Scintigraphic Detection of Intrapulmonary Bleeding Using Technetium-99m Sulfur Colloid: Concise Communication

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Radionuclide imaging has been successfully used clinically to determine sites of gastrointestinal hemorrhage, but its use in hemoptysis has not been studied. A dog model of intrapulmonary hemorrhage was devised. Utilizing technetium sulfur colloid, at doses of 4 and 15 mCi, bleeding rates of 0.1–0.2 cc/min were detected. In some dogs, however, significantly higher bleeding rates were not detected. The largest source of error arose from bleeding into a large bronchus, which causes a diffuse distribution of the radionuclide.

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In patients with hemoptysis, the site of bleeding may be difficult to locate, particularly if bilateral or diffuse pulmonary disease is present. Location of the hemorrhage can expedite therapy if transcatheter bronchial embolization or surgical resection for hemorrhage is contemplated. Radionuclide imaging has been used clinically for the detection of gastrointestinal hemorrhage (*1–8*), and less frequently in cases of pulmonary hemorrhage (*9,10*). Experimental evaluation of the use of radionuclide imaging in pulmonary hemorrhage is reported.

METHODS

Seventeen mongrel dogs (20–30 kg) were studied. They were anesthetized with sodium pentobarbital (30–40 mg/kg). An endotracheal tube was inserted but spontaneous respiration was allowed. Heparin (3000 units) was administered intravenously.

A #5 French catheter was inserted into the endotracheal tube and passed into the lung until slight resistance was met (Fig. 1), and was taped in place to prevent change in its position. The position of the catheter tip was established at the end of the experiment with AP and lateral radiographs.

Immediately following injection into a front paw vein of 4 mCi (9 dogs) or 15 mCi (7 dogs) of Tc-99m sulfur colloid, 3-cc peripheral-venous blood samples were withdrawn every 3 min. One cc of each sample was counted in a gamma well counter and blood disappearance curves plotted to establish the half-time of Tc-99m SC in the dogs studied. The remaining 2 cc of each sample was used to mimic pulmonary hemorrhage in the following manner. With a Harvard infusion pump, the venous blood was passed through the endotracheal tube whose tip was positioned in the lung at the desired site of experimental pulmonary hemorrhage. "Bleeding rates" in the lung were varied from 0.8 to 0.05 cc/min (Fig. 1).

Images were obtained at 3- to 5-min intervals using a 37-PM-tube, portable scintillation camera equipped with a low-energy, high-resolution collimator. A 20% window was centered on the 140-keV peak. Images were collected for 100,000 or 200,000 counts on Polaroid film for 60–90 min after tracer injection and onset of simu-

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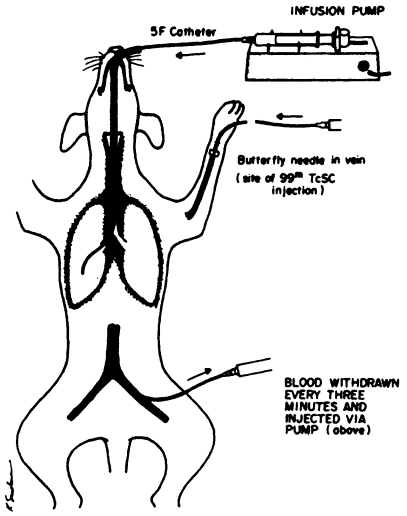

FIG. 1. Diagram of experimental method. Technetium-99m sulfur colloid is injected into peripheral vein, then samples are withdrawn every 3 min from femoral vein, and an aliquot of each infused into endotracheal catheter, whose tip models site of "pulmonary bleeding."

lated pulmonary hemorrhage, which was continued at the determined controlled bleeding rate for the duration of the experiment.

The end point of the experiment was detection of a definite area of increased activity on the Polaroid scintiphoto. If no focal photon concentration was seen, the experiment was terminted at 90 min after injection.

The least amount of activity "bled" into the lung, that sufficed to make a visible focus on the scintiphotos, was calculated for dogs that received 4 mCi of Tc-99m SC (Table 2). The volume of the simulated hemorrhage was derivable from the known rate of injection and the time elapsing until a focus became visible in the scintigrams, and μCi/cc for the appropriate 3-min blood samples were found by comparison of their counts with those from an aliquot of the Tc-99m SC dose.

