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DISTRIBUTION OF RADIOCERIUM AND RADIOPROMETHIUM IN MICE

An autoradiographic study

by

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The lanthanides have received considerable attention in recent years, and these rare earths are now used industrially in alloys (BAUMANN 1954, KYKER 1962), in medicine as antithrombosis agents (HARA & SATO 1955, VINCKE 1960) and as radioactive isotopes for the treatment of certain types of tumour (LEWIN et coll. 1953, CHRISTOPHERSSON et coll. 1956). Fission releases yttrium and large amounts of the lighter lanthanides; niobium and yttrium, for instance, predominate from the seventieth day to six years after the fission of uranium 235 (LÖW & BJÖRNERSTEDT 1957).

Metabolism of the lanthanides has been touched upon in previous papers (KYKER 1962, MAGNUSSON 1963). The blood level declines rapidly after the intravenous injection of lanthanides, which accumulate particularly in the liver and skeleton. There is little absorption from the gastrointestinal tract after oral administration, even in ruminants (EKMAN & ÅBERG 1961). Autoradiographic studies on particular tissues, such as the liver, spleen, and bone, have been reported (LASZLO 1956, JOWSEY et coll. 1958 and AEBERHARDT et coll. 1961).

Submitted for publication 17 June 1963.

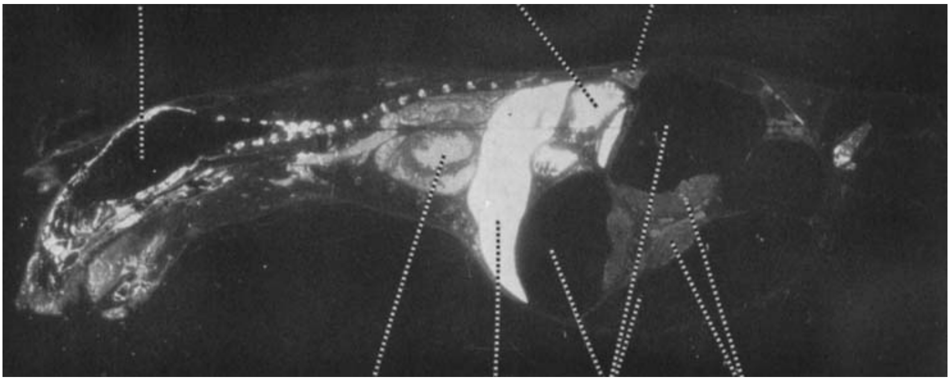

Fig. 1. Pregnant mouse 20 minutes after intravenous injection of ^{144}Ce; high concentration in the gastric contents.

An autoradiographic survey of the distribution in the body of the light lanthanides, cerium and promethium, is presented in this communication. The distribution of the heavy lanthanides, terbium, holmium, and ytterbium, will be dealt with in a forthcoming publication.

Material and Methods. The isotopes, ^{144}Ce and ^{147}Pm were obtained from Amersham, England, and injected into eleven female mice, 9 of which were pregnant and due to litter within two days. The pregnant mice had a mean weight of about 40 g and the non-pregnant of about 20 g. Five of the mice were injected with ^{144}Ce and six with ^{147}Pm. Both isotopes were injected intravenously as chlorides in a carrier-free solution at pH 3 in a single dose of approximately 1 μC/g bodyweight. The mice were killed at intervals after injection by immersion in a mixture of hexane and solid carbon dioxide (— 70°C). The ^{144}Ce mice were killed at 5 and 20 minutes and at 1, 4, and 24 hours after the injection, and the ^{147}Pm mice at 20 minutes and at 1, 4, and 24 hours. Sagittal sections through the frozen bodies were cut with a microtome, picked up on tape and dried in a cold room at — 10° C. The sections were apposed to Gevaert Structurix X-ray film for exposure for one to seven days. The autoradiographic technique has been described in detail by ULLBERG (1958).

