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DISTRIBUTION OF RADIOTERBIUM, RADIOHOLMIUM AND RADIOYTTERBIUM IN MICE

An autoradiographic study

by

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The medical and industrial uses of the lanthanides were briefly touched upon in a previous paper on autoradiography with the light lanthanides, radiocerium and radiopromethium (EWALDSSON & MAGNUSSON 1964). The present report represents an extension of the autoradiographic studies to cover radioterbium, radioholmium, and radioytterbium. These elements lie at the upper end of the lanthanide scale and for this reason are referred to as the heavy lanthanides.

Material and Methods. The isotopes ^{160}Tb, ^{166}Ho, and ^{169}Yb were purchased from Amersham, England, as chlorides in aqueous solution with pH 3. Eighteen female mice were used in the experiment; 13 of them were pregnant and expected to litter within two days and had a mean weight of 40 g; the 5 non-pregnant females weighed about 20 g. The isotopes were injected into a tail vein in a single dose corresponding to approximately 1 μC/g bodyweight. Eight mice were injected with ^{160}Tb, three with ^{166}Ho, and seven with ^{169}Yb. Mice injected with ^{160}Tb were killed at 5 and 20 minutes and at 1, 4, and 24 hours. The ^{166}Ho mice were killed at 1, 4, and 24 hours, and the ^{169}Yb mice at 5 and 30 minutes and at 1, 4, and 24 hours after injection.

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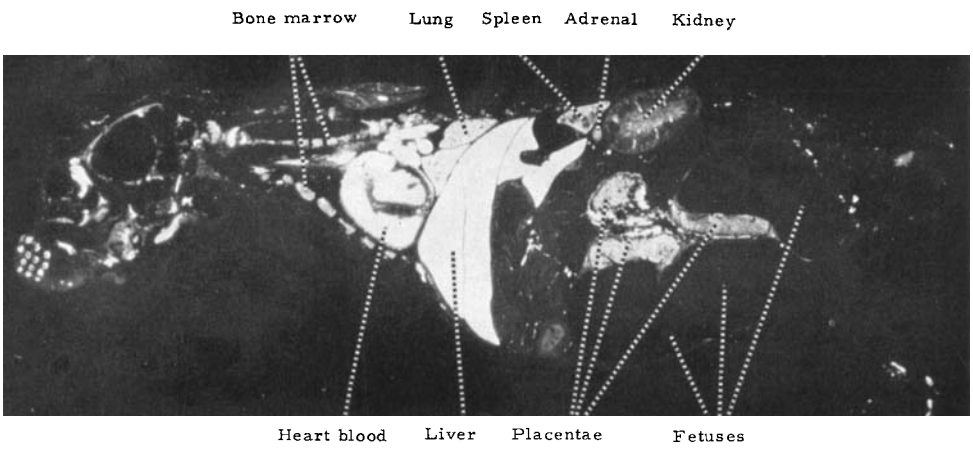

Fig. 1. Distribution of ^{160}Tb in body of pregnant mouse an hour after intravenous injection. White areas correspond to high radioactivity; radioterbium content is high in the blood and liver.

The autoradiographic technique has been described by ULLBERG (1958). Twelve sagittal sections, 10 to 20 μ thick, were taken at different levels from each mouse, dried, and exposed, all at — 10° C; they were then apposed to Structurix (Gevaert) film for periods ranging from two to seven days.

Results

Blood. During the first hour the high level of activity in the blood dominated the autoradiograms for all three isotopes (Fig. 1). At one hour after injection, the ^{160}Tb activity was as great in the liver as in the blood; at this time there was greater ^{166}Ho activity in the blood than in the liver and less ^{169}Yb activity in the blood than in the liver. The blood activity declined at different rates for the isotopes. The blood levels of ^{160}Tb and ^{169}Yb dropped more rapidly than that of ^{166}Ho. There was much more ^{166}Ho than ^{160}Tb or ^{169}Yb activity in the blood at four hours after injection. None of the isotopes could be detected in the blood in the autoradiogram at 24 hours after injection.

