

# Distribution of Unbound Reduced Technetium-99m in Animals

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*In order to assess the distribution of radioactive contaminants of common radiopharmaceuticals, unbound reduced Tc-99m at three different pH levels was injected into rabbit, dog, and rhesus monkey. Animals were monitored for 24 hr after Tc-99m injection with static images taken at selected times. Localization of unbound reduced Tc-99m was remarkably constant from species to species and at all three pH levels. Localization of this compound reflects the distribution of reticuloendothelial cells. The wide variance between the distribution of unbound reduced Tc-99m and that of free pertechnetate permits identification of either contaminant in radiopharmaceutical preparations.*

Nuclear medicine personnel deal with three common forms of Tc-99m: unreduced unbound Tc-99m (also known as free pertechnetate); reduced bound Tc-99m; and reduced unbound Tc-99m. The biological distribution and fate of free pertechnetate is well reported (1,2) and the distribution of reduced bound Tc-99m is that of the compound to which it is bound. However, the distribution of unbound reduced Tc-99m, which may be present as a contaminant in radiopharmaceutical preparations, is not widely known. To determine this distribution, we injected reduced unbound Tc-99m at several pH levels into rabbits, dogs, and monkeys.

## Materials and Methods

Sodium pertechnetate eluent from a technetium generator was reduced using 25  $\mu$ l of stannous chloride solution added to 1–5 ml of pertechnetate solution. The stannous chloride solution was freshly prepared by adding 40 mg of SnCl<sub>2</sub>·2H<sub>2</sub>O to 1 ml of oxygen-purged HCl. Complete reduction was verified via paper chromatography in normal saline and silica ITLC (Gelman, Ann Arbor, MI) in 100% acetone. Prior to injection, the pH, initially 1.5, was adjusted to 1, 3, or 6 using 0.1 N HCl or 0.1 N NaOH.

New Zealand white rabbits, ranging in size from 2.0 to 4.0 kg, were sedated with sodium pentobarbital and injected intravenously via a marginal ear vein with 0.5 to 1.0 mCi of reduced unbound Tc-99m. Pure-bred beagles

were tranquilized with a mixture of xylazine and ketamine HCl 1:1 injected intramuscularly and then injected with approximately 1.0-mCi reduced unbound Tc-99m via the saphenous vein. Rhesus monkeys were similarly injected after sedation with Sernylan® (phencyclidine HCl) intramuscularly. At least one animal of each species was injected with Tc-99m at each adjusted pH.

All animals were imaged continuously for the first 3 hr and then at 4, 6, and 24 hr (all times mentioned subsequently are postinjection). A Searle LFOV camera with data store, 140 keV high-resolution, parallel hole collimator, and 20% technetium window was used. Scintiscans of 400,000 counts each were taken every 10 min for the first 3 hr and at each subsequent time period. Video tape recordings of 5 min each were taken at the same time as the scintiscans.

Information was fed from the data store to a Xerox 530 computer for analysis. The computer summed the data into 1-min time frames and printed hard copy of each time frame. Regions of interest for liver, lung, spleen, and femur were outlined on hard copy. The computer then calculated the counts in each organ as a percent of the total counts in the field-of-view. Since the entire animal was in the field-of-view, these values then became the percent of injected dose.

**TABLE 1. Percentage of Injected Dose in Organs of Rabbit, Dog, and Monkey 1 Hr after Intravenous Administration of Reduced Tc-99m.**

	Liver			Urinary Bladder			Spleen		
	pH			pH			pH		
	1	3	6	1	3	6	1	3	6
Rabbit	47	54	68	18	8	7	1	4	2
Dog	57	54	58	1	6	7	7	6	6
Monkey	—*	66	59	—	10	14	—	0	2

\*Analysis not performed.

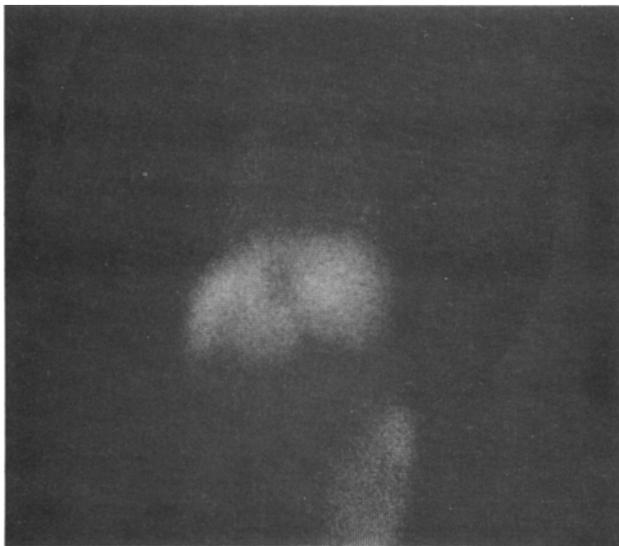
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## Results

