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DISTRIBUTION OF YTTRIUM 91 IN MICE STUDIED BY WHOLE BODY AUTORADIOGRAPHY

by

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Among the fission products formed in a reactor and in nuclear weapons are several isotopes of yttrium (KYKER 1962). As yttrium 90 is a daughter of strontium 90, this radionuclide also contributes to the body burden after ingestion of ^{90}Sr. When considering the problems of the internal radiation the relatively long range of the ^{90}Y betas should be remembered (max. energies: ^{90}Y: 2.24 MeV; ^{90}Sr: 0.61 MeV). In this connection it is also of interest to know whether or not the ^{90}Y found in the body as a daughter product of ^{90}Sr is relocalized away from the strontium deposit sites.

The distribution in the body of yttrium is also of importance from a hygienic viewpoint in relation to its industrial use, and because of its therapeutic use for local irradiation, especially of tumours covering membranes of the body cavities (WALKER 1964). A review article on the metabolism of radioyttrium was published by Eileen RAMSDEN (1961).

In the present work the distribution of ^{91}Y in mice has been studied by whole body autoradiography, and it was chosen because its radiation properties

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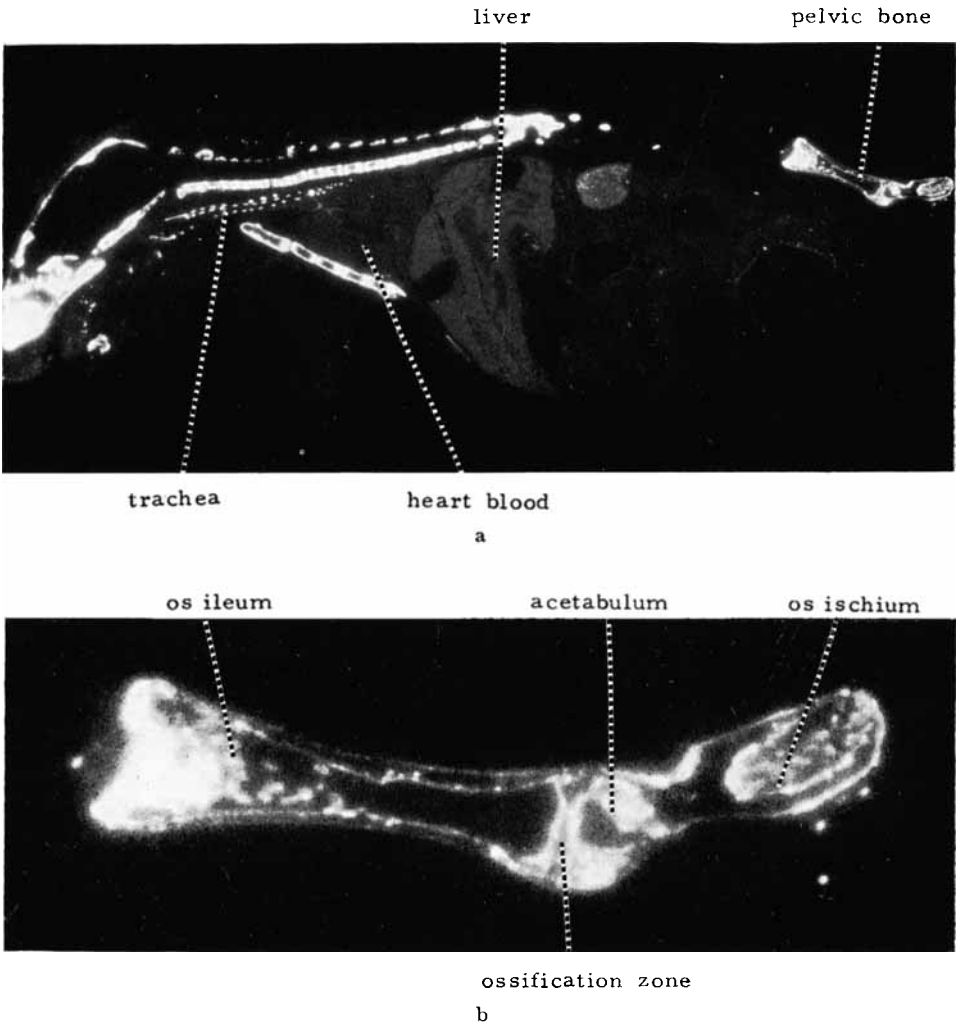