Blood vessels. There was some accumulation of ^{160}Tb and ^{166}Ho but no ^{169}Yb activity in the walls of the larger blood vessels after 24 hours.

Skeleton. All three isotopes began to accumulate in the skeleton a short time after administration. The levels rose steadily throughout the experiment. Most activity was present in the bone marrow; there was some in the periosteum but none in the cortex.

Teeth. ^{160}Tb and ^{169}Yb activities were present from 4 to 24 hours after injection, mainly in the pulp, and to a slight degree in the enamel; there was none in the dentine.

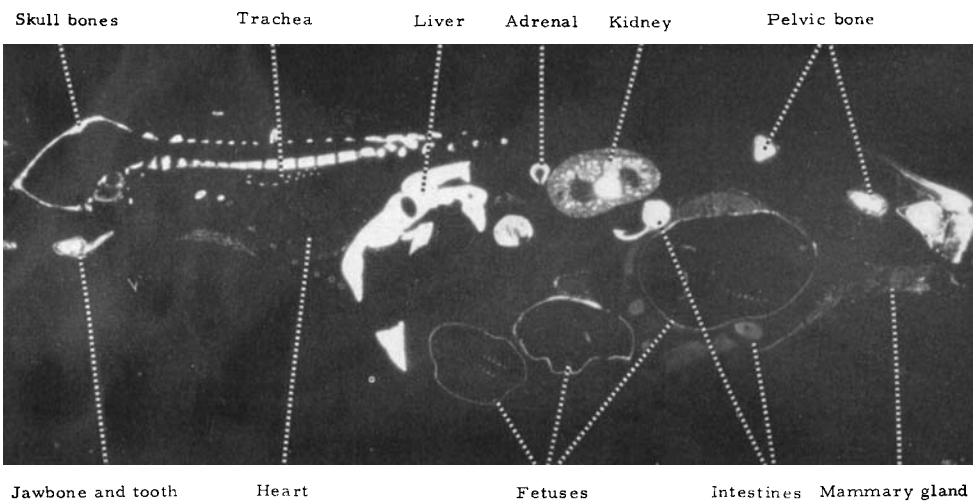

Fig. 2. Distribution of ^{166}Tb in body of pregnant mouse 24 hours after injection. The highest radioactivity lies in the liver, bone marrow, tracheal cartilage, adrenal cortex and intestinal contents.

Cartilage. ^{160}Tb and ^{166}Ho activities appeared in the tracheal rings at 24 hours after injection (Fig. 2). No ^{169}Yb activity could be detected in cartilage.

Skeletal musculature. There was only slight accumulation of the three isotopes.

Myocardium. The activity here was slightly greater than in the skeletal musculature.

Skin and subcutaneous tissues. Slight activity was present in the subcutaneous fatty tissue during the first four hours after injection of the three isotopes. There was a relatively high level of activity in the follicles of the tactile hairs during the first few hours.

Stomach. All three isotopes accumulated to some degree in the surface epithelium as a sign of excretion (Fig. 3). This appearance persisted throughout the experiment. Some activity could at times also be recorded in the gastric contents.

Intestines. Activity was present in the intestinal contents 4 and 24 hours after injection of the isotopes (Fig. 4).

Liver. All three isotopes accumulated rapidly and in large amounts in the liver (Figs 5 and 6). Activity reached its peak within an hour or so after injection, and persisted throughout the experiment. At 24 hours after injection, the distribution patterns were dominated by the high activity levels for all three isotopes in the liver and skeleton. Liver activity in relation to blood activity is described under subheading 'blood'.

Gallbladder. All three isotopes were present in the bile at some time or other throughout the experiment.

Respiratory system. The lungs at 24 hours contained a little ^{166}Ho and ^{169}Yb activity but no ^{160}Tb activity.