The percentage of injected dose in dog liver was approximately 55% (range: 49–60%) from 3 min to 6 hr regardless of the pH of the injected Tc-99m (Table 1). At 24 hours, 47% of the radioactivity remaining in the dog was in the liver. The radioactivity level in the dog spleen was constant at 6%. In addition, some radioactivity was seen in the kidneys during the first hour. By 2 hr postinjection, the kidneys were no longer visible, but approximately 7% of the radioactivity was seen in the urinary bladder. Radioactivity was not visualized in any other part of the body, including background. The distribution of radioactivity in monkeys was essentially the same as that in dogs. Figure 1 demonstrates typical distribution of reduced technetium in dog and monkey.

Rabbit liver radioactivity (at pH of 6) increased rapidly, reaching 62% in 1 min. By 10-min postinjection, it reached 68% and maintained this level through 24 hr (Fig. 2). Rabbit spleen radioactivity was 1–4% at all pH levels and all times, while urine radioactivity varied from 7–18%. In addition, approximately 10% of the radioactivity was seen in the lungs and the bones of the legs in some rabbits at all pH levels.



**FIG. 1.** Radioactivity present in liver and spleen of dog at 20 min after intravenous administration of reduced unbound Tc-99m at pH 1.

Distribution of reduced unbound Tc-99m bears no resemblance to the distribution of free pertechnetate as seen in Fig. 3. The distribution of reduced unbound Tc-99m does, however, suggest entrapment of colloidal particles by the reticuloendothelial system (RES). In humans, 70 to 80% of injected moderately sized colloidal particles appears in the liver, 4 to 8% in the spleen and the rest in bone marrow, and to a lesser extent (2%) in lung (3,4). This accurately reflects the distribution of RE cells in the body. Uptake of radioactivity in the animals examined in this study indicates that reduced unbound Tc-99m distributes in the RES as a colloidal complex with tin hydroxide.

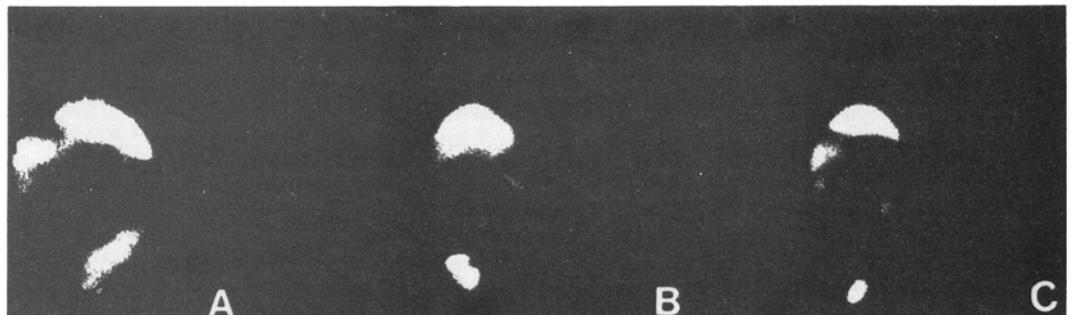
There is some radioactivity excreted by the kidneys, however, and this appears to be noncolloidal reduced Tc-99m. Since there is virtually no circulating radioactivity after the first few minutes postinjection in each study, it is unlikely that reduced unbound Tc-99m forms complexes with serum proteins.

The distribution of radioactivity in each organ at each pH value examined (1,3,6) showed no significant difference. This is in contrast to a report that pH influences the distribution of Tc-99m tin hydroxide (5).



**FIG. 3.** Whole-body radioactivity present in rabbit 60 min after intravenous administration of sodium pertechnetate. Scintiscan shows salivary glands, thyroid, intestine, and urinary bladder.

**FIG. 2.** Radioactivity present in rabbit 60 min after intravenous administration of reduced unbound Tc-99m; A, B, and C represent pH 1, 3, and 6 respectively. Liver, spleen, kidneys, and urinary bladder can be seen.



Regardless of pH, the distinctive distribution pattern of unbound reduced Tc-99m should alert nuclear medicine personnel to the possibility of contamination of the injected radiopharmaceutical by this form of technetium. Additional quality control procedures on the uninjected portion of the compound should be employed either to confirm or rule out such contamination.

## References

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