Fig. 1. a) Autoradiogram showing the distribution of ^{91}Y one hour after injection. White areas correspond to high radioactivity. No detectable ^{91}Y left in the blood; the uptake is highest in the skeleton and in the tracheal cartilage; a slight accumulation can also be seen in the blood vessel walls, liver and kidney. b) Detail of (a). In the pelvic bone, high concentration in ossification zones and in periosteal and endosteal layers.

(1.55 MeV betas, half-life 57 days) are more favourable for autoradiography than are those of ^{90}Y. Chemically, yttrium is closely related to the lanthanides. Distribution investigations of certain lanthanides, using the same autoradiographic technique have been published earlier (EWALDSSON & MAGNUSSON 1964).

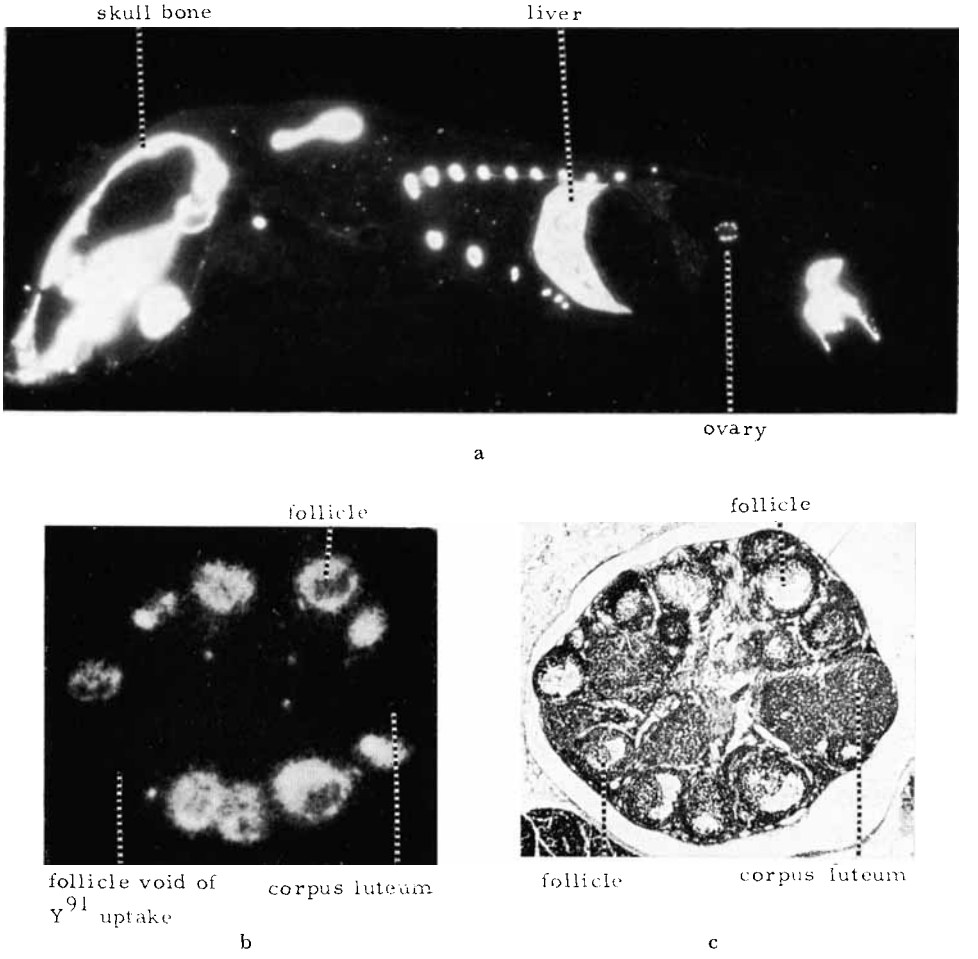

Fig. 2. a) Autoradiogram of ^{91}Y in non-pregnant mouse 2 hours after injection. Uptake of radio-yttrium only in skeleton, liver and ovary. b) Autoradiogram of ovary. High concentration in the walls (apparently mainly in the granulosa layer) of most but not all follicles. c) Section stained with hemalum-eosin, corresponding to the ovary autoradiogram.