Results

Blood. Blood levels of both radiocerium and radiopromethium rapidly declined and at 20 minutes after injection the blood contained less activity than the liver, skeleton and kidneys. It would appear that radiopromethium leaves the blood more readily than radiocerium. There was no autoradiographic evidence

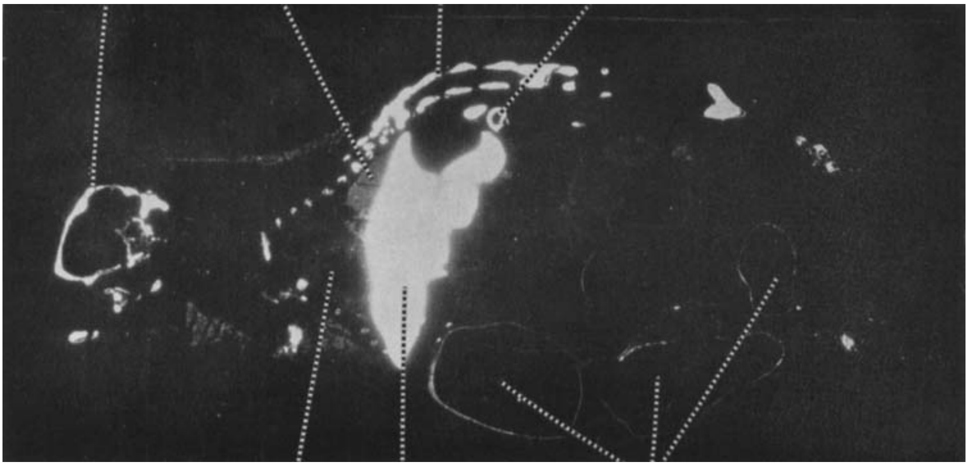

Fig. 2. Pregnant mouse 24 hours after intravenous injection of ^{144}Ce; high concentrations in liver, skeleton and adrenals.

of radiopromethium in the blood after 4 hours nor of radiocerium after 24 hours.

Blood vessels. The walls of the larger vessels accumulated some of both isotopes from one to 24 hours after injection.

Skeleton. Both isotopes accumulated early and to a considerable degree in the skeleton. Activity in the skeleton rose steadily so that after 24 hours the accumulation in the skeleton as well as in the liver and kidneys dominated the distribution pattern. Both lanthanides collected particularly in the endosteum and periosteum. Activity in the bone marrow was relatively low, particularly in the case of radiopromethium.

Teeth. There was an intense accumulation of both isotopes in the enamel and pulp at all the intervals studied; the activity in the former was limited to the ameloblast layer. There was very little activity in the dentine.

Cartilage. Both isotopes collected in the tracheal rings, radiocerium to a lesser degree than radiopromethium. The level of radiopromethium in the cartilage after 24 hours approached the degree of activity evident in the liver and skeleton (Fig. 4).

Skeletal musculature. There was very little activity of either isotope throughout the period of observation.

Myocardium. There was slightly more activity than in the skeletal musculature.

Skin and subcutaneous tissues. Neither isotope collected in the skin. There was slight activity in the follicles of the tactile hairs of the nose during the first 4

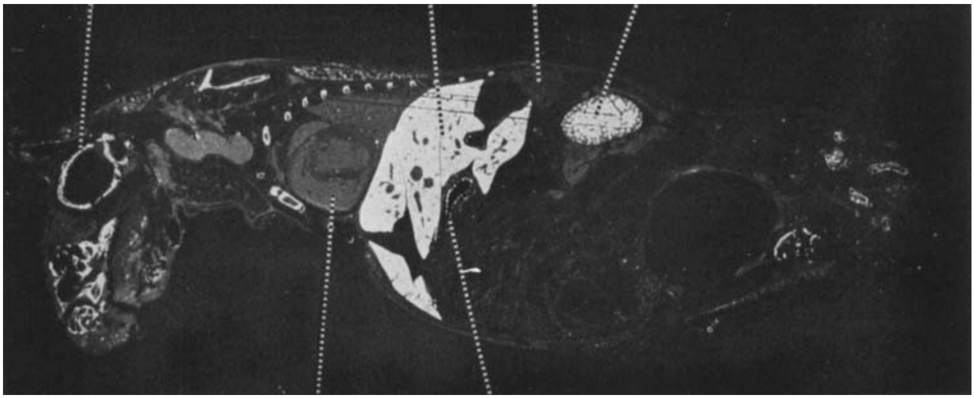

Fig. 3. Distribution of ^{147}Pm in a pregnant mouse 20 minutes after intravenous injection; high concentrations in liver, kidneys, bones and gastric mucosa.

hours after injection. At the same time there was a slight accumulation of radiocerium in the subcutaneous fatty tissue but none of radiopromethium.