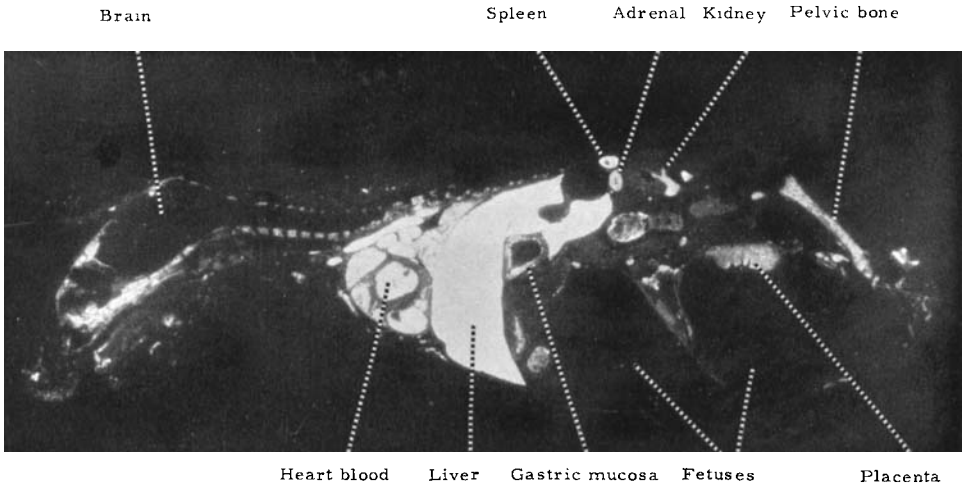

Fig. 3. Distribution of ^{166}Ho in body of pregnant mouse 4 hours after injection. High radioactivity in the blood, liver, spleen and gastric mucosa.

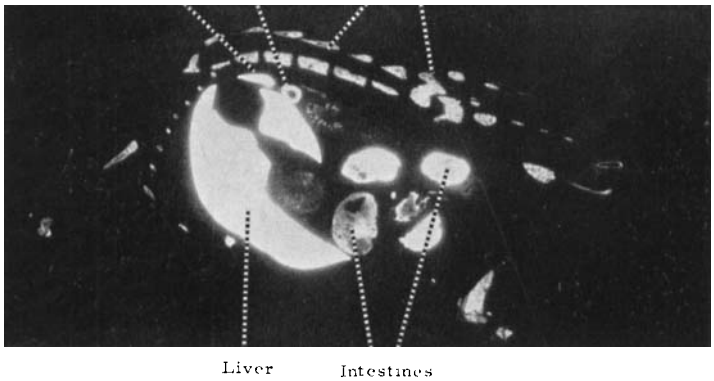

Fig. 4. Distribution of ^{160}Ho in abdomen of mouse 24 hours after injection. High radioactivity in the liver, adrenal cortex, bone marrow and intestinal contents.

Kidneys. All three isotopes were present to some extent in the kidneys throughout the experiment. There was distinct activity in the renal pelvis and the urinary bladder, as a sign of excretion, at five minutes after the injection of ^{160}Tb and until the end of the observation period. Corresponding signs of renal excretion could not be demonstrated for ^{166}Ho or ^{169}Yb. There was some focal activity in the renal cortex in the autoradiograms for all three isotopes at all the intervals studied.

Ovaries. All three lanthanides could be demonstrated in the ovaries with the

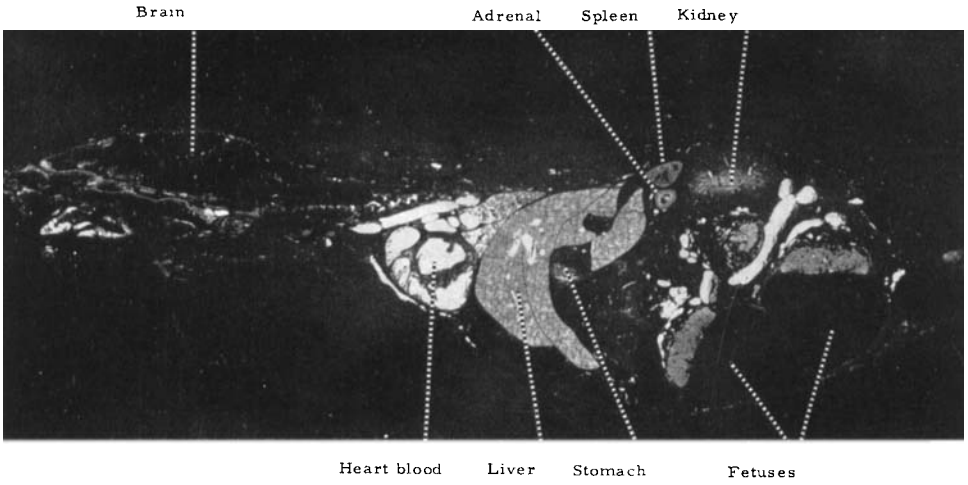

Fig. 5. Distribution of ^{169}Yb in body of pregnant mouse an hour after injection.

highest activity levels in the corpora lutea and the interstitium but no detectable activity in the follicles. There were no topographic differences in the distribution patterns of the isotopes.

Spleen. All three lanthanides accumulated in the spleen. Accumulation began shortly after injection and steadily increased to reach a high level of activity at 24 hours. Activity was limited to the red pulp.

Adrenals. While all three isotopes accumulated in the adrenal cortex, the uptake of ^{160}Tb was most rapid, and there was intense activity of this isotope in the cortex at 20 minutes after injection. The activity of ^{160}Tb and ^{166}Ho at 24 hours was as great in the adrenal cortex as in the liver. The ^{166}Ho and ^{169}Yb activities during the first hour after injection were limited to the cortico-medullary junction, and the ^{160}Tb activity was more diffusely distributed throughout the cortex. None of the isotopes could be detected in the adrenal medulla.

Foetus. Some ^{160}Tb and ^{166}Ho activities were present in the foetal skeleton after 24 hours, and slight ^{166}Ho activity was present in the foetal intestines. No ^{169}Yb activity could be detected in the autoradiograms for the corresponding periods.

Placenta. The activity in the placenta during the first hours after injection corresponded to the blood levels of the nuclides. There was a low level of activity for all three lanthanides in the placenta at 24 hours when there was no longer any detectable activity in the blood.

Foetal membranes. A rapid uptake, and persistent activity of ^{160}Tb was noted in the foetal membranes, but no definite ^{166}Ho or ^{169}Yb activities could be detected at any time.

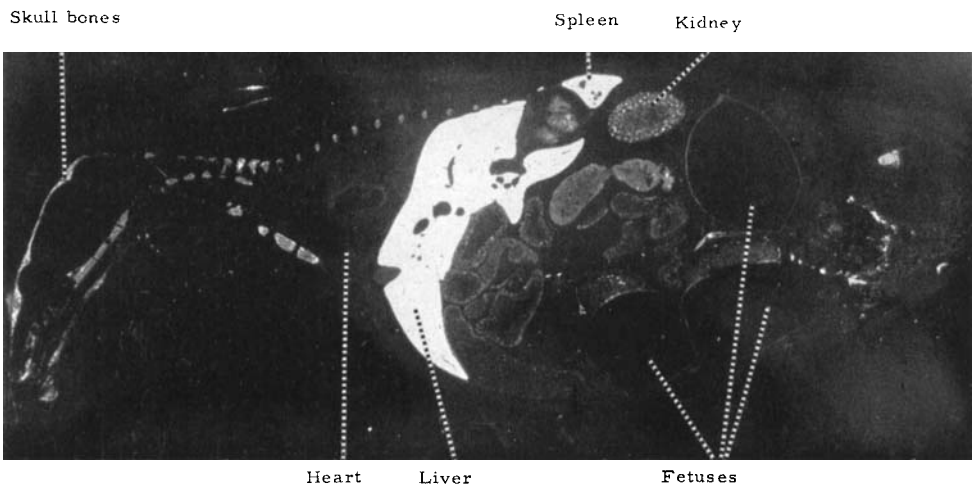

Fig. 6. Distribution of ^{169}Yb in body of pregnant mouse 24 hours after injection. The highest radioactivity lies in the liver and spleen.

Mammary glands. Activity in the mammary glands was very low and first discernible after 24 hours.

Discussion

The uptake of lanthanides by the liver and skeleton evident in the autoradiograms confirms the reports of HAMILTON (1948), DURBIN et coll. (1956), and MAGNUSSON (1963), among others. Other tissues also accumulate appreciable amounts of these lanthanides; ^{160}Tb is accumulated particularly by the spleen, cartilage, adrenal cortex and kidney, ^{166}Ho by the spleen, adrenal cortex and kidney, and ^{169}Yb by the spleen and kidney.

Great similarities in the distribution patterns of these heavy lanthanides and those of the light lanthanides, radiocerium and radiopromethium, exist (EWALDSSON & MAGNUSSON 1964).

Radiocerium is accumulated not only by the liver and skeleton but by the kidneys, spleen, cartilage, and adrenal cortex, and radiopromethium by the kidneys and cartilage. The blood activity of ^{160}Tb, ^{166}Ho, and ^{169}Yb declines much more slowly than the blood activity of radiocerium and radiopromethium. The light lanthanides then leave the blood for the tissues, particularly the liver and skeleton, much more rapidly than the heavy lanthanides. DURBIN (1962) made a similar observation.

There is autoradiographic evidence of excretion of all three lanthanides by the stomach and in the bile, an observation that was also reached by CASTELLINO et coll. (1962) and MAGNUSSON (1963).

A strong uptake of radiocerium and radiopromethium by hyaline cartilage

is apparent (EWALDSSON & MAGNUSSON 1964); ^{160}Tb follows the same pattern; ^{166}Ho was accumulated to a much lesser degree by cartilage and ^{169}Yb apparently not at all. Yttrium is bound in cartilage to chondroitin sulphuric acid (ÅBERG & EKMAN 1959) and so, probably, are the lanthanides. The autoradiographic distribution patterns suggest that the lanthanides have different degrees of affinity for chondroitin sulphuric acid.

There is autoradiographic evidence of the renal excretion of ^{160}Tb but not of ^{166}Ho or ^{169}Yb. The three heavy lanthanides and radiocerium, but not radiopromethium (EWALDSSON & MAGNUSSON 1964), are accumulated fairly strongly by the spleen. Some lanthanides collect in the adrenal cortex while the medulla remains practically free. Radiocerium is accumulated by the cortex (EWALDSSON & MAGNUSSON 1964), as are ^{160}Tb and ^{166}Ho.

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SUMMARY

The distribution patterns of ^{160}Tb, ^{166}Ho, and ^{169}Yb were studied by whole body autoradiography. These lanthanides were accumulated mainly in the liver, skeleton, spleen and kidney; ^{160}Tb was also accumulated by the adrenal cortex and cartilage, and ^{166}Ho by the adrenal cortex. The distribution patterns are compared with those of the lanthanides, ^{144}Ce and ^{147}Pm, previously studied by the same technique.

ZUSAMMENFASSUNG

Die relative Verteilung im Körper von ^{160}Tb, ^{166}Ho und ^{169}Yb wurde mittels Autoradiographie studiert. Diese Lanthanide wurden hauptsächlich in der Leber, dem Skelett, der Milz und den Nieren aufgespeichert; ^{160}Tb wurde auch in der Nebennierenrinde und im Knorpel angereichert, ^{166}Ho in der Nebennierenrinde. Die proportionelle Verteilung wird verglichen mit der der Lanthanide ^{144}Ce und ^{147}Pm, die vorher mit derselben Methode untersucht worden war.

RÉSUMÉ

La distribution de ^{160}Tb, ^{166}Ho et ^{169}Yb a été étudiée par autoradiographie corporelle totale sur des souris. Ces lanthanides s'accumulent surtout dans le foie, le squelette, la rate et les reins; ^{160}Tb s'accumule aussi dans le cortex surrénal et le cartilage, et ^{166}Ho dans le cortex surrénal. Leur répartition est comparée à celle des lanthanides ^{144}Ce et ^{147}Pm déjà étudiés par la même technique.

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