Methods. Carrier-free ^{91}Y was obtained from the Radiochemical Centre, Amersham, England. The isotope was delivered in 1 N hydrochloric acid. The pH was adjusted to 2—2.5 before injection by addition, drop by drop, of 0.1 N sodium hydroxide and checking the pH with very small strips of indicator paper (Merck 0.5—5.0). Below pH 2.5 yttrium is ionic.

Fourteen CBA mice were injected intravenously in a tail vein with a single dose of ^{91}Y corresponding to approximately 1 μCi/g bodyweight. Six of the

mice were pregnant in late gestation state. They were killed at the following times after injection: 5 min, 20 min, 1 hour, 4 hrs, 24 hrs and 96 hrs. Four male and 4 female adult mice were also injected. They were killed 5 min, 20 min, 2 hrs, and 24 hrs, respectively, after injection. The autoradiographic technique has been described in detail previously (ULLBERG 1954, 1958). Sectioning, drying and exposure were carried out at —10°C. Twenty micron thick sagittal sections were taken at various levels. The sections were freeze-dried and pressed against 'Structurix (Gevaert) X-ray' film. After exposure ranging from 2 to 15 days the roentgen films were developed and some of the corresponding sections stained (while still kept on the tape).

Results

The radioactivity gradually disappeared from the blood, a process which was largely completed after 4 hours. Part of the ^{91}Y was excreted, mainly through the kidneys and the bulk of the remaining portion was taken up in the skeleton, where it remained throughout the experiment (4 days). In addition, some soft tissues also showed a slight tendency towards specific uptake and retention of the radioyttrium. The soft tissues that showed the highest concentrations were kidneys, ovaries, gastric mucosa, mammary glands and parts of the placentae. A more detailed description of the distribution pattern is given below.

Skeleton. Within the bones the highest uptake was seen in the epiphyseal mineralisation zones and subperiosteally. In the fetuses, where localization was seen exclusively in the skeleton (Fig. 3), the highest uptake is also found in the epiphyses.

Cartilage. In the adult mice, uptake was seen in the cartilage of the trachea, ribs and ear. In the fetal bones, however, no uptake of ^{91}Y in the cartilage could be observed (see Fig. 3).

Myocardium and blood vessels. The myocardium in all time intervals studied, had a slightly higher activity than the skeletal muscles. In addition to a homogenous distribution a few very hot spots were seen. The walls of the large arteries (e.g. aorta and the pulmonary artery) were very accentuated.

Kidney. The main path of excretion of yttrium seems to be through the kidneys. Five minutes after the injection, the kidney showed a rather strong radioactivity fairly evenly distributed, indicating a rapid onset of excretion. Two

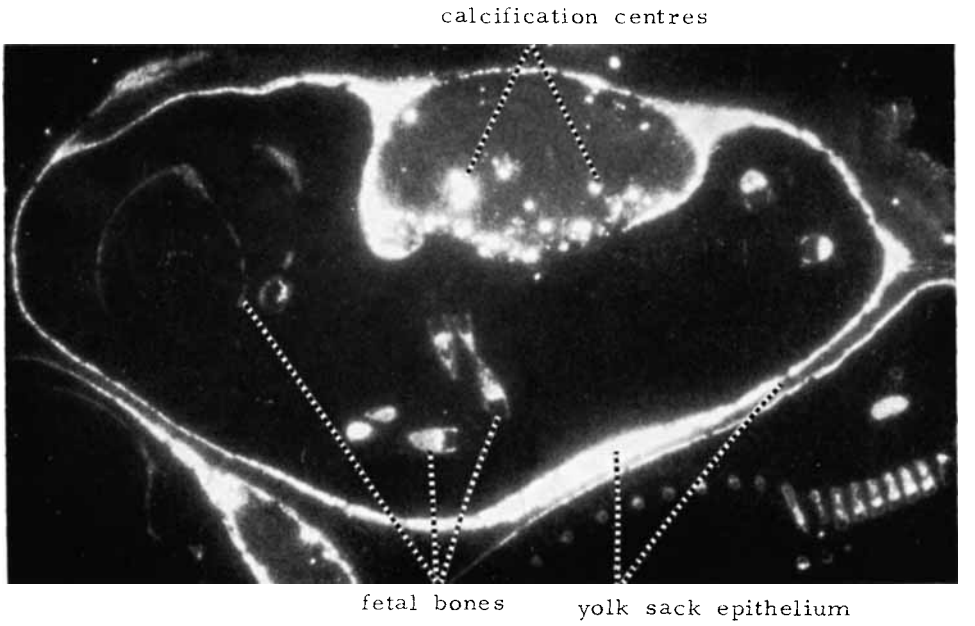

Fig. 3. Detail of whole body autoradiogram of pregnant mouse 4 hours after injection of ^{91}Y showing part of uterus. Selective localization in the bones of the fetus, especially in the epiphyseal ossification zones; no uptake in the epiphyseal cartilage is detectable. Strong uptake also in the yolk sac epithelium and in degenerative calcification centers in the chorioallantoic placenta.

hours after the injection the distribution in the cortex was spotty. This persisted throughout the investigation. The urinary bladder showed a very high amount of ^{91}Y in the first 4 hours of the experiment, followed by a slight decrease.

Digestive system. The liver showed intermediate activity and no apparent excretion through the bile could be detected. The gastric mucosa showed a very strong uptake with a mostly spotty pattern in all the time intervals studied. The isotope concentration of the intestines was very low both in the walls and in their contents, with the exception of some scattered hot spots.

Lungs. In some animals scattered hot spots could be seen in the lungs, probably due to radiocolloid formation.

Ovaries. The ovaries rate among the soft tissues which show the highest uptake in the body. The strongest accumulation was in the follicle walls of the non-pregnant females (Fig. 2b). No specific accumulation was seen in corpora lutea.

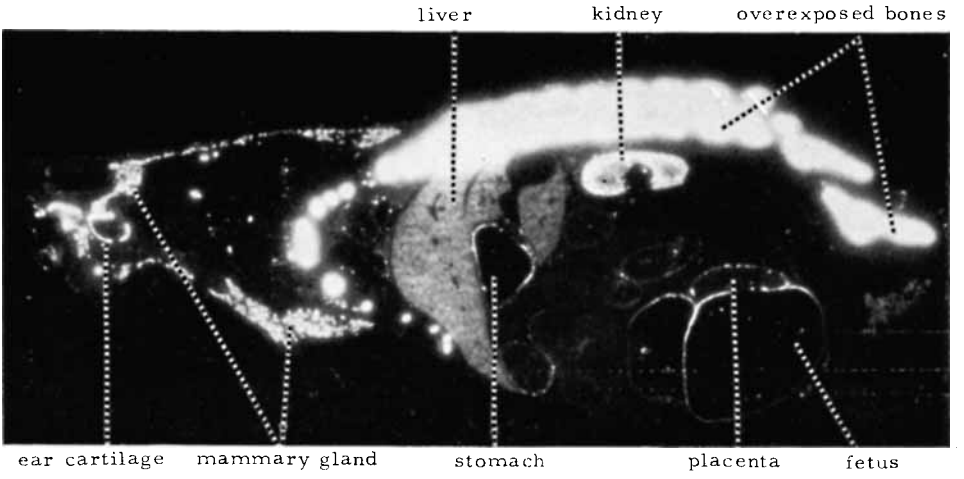

Fig. 4. Autoradiogram of a sagittal section from the lateral portion of a pregnant mouse 4 days after injection of ^{91}Y. The film is partly overexposed from ^{91}Y in bones. Specific uptake can also be seen in the kidney, gastric mucosa, liver, mammary glands, fetal membranes and placenta.

Testes. No specific localisation in the testes.

Mammary glands. The mammary glands of the pregnant mice showed a strong uptake, apparently confined to the parenchyma of the gland.

Placentae. The chorioallantoic placenta showed a slight uptake of evenly distributed ^{91}Y which could be seen also after the blood activity had disappeared. A few localized areas with very strong uptake of radioyttrium, corresponding to sites of degenerative calcification, were also observed. Outlining the chorioallantoic placenta on the maternal side, a spotty line of high uptake was seen. On the fetal side of the chorioallantoic placenta, a very strong accumulation was noted, probably higher than in any other soft tissue and apparently confined to the yolk sac epithelium.

Discussion

The distribution picture was dominated by the uptake in the skeleton but the hard tissue localization was not selective, as a few other organs also took up and retained ^{91}Y, although to a lower degree.

When the distribution pattern is compared with the pattern obtained in similar autoradiographic investigations with ^{90}Sr (NILSSON & ULLBERG) it can be noted that radiostrontium rapidly and exclusively was taken up by the skeleton. No tendency of the radioactive material to reappear in any soft

tissues, indicating a relocalization of the ^{90}Y formed in the body as a ^{90}Sr daughter, could be noticed, not even long after ^{90}Sr-injection or in heavily overexposed autoradiograms.

The autoradiograms of yttrium in bone did not differ significantly from those of calcium (ULLBERG 1965) and strontium. The radioactivity was in all cases localized in epiphyseal growth lines. This was especially accentuated in the fetal bones.

RAMSDEN (1961) has suggested that the tendency to localize in soft tissues is dose-dependent, tracer doses being more exclusively localized to bones. In the present work, however, a soft tissue localization was observed, although a tracer dose was given.

RAMSDEN also claimed that with a larger dose radiocolloid formation is relatively increased and that the radiocolloid is responsible for the soft tissue localization. In our work the autoradiographic pattern shows a partially even distribution and a partially spotty localization.

The initial accumulation in the kidney obviously can be related mainly to excretion, but the spotty uptake in the renal cortex is apparently due to specific retention in the walls of the renal tubules. A similar renal tubular uptake has been observed also for ^{203}Hg and cadmium. The uptake of activity in the gastric mucosa was remarkably high.

Concerning the radiation hazards of yttrium taken up by the body the strong uptake in the follicular walls of the ovary deserves to be mentioned. This may involve risks for beta radiation of the developing ova, with possible genetic consequences.

The fetus seems to be fairly well protected as the placental transfer was partially blocked. However, some ^{90}Y passed the placenta and localized in fetal bones. The intense accumulation in the yolk sac epithelim may be related to a fetal discrimination mechanism.

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SUMMARY

The distribution of ^{91}Y in mice was studied by means of whole body autoradiography. Yttrium is predominantly taken up by the hard tissues with a localization similar to that of strontium. In addition, some soft tissues, such as renal cortex, ovaries, gastric mucosa and, in pregnant animals, the mammary glands and parts of the placenta, show a specific uptake. Of especial interest is the strong concentration in the follicular walls of the ovaries with possible genetic consequences. The fetal uptake is relatively limited and concentrated to the fetal skeleton.

ZUSAMMENFASSUNG

Die Untersuchungen zeigen, dass Yttrium 91 hauptsächlich von den harten Geweben aufgenommen wird, wobei es ähnlich dem Strontium gelagert wird. Spezifische Speicherung fand in einigen weichen Geweben wie Nierenrinde, Eierstöcke, Magenschleimhaut und, bei graviden Tieren, in den Brustdrüsen und Teilen der Plazenta statt. Besonders interessant ist die starke Konzentration in den Follikelwänden der Eierstöcke, wobei genetische Folgen möglich sind. Die Aufnahme durch den Foetus ist verhältnismässig gering und auf das foetale Skelett beschränkt.

RÉSUMÉ

Ces recherches ont montré que l'yttrium 91 est fixé principalement par les tissus durs avec une localisation semblable à celle du strontium. On a constaté une fixation spécifique dans certains tissus mous tels que le cortex rénal, les ovaires, la muqueuse gastrique, et, chez les animaux gravides, les glandes mammaires et des parties du placenta. Particulièrement intéressante est la forte concentration dans les parois folliculaires des ovaires, pouvant avoir des conséquences génétiques. La fixation foetale est relativement limitée et concentrée sur le squelette foetal.

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