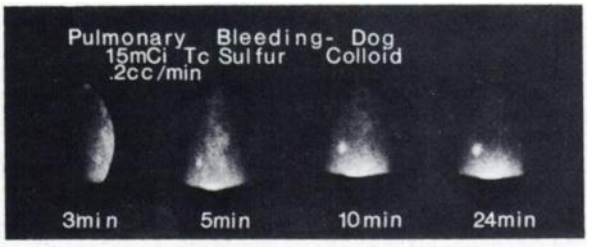

FIG. 2. Scintiphotos of lungs of dog given 15 mCi of Tc-99m SC I.v. Blood was injected through endotracheal catheter at 0.2 cc/min. On the earliest image, at 3 min after onset of "pulmonary bleeding," focus of increased activity can be seen in lower right lung field.

RESULTS

In some dogs from both the high- and the low-dose groups, bleeding rates as low as 0.1–0.2 cc/min created foci of increased activity on the scintiphotos (Figs. 2 and 3). Nevertheless, bleeding at rates above 0.2 cc/min were not always identified (Table 1). The ease with which an area of increased activity could be detected and the bleeding time required varied greatly. In some dogs, a discrete, well-visualized focus of activity was present (Fig. 2). In others an ill-defined smudge appeared. When the bleeding site was very discrete, it was identified within 5 min. A 200,000-count-image, rather than a 100,000-count one, made a definite difference in time of detectability of the bleeding site in nine of 13 dogs that had images at both count accumulations (see Table 1). In two dogs, the bleeding site was invisible in 100,000-count images, but could be seen with 200,000 counts at 33 and 58 min.

Representative graphs of blood activity against time for dogs receiving 4 mCi and 15 mCi of Tc-99m SC (Figs. 4a and 4b) show half-times of ~3 min. At 20 min, blood activity levels had decreased to less than 5% of that at time zero.

DISCUSSION

Alavi et al. (*1*) utilized a similar model to evaluate gastrointestinal hemorrhage in dogs, and reported detection of bleeding at rates from 0.05 to 0.1 cc/min. However, the procedure they used was different from ours. The blood disappearance rate for Tc-99m SC, due primarily to trapping in the liver and spleen, is rapid ($t_{1/2}$ = 3 min). Therefore, due to the time lag between the

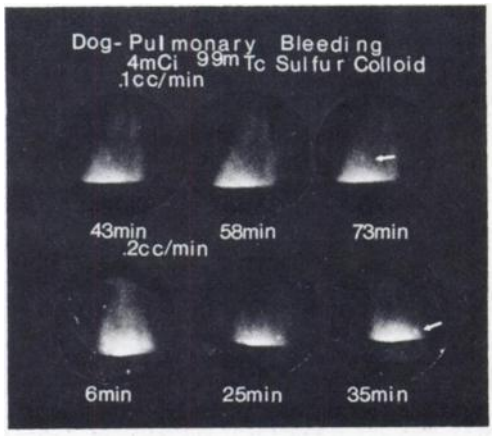

FIG. 3. Scintiphotos of lungs of two dogs given 4 mCi of Tc-99m SC I.v. Upper panel shows "pulmonary bleeding" at 0.1 cc/min, with site becoming visible in lower right lung (arrow) at 43 min. Lower panel shows images from dog "bleeding" at 0.2 cc/min, showing positive focus in lower left lung (arrow) at 25 min.

TABLE 1.

Tc-99m SC (mCi)	Flow rate (cc/min)	Time (min) at which bleeding site was detected (200 K cts)	(100 K cts)
15	0.8	4	*
15	0.5	15	27
15	0.4	Never	Never
15	0.4	2	4
15	0.2	5	*
15	0.11	30	*
15	0.1	Never	Never
4	0.5	18	32
4	0.4	33	Never
4	0.3	10	16
4	0.3	3	4
4	0.2	15	25
4	0.2	Never	Never
4	0.2	20	45
4	0.11	58	Never
4	0.05	Never	Never

* Data not available.