Stomach. There was intense activity for both isotopes in the superficial gastric mucosa, a sign of excretion during the first hours after injection. This activity persisted throughout the period of observation. The gastric contents also presented a high level of activity at 20 minutes after the injection of radiocerium (Fig. 1).

Intestine. At some time or other throughout the experiment various segments of the intestine presented some degree of activity for both isotopes. Radiocerium activity was evident after one hour and radiopromethium activity as early as at 20 minutes.

Liver. Both isotopes accumulated early and at a high level in the liver, which at 20 minutes after the injection contained 3 to 5 times more activity than the blood; the liver retained this high level of activity throughout the experiment.

Respiratory organs. There was fairly strong radiocerium activity in the lung tissue from 4 hours onwards but no radiopromethium activity was apparent at any time.

Kidneys. There was strong accumulation of both isotopes in the kidneys at all intervals studied. The level of radiocerium in the kidney at 20 minutes after injection was twice that of the blood and that of radiopromethium 7 to 8 times that of the blood. The activity of both isotopes predominated in the cortex and was intense in certain regions (Fig. 3). The radiopromethium in the renal medulla was more evident than the radiocerium. The renal pelvis had much less activity for either isotope than other parts of the kidney.

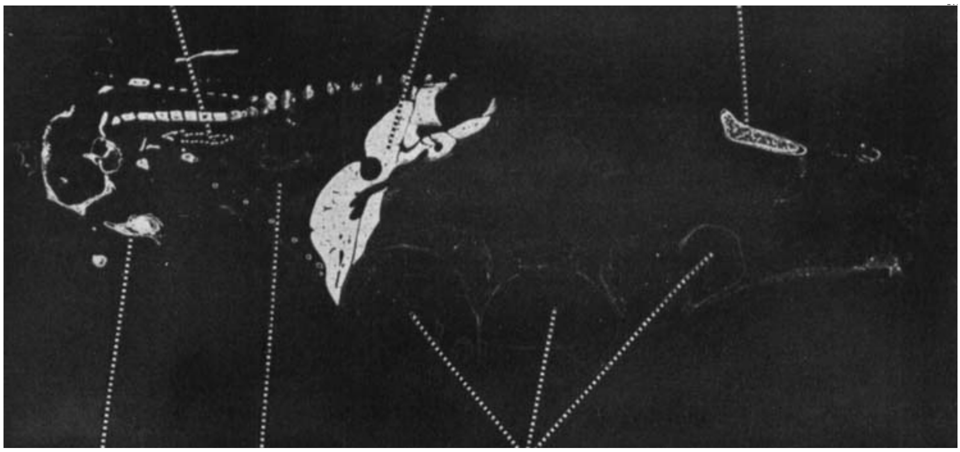

Fig. 4. Distribution of ^{147}Pm in a pregnant mouse 24 hours after intravenous injection; high concentrations in liver, bones, cartilage of the trachea, and pulp of the teeth.

Urinary bladder. There was some promethium activity as evidence of renal excretion throughout the experiment. Radiocerium activity was not detected in the bladder.

Ovaries. Radiocerium was accumulated by the ovaries to a greater extent than radiopromethium. One and 4 hours after injection the ^{144}Ce activity was on a par with that of the blood. The ^{147}Pm activity in the ovaries was low at all the intervals studied.

The radiocerium activity within the ovaries was greater in the corpora lutea and the stroma than in the follicle contents. Radiopromethium, on the other hand, was mainly accumulated by the follicle contents, and other parts of the ovaries from one hour onwards had no detectable activity.

Spleen. Promethium activity in the spleen was low during the experiments. There was greater splenic uptake of radiocerium and the uptake increased steadily to reach the same level as in the liver and skeleton after 24 hours. Activity was concentrated to the red pulp.

Adrenals. There was little radiopromethium activity in the adrenals but the level increased to some extent with time. The adrenals accumulated radiocerium to a greater degree. Cortical activity predominated, particularly along the corticomedullary border, for both isotopes. By 24 hours, activity was evident only in the cortex, where the activity of radiocerium was very high and only slightly less than in the skeleton (Fig. 2).

Placenta. The activity in the placenta was much the same as in the blood.

Fetal membranes. There was some accumulation of both lanthanides in the foetal membranes. Radiopromethium activity was low and first evident after 24 hours. Radiocerium was accumulated to a greater degree, and by one hour after injection the activity was greater than in the blood.

Fetuses. Slight uptake of both radiopromethium and radiocerium was evident in the fetal skeletons at 24 hours after injection.

Mammary glands. Both lanthanides were accumulated to some extent. Radiopromethium activity was visible from 20 minutes, and radiocerium activity from one hour onwards.

Brain. No activity was detected in the central nervous system.

Discussion

The distribution patterns for radiocerium and radiopromethium were dominated by the accumulation in the liver and skeleton. These observations accord with results obtained previously with other methods (HAMILTON 1948, DURBIN et coll. 1956, MAGNUSSON 1963). There was a relatively marked radiocerium accumulation in the kidneys, spleen, cartilage and adrenal cortex, and relatively strong radiopromethium activity in the kidneys and cartilage. Although there were similarities in the distribution pattern for the two lanthanides there were also some differences.

The liver is important in lanthanide metabolism. Shortly after the intravenous injection, the liver contains more than 50 per cent of the dose given (MAGNUSSON). Radiocerium is uniformly distributed in the liver tissue, according to the autoradiographical studies of AEBERHARDT et coll., and this was confirmed in the present series. The intrahepatic distribution of radiopromethium, on the other hand, was somewhat irregular, and it is conceivable that the two lanthanides differ in this respect; microautoradiography would appear to offer the only means of producing definite evidence.

The skeletal patterns were similar for both radiocerium and radiopromethium. Both lanthanides accumulated in the periosteum and the endosteum but not in the cortex; DURBIN (1962) made similar observations. The collection of both isotopes was remarkably high in the dental pulp, presumably as an expression of the intense metabolic activity.

Both foreign and natural substances, dextran and albumin for example, may be excreted by the gastric mucosa (ÅBERG 1952, ULLBERG et coll. 1960, ÅBERG et coll. 1961). The present authors have also obtained autoradiographic evidence of the gastric excretion of radiocerium and radiopromethium. Both gastric and biliary excretion of these isotopes occurs, according to the results published in the paper by MAGNUSSON, although biliary excretion could not be observed autoradiographically during the course of the present experiment.

The isotopes in the adrenal accumulated particularly in the cortex, possibly because of the high lipid content present and the tendency of lanthanides to react with phosphatides (BAUMANN 1954).

Acknowledgement

The investigation was aided by grants from Statens Råd för Atomforskning, Jordbrukets Forskningsråd, Cancerfonden and Wallenbergstiftelsen.

SUMMARY

The distribution pattern of ^{144}Ce and ^{147}Pm have been studied by wholebody autoradiography. Both lanthanides accumulated most in the liver and skeleton. There was also a high uptake of radiocerium by the kidneys, spleen, cartilage, and adrenal cortex and of radiopromethium by the kidneys and cartilage.

ZUSAMMENFASSUNG

Die proportionale Verteilung im Körper des ^{144}Ce und des ^{147}Pm wurde mittels Autoradiographie des ganzen Körpers studiert. Beide Lanthanumsalze speicherten sich vorzüglich in der Leber und im Skelett. Radiocerium wurde in grösseren Mengen in den Nieren, der Milz, dem Knorpel und den Nebennierenrinden gefunden, Radiopromethium fand sich in den Nieren und im Knorpel.

RÉSUMÉ

La distribution de ^{144}Ce et de ^{147}Pm a été étudiée sur des souris par autoradiographie du corps entier. Ces deux lanthanides s'accumulent surtout dans le foie et le squelette. Il y a aussi une fixation importante de radiocérium dans les reins, la rate, le cartilage et le cortex surrénal, et de radioprométhéum dans les reins et le cartilage.

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