EXPERIMENTAL BIOLOGY

THE EFFECT OF IONIZING RADIATION OF DIFFERING INTENSITY ON THE REGENERATION OF BONE*

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The problem of the effect of the chronic, continuous action of radiation on the body has recently acquired great importance.

In spite of the large volume of work [1-7] devoted to the study of the action of ionizing radiation on bone tissue, the question of the chronic action of small doses of radiation on the reparative processes in bone tissue has not yet been adequately dealt with in the literature.

The immediate purpose of our research was to compare the action of the radiation from radioactive cobalt (Co^{60}) when applied once in high intensity and when given as prolonged continuous irradiation of low intensity.

EXPERIMENTAL METHOD

Experiments were carried out on male white rats weighing 150-170 g and ages 5-6 months.

In order to induce a process of regeneration which could be kept under observation, trepanning of the middle third of the diaphysis of the femur was performed on all the animals under aseptic conditions by means of a No. 3 dental drill. By the use of this method it was possible to produce bone defects which were equal in all respects with each other, which was essential for comparison of the material.

The process of healing of the bone wounds was studied in histological preparations taken 3, 5, 7, 9, 12, 14, 18, 21 and 30 days after the operation.

Altogether 3 series of experiments were carried out on 200 animals. In the first series unirradiated animals were used. In the 2nd series a single total exposure to γ-ray irradiation was applied, the doses being 1000 and 1500 r, with a dose rate of 15.5 r/min and exposure times of 3 and 4.5 hours respectively.

Operation was performed on some of these animals immediately after irradiation, and on the others in this series during a period of 3 months after irradiation. These times were chosen for the operation so that the duration of the sequelae of irradiation on bone tissue could be determined.

The animals of the 3rd series were exposed to prolonged, chronic irradiation with γ-rays, which was given in a special room from a special constant-action gun loaded with Co^{60}. The total doses in these experiments (1000 and 1500 r) were of the same magnitude as those given in irradiation of short exposure. The animals irradiated for 12 days (dose rate 125 r/day), for 2 months (25 r/day), 3 months (16.7-11.1 r/day) and 6 months (8.3-5.5 r/day).

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In comparing the experimental material consideration was taken of the periosteal reaction, the size of the callus formed, and the rate of occurrence of the individual phases of its development. Changes in the bone marrow were also considered.

EXPERIMENTAL RESULTS

The process of healing of the bone wound in the control animals corresponded to the descriptions given in the literature [1, 2, 3], differing only in the times of occurrence of the individual phases of development in accordance with the method of our choice. In the first series, therefore (control animals), we confined our attention mainly to the more precise definition of the times of healing of bone defects.

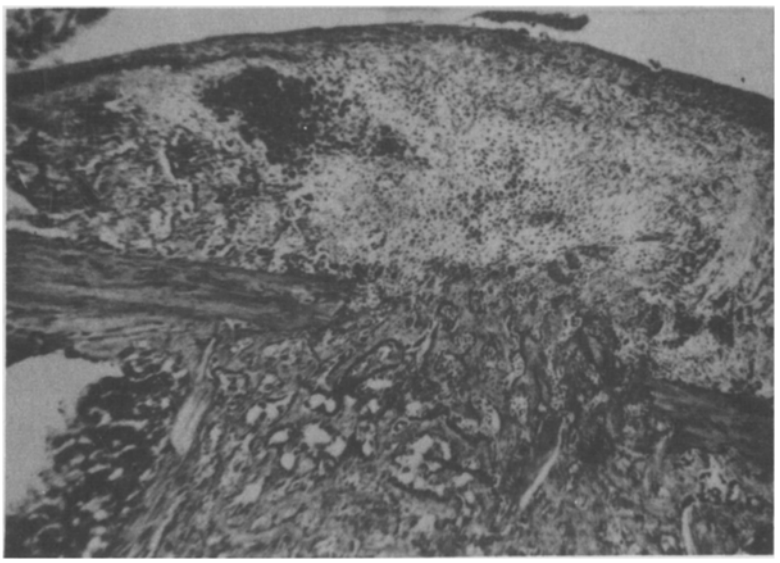

Fig. 1. Regeneration of a bone defect in a control (unirradiated) animal. Time of regeneration 9 days. Microphotograph. Magnification 40 times.

The process of formation of provisional callus in the control animals began on the 3rd-5th day after operation and reached its highest development on the 7th-9th day. At this period differentiation of cells of osteoblastic tissue took place, with the formation of cartilage and of bony trabeculae. Next the reorganization of the provisional callus began, including destruction of cartilaginous tissue and the formation of new elements of woven bone.

This reorganization took place on the 14-15th day of regeneration, after which regression of the callus supervened, with the formation of a marrow cavity, hitherto obliterated.

The microphotograph (Fig. 1) shows the picture of formation of bony callus in a control animal on the 9th day of regeneration. The periosteal callus, covering the site of the defect and consisting mainly of cartilaginous tissue, has reached at this stage the peak of its development. From osteogenic tissue, ingrowing from the side of the periosteum and filling the trepan hole, osteoid and young bony trabeculae have been formed.

An analogous process was also observed in connection with the endosteum, where it was more pronounced and led to obliteration of the marrow cavity. In all parts of the bony callus, parallel with the process of formation of bone tissue, its partial destruction by osteoclasts also took place.

The experiments in which a single total γ -ray irradiation was given showed that, in the doses used (1000 and 1500 r), obvious suppression of the process of regeneration of bone was caused, which was particularly marked when compared with the control animals on the 7th, 9th and 14th days after operation. At later times (21st to 30th days) the differences in the rate of regeneration of the irradiated and unirradiated animals became less pronounced.

The process of formation of bony callus in the irradiated animals passed through the same stages of development as in the controls. It was distinguished, however, by a much slower course. The periosteal part of the callus was constantly of smaller dimensions. In certain cases development of bone tissue took place without

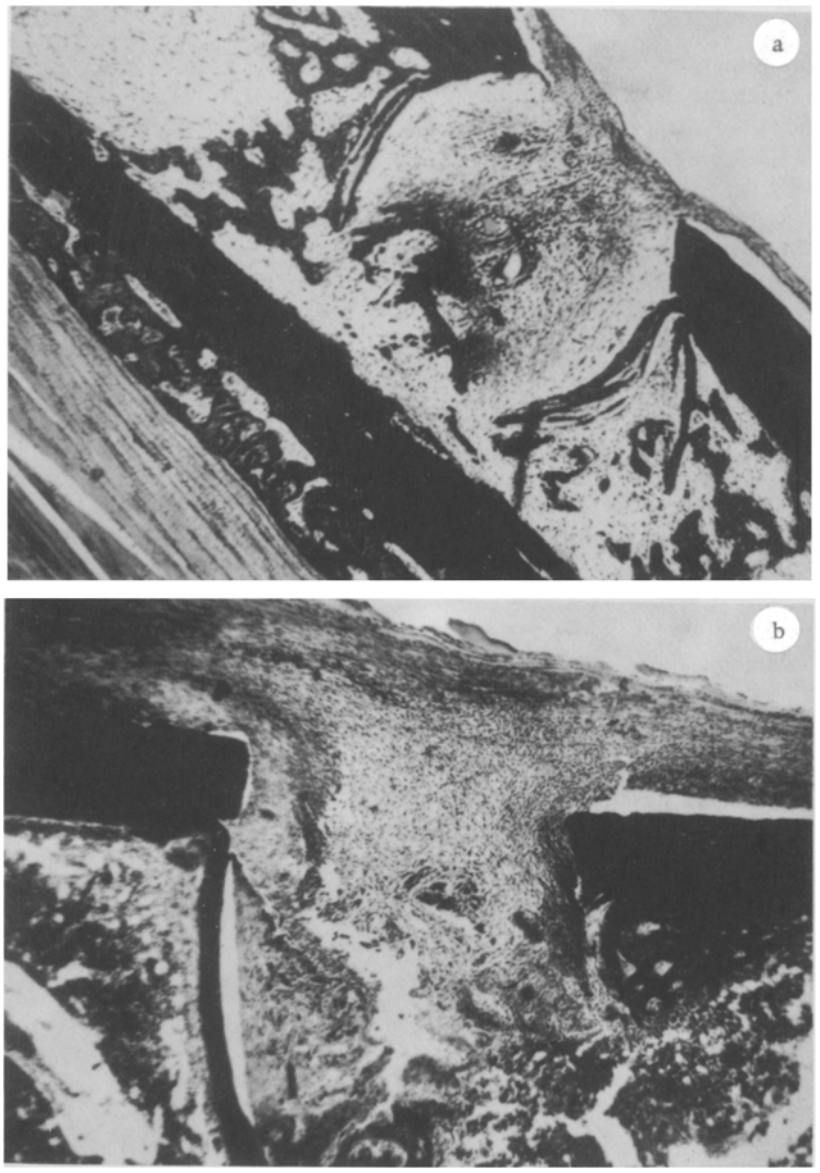

Fig. 2. Regeneration of bone after total γ-ray irradiation with short exposure. a) Operation performed immediately after irradiation; b) operation performed 3 months after irradiation. Dose 1000 r. Time of regeneration 9 days. Microphotograph. Magnification 40 times.

passing through the cartilage. Endosteal osteogenesis was also suppressed. The structure of the bone marrow was grossly disturbed, particularly in the intital period after irradiation.

On the microphotograph (Fig. 2, a) is shown the picture of healing of the bony defect after total γ-ray irradiation of the rat with a short exposure and a dose of 1000 r (the operation was performed 2 hours after irradiation and the time of regeneration was the 9th day). The periosteal part of the callus, covering the bony defect, was almost completely absent. No cartilage tissue was formed in it. The bone wound was filled with undifferentiated granulation tissue. Fibrous bands were predominant in it and recent hemorrhages were often

seen. From time to time islets of chondroid tissue were observed, and young bony trabeculae were seen, but they were smaller in size and fewer in number than in the control animals. No closure of the lumen of the medullary canal took place here. In the preparation, a process of severe impoverishment of the bone marrow in myeloid cells was seen. The remains of the bone marrow tissue consisted mainly of a reticular framework.

Supression of the process of osteogenesis was no less pronounced also in those cases of irradiation with short exposure in which the injury to the bone was inflicted not at the climax of the radiation sickness but 3 months after irradiation (1000 r), i.e., at a period when the signs of radiation sickness, to judge by the peripheral blood picture and other indices, were less marked.

The microphotograph (Fig. 2, b) shows such a picture. It differs little from that shown in Fig. 2, a.

No cartilaginous callus has been formed from the periosteum, the process of differentiation of the cells of the callus into cartilaginous and bony tissue has been severely retarded, and endosteal osteogenesis has been suppressed.

Despite the fact that regeneration of bone tissue was found to be suppressed 3 months after irradiation of short exposure, no severe changes were found in the bone marrow tissue, probably on account of the partial restoration of hemopoiesis.

In the experiments with chronic (continuous) irradiation, lasting 12 days, 2 and 3 months, with total doses of 1000 and 15000 r, the effectiveness of the action of the radiation on the process of regeneration of bone tissue was not lowered, and sometimes was even higher. Prolonged chronic irradiation significantly retarded the process of osteogenesis, which was shown in both earlier (7th-9th day) and later (21st-30th day) stages.

It must be mentioned that the reaction in the bone marrow was feebly expressed. In all the cases of chronic irradiation, the radiation sickness followed a less acute course than after irradiation with the same doses but a short exposure.

On the microphotograph (Fig. 3) is shown the picture of healing of a bone defect after continuous γ-ray irradiation for a period of 2 months (dose 1000 r, time of regeneration 9th day). As may be seen from the microphotograph, the periosteal reaction and the process of endosteal osteogenesis were very feebly expressed,

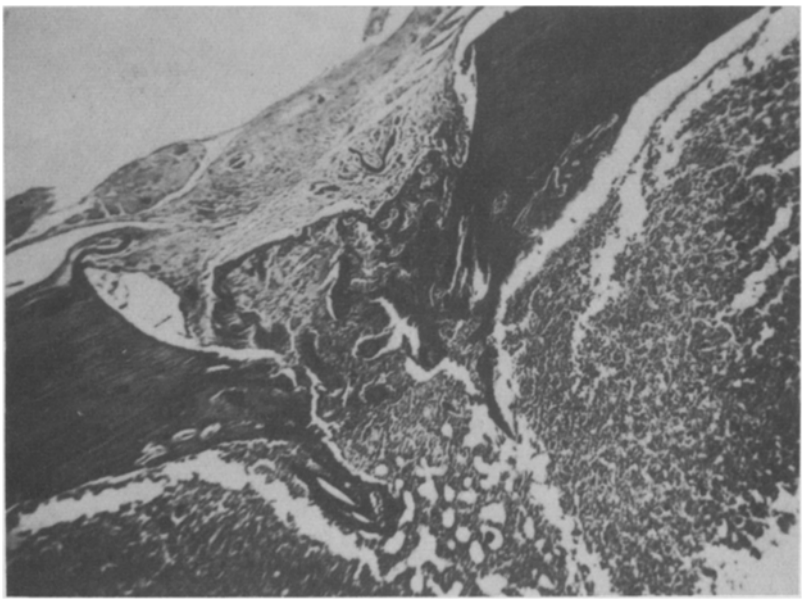

Fig. 3. Regeneration of bone after chronic irradiation for 2 months. Dose 1000 r. Time of regeneration 9th day. Microphotograph. Magnification 40 times.

and the osteogenic trabeculae were few in number and no cartilage tissue was formed. The marrow tissue was compactly filled with cells, among which are seen many megakaryocytes. It has undergone relatively little change.

In the experiments with chronic irradiation lasting 6 months (dose 1000 r), from preliminary findings the suppression of the regenerative power of the bone tissue was more weakly expressed than after less prolonged (for 2 or 3 months) irradiation with the same dose.

Our observations showed that after chronic irradiation with a low intensity, the action of the radiation on the bone accumulated and suppressed the regenerative power of the bone tissue to the same degree as after irradiation with high intensity and short exposure. This occurred even in those cases when the dosage power was considerably reduced and the duration of the irradiation was increased to 3 months.

At the same time it was discovered that the effect of the sequelae of irradiation of short exposure (shown by suppression of the regenerative process) on the bone was very prolonged. From our findings this effect lasted over 3 months. This agrees with the reports in the literature [5, 6, 7].

In contrast to the foregoing, the study of the changes in the bone marrow showed that this suffers only slight damage from chronic irradiation but severe from the single irradiation, although in the latter case its structure was soon restored.

The difference observed in the reaction of the bone tissue and the bone marrow may be explained by their unequal power of repair of the radiation lesion. According to G. S. Strelin [3], such differences are due to peculiarities of the physiological regeneration of the tissues.

SUMMARY

Single radiocobalt (Co^{60}) γ-irradiation of white rats in doses of 1000 and 1500 r caused a distinct suppression of regeneration following trepanation of the femur (the medial third of its diaphysis) by means of a dental drill No. 3 (on the 7th-14th day after the operation). Retarded bone formation could be also observed with the injury of the bone inflicted 3 months after the irradiation (1000 r).

In experiments with chronic irradiation lasting 12 days, 2 and 3 months (the sum total doses being 1000 and 1500 r) the efficacy of the radiation action on the bone tissue would not diminish and at times appeared to be even somewhat higher.

In chronic irradiation the bone marrow tissue showed but slight injuries, but would become acutely disturbed following single irradiation with its structure, however, being rapidly restored in the latter case.

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