withdrawal and reinfusion of blood following an intravenous dose of the colloid, the activity of the infused blood will be greater than the background due to the in vivo blood pool. To simulate actual bleeding, the blood issuing from the catheter tip should have the same activity as the dog's blood at that time. In these experiments, an infusion pump was used to control the simulated bleeding rate and deliver radioactive intrapulmonary blood with activity as close as possible to that of the dog's background blood pool. Every 3 min venous blood was withdrawn for pulmonary infusion. If blood were withdrawn soon after the Tc-99m SC injection, and then reinfused for the duration of the experiment, the activity of the infused blood would be high compared to background, falsely improving the chance for visualization. Alavi attempted to eliminate this source of error by withdrawing arterial blood for a 12-min period before reinfusing it into the GI tract. This still created a high infusion-to-background activity ratio, since the mean activity of blood collected over a 12-min period is higher than the mean blood activity level during most of the infusion. This difference in experimental method may account for the slight difference in sensitivity between the tests (their threshold bleeding rates of 0.05 cc/min against the 0.1 cc/min reported here).

Assuming inconsequential time from blood withdrawal to insertion of the blood-filled syringe into the infusion pump, the maximum error in our model is due to the dead space in the catheter, which was 0.75 cc. At a high flow rate (0.8 cc/min), new blood reaches the catheter tip in less than one minute. At slow flow rates (0.1 cc/min), 7.5 min lapse before the catheter is filled. This implies a falsely high ratio of catheter-tip blood to background blood-activity ratio, since background Tc-99m SC blood levels will fall during 7.5 min.

To minimize this error at low flow rates, the catheter was partially filled with 0.5 cc of radioactive venous blood before the first, and only the first, infusion. This slightly increases the time that blood of higher activity

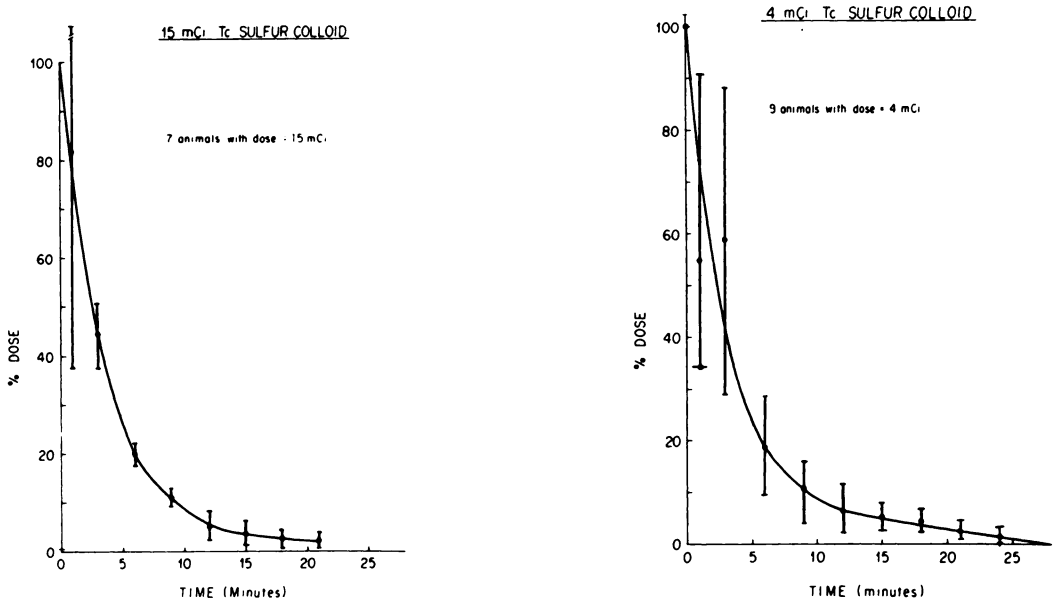

FIG. 4. (a) Blood disappearance curve for 15 mCi of Tc-99m SC injected intravenously in seven dogs. Ordinate is percent dose per ml of blood, scaled upward to reflect total blood volume. 50% of the activity has disappeared from blood by ~3 min after injection. Standard deviations are indicated by vertical lines. (b) Disappearance of Tc-99m SC from blood in 9 dogs injected with 4 mCi. Half-time is ~3 min. Standard deviations are indicated by vertical lines.

TABLE 2. THRESHOLD ACTIVITY REQUIRED FOR VISUALIZATION OF BLEEDING SITE. (DOSE = 4 mCi Tc-99m SC.)

Flow rate (cc/min)	Calculated threshold activity (total μCi)
0.5	6.9
0.3	2.3
0.3	1.5
0.2	8.5
0.1	2.1

is infused, but it greatