EXPERIMENTALLY INDUCED OSTEONECROSIS IN ANIMALS

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Kent Smith is to be congratulated on being the first to produce and demonstrate bone lesions in large mammals following multiple exposures to high pressure. The difficulty in inducing dysbarism-related osteonecrosis experimentally in these animals has been a stumbling block in the study of the disease for many years. Dr. Smith's success is unlikely to be repeated in every laboratory, however, as it appears that mini-pigs, with which his work was done, are so ferocious that it takes a brave man to insult them repeatedly!

Interestingly enough, the osteonecrotic lesions found in these mini-pigs do not appear to be identical with either form of the disease known to be typical in man. Two distinct types of lesions are seen in experienced divers and compressed-air workers. In one, the subcortical regions of the heads of the humerus and femur are involved (Fig. 1). In the other, the shafts of the femur and tibia are affected, so that the changes are localized primarily in the medullary cavity (Fig. 2).

FIG. 1. Juxta-articular lesions of aseptic osteonecrosis in all 4 major joints of compressed-air worker.

FIG. 2. Osteonecrotic medullary lesion at lower end of human femoral shaft.

Whether or not the lesions seen in Dr. Smith's mini-pigs and those seen in man have similar causality, it is still necessary to determine their etiology. Are all these lesions the result of interruptions in blood circulation within bone — for instance, by gas bubbles or other embolic material arising as a secondary phenomenon in decompression? Or is there some other explanation, such as osmotic pressure effects or hormonal disturbances?

Many research workers over the years have attempted to find answers to these questions by experiments in which animals have been exposed to hyperbaric conditions, but success has been minimal. In an effort to throw light on this problem, therefore, the effect of mechanically interfering with the blood supply to the femoral head in sheep has been investigated at the University of Newcastle upon Tyne's Department of Surgery.

In all, 18 sheep were operated upon. The lateral or superior epiphyseal vessels to one femur and its capsule were cut. The femoral head was thereafter supplied only by a small leash of vessels known as the medial or inferior epiphyseal vessels; possibly a few vessels passing through the ligamentum teres were left as well.

The 18 sheep were then put out to graze, and both hip joints of each animal were X-rayed at regular intervals. Eight of the 18 sheep developed radiologically detectable lesions, about which there could be no doubt, in the femoral head of the side operated upon. Six developed radiological signs that may or may not have indicated lesions; and four developed no abnormalities, despite the gross operative procedure.

The first radiological signs in the sheep appeared after approximately 2 months, but it took about 3 months before it was possible to identify positively the changes as being osteonecrotic lesions. The progress of the lesions was then followed for 3 to 4 months and, in some cases, for as long as 19 months. Unexpectedly, rather than the lesions becoming more and more pronounced radiologically, they regressed. In fact, some of the lesions observed for the longest period of time ultimately could not be detected radiologically at all. Insofar as the radiological changes are concerned, the lesions apparently repaired themselves completely.

In man, osteonecrotic lesions progress at different rates — sometimes very slowly. Figure 3 of the chapter entitled "Management and Treatment of Osteonecrosis" (Walder, this volume) shows just how slowly these changes may occur — in this instance, in the humeral head of a compressed-air worker over a period of five years. Even after so long a period, the surface of the humerus has not collapsed. It is possible that the man's condition may never deteriorate to the extent that he will require surgical treatment.

By contrast, other lesions develop very quickly. As an example, the humeral head shown in Fig. 3 was normal in February 1967. Four months

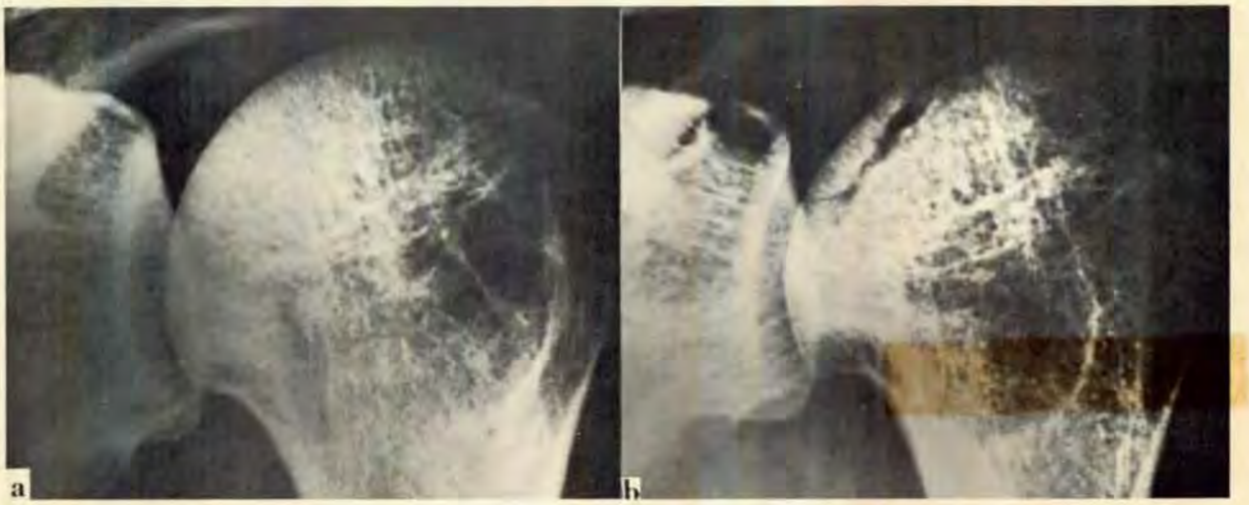

FIG. 3. (*a*) Lesion in humeral head, which (*b*) rapidly deteriorated over period of 4 months.

later a lesion had advanced to such an extent that pieces of bone were flaking off. Just one month later, further severe changes were evident.

Osteonecrosis in animals not only can progress very quickly, but also can resolve itself. One must be careful not to miss similar changes in man, however slow or subtle. The following interesting case illustrates this fact:

An experienced compressed-air worker unfortunately suffered a bronchospasm during a decompression; he developed decompression sickness and died. At the postmortem examination, one of his femoral heads was removed for histological examination. Transverse sections of this piece of bone are shown in Fig. 4. A slab radiograph revealed a typical lesion of osteonecrosis at the articular surface, demonstrated by a band across the head of the bone with what appears to be relatively normal bone tissue deeper in the head. On microscopic examination, however, a large area was found. It consisted of dead trabeculae on top of which new bone had been laid down. In other words, histological evidence is that a very much larger area of the bone was involved in the osteonecrotic process than is apparent from the X-ray, presumably because natural repair had occurred. The crosshatching shows the area of the head that, from the histological evidence, has been dead in the past.

In the case of this compressed-air worker, enormous repair had taken place, just as occurred with the sheep in our experimentation. In fact, it is tempting to postulate that bones can become damaged in decompression, then repair themselves without anything abnormal ever being detected by radiological examination. The results of our work with sheep tend to support this hypothesis.

It is more difficult to sever specific blood vessels to the lower end of the femur to produce lesions in it than in the femoral head. An attempt was therefore made to reproduce this type of lesion by using artificial emboli — namely, glass beads, 120 microns in diameter, which were introduced into the common iliac artery of rabbits. Figure 5 shows the lines of these beads, which have embolized the marrow, giving rise to histological changes similar in appearance to those seen in osteonecrotic lesions affecting the lower ends of the human femora.

The work being done at the University of Newcastle upon Tyne appears to complement that of Dr. Smith in Seattle. In the study of dysbarism-related osteonecrosis, both experimental approaches are necessary in the attempt to *1*) sub-

FIG. 4. Femoral head with subcortical lesion. (*a*) Slab radiograph shows apparent limits of osteonecrosis; (*b*) histological section shows same limits; and (*c*) histological section is crosshatched to show extent of area originally involved in osteonecrosis.

stantiate the hypothesis that the disease is caused by blockage of the blood vessels; and 2) refute the contention that agents *not* connected with vascular supply to bone are important in the production of this condition.

FIG. 5. Microfocal radiograph of rabbit femoral shaft showing glass beads of 120-micron diameter in descending branch of nutrient artery.