microscopic indication of ischaemia may be given by changes in the bone marrow. In haemopoietic areas from the second day onwards, round and ovoid spaces appear, presumably filled with fat: they are surrounded by cells which from about the fourth day lose their nuclear staining (Fig. 2.1), later becoming eosinophilic and finally ghosted (Fig. 2.2). A similar but less conspicuous loss of nuclei occurs in the sparsely cellular fatty marrow after about the fifth day and at the same time

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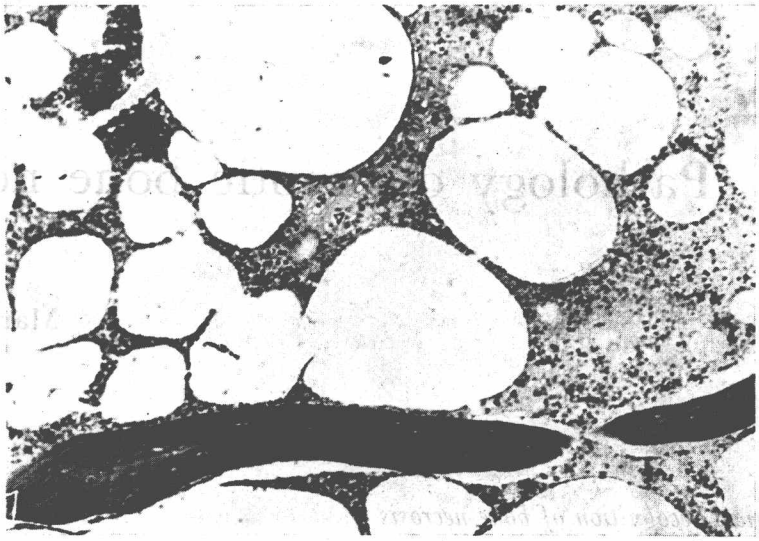

Fig. 2.1.* Five days after femoral neck fracture haemopoietic marrow from the femoral head shows loss of nuclear staining and formation of large fat-filled spaces. Osteocytes are still present in the bone trabecula. (× 100).

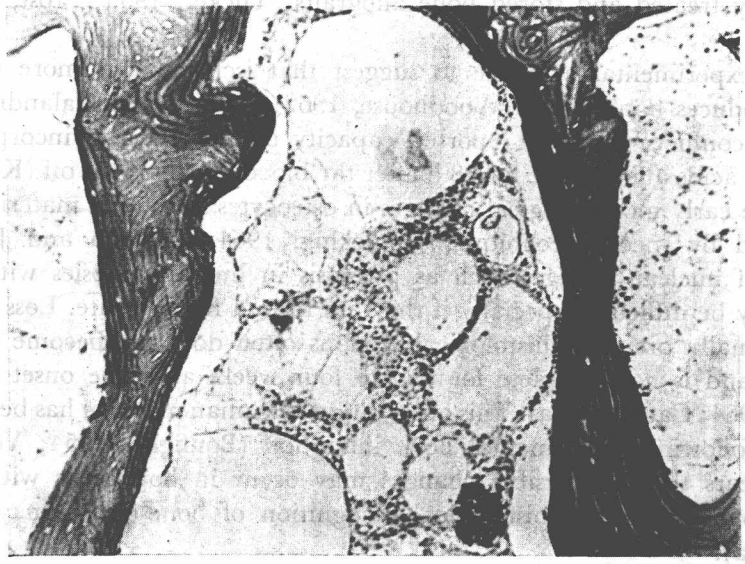

Fig. 2.2.* Seventeen weeks after injury all the osteocyte lacunae of the bone trabeculae are empty and the marrow is 'ghosted'. (× 100).

* Denotes figures reproduced by courtesy of the Journal of Bone and Joint Surgery. All the histological sections are stained with haematoxylin and eosin unless otherwise stated.

the walls of the small blood vessels of the marrow show evidence of necrosis (Johnson, 1964; Sevitt, 1964; Catto, 1965a).

2.2 Histological features of revascularisation

Where the necrotic zone abuts on live marrow, proliferated capillary leashes accompanied by fibroblasts and macrophages may advance into the dead tissue (Fig. 2.3). Foamy cells containing lipid are seen and may, along with foreign body giant cells, surround oil-filled spaces resulting from the breakdown of necrotic fatty marrow (Fig. 2.4). Sometimes the marrow is replaced by poorly vascular collagenous tissue in which dead bone trabeculae remain unaltered (Fig. 2.5) but when the blood supply is more completely restored osteoclasis of dead bone occurs and viable woven bone (Fig. 2.6) is laid down on the surface of dead bone and, less frequently, as new trabeculae in the marrow spaces. Phemister (1915) in adopting the term 'creeping substitution', contrasted this slow replacement of aseptic dead bone with the resorption or sequestration of dead bone associated with severe infection (Phemister, 1930).

The preponderance of one or other component of creeping substitution varies with circumstances. When the patient is immobilised osteoclasis tends to be more marked and revascularisation of dead marrow is accompanied by loss of bone due to disuse, while in the mobile patient apposition of new bone may be more prominent and in many cases resorption is slight or slow in following so that the term 'creeping apposition' might be more appropriate (Bohr and Larsen, 1965; Kenzora et al., 1969).

While the marrow may eventually return almost to normal, much dead bone may remain unresorbed and persist, sometimes entombed within new living bone for many

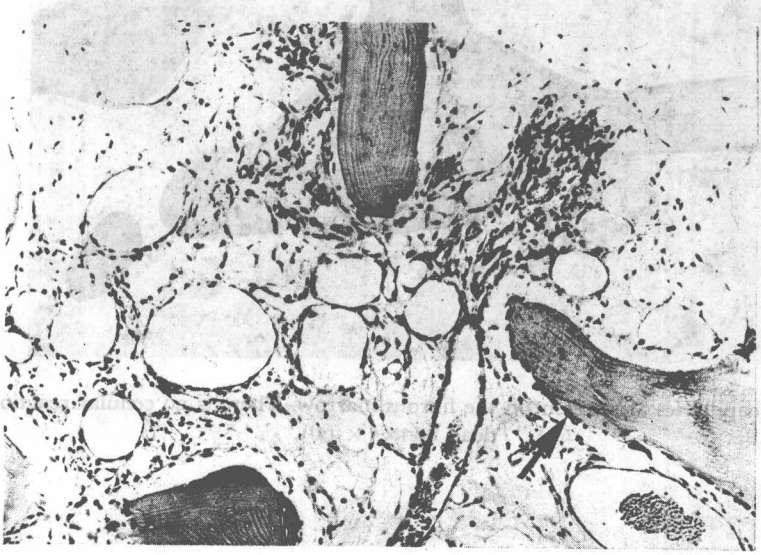

Fig. 2.3. A leash of capillaries along with fibroblasts and macrophages has advanced into necrotic marrow. Plump osteoblasts are seen covering one bone surface (arrow). (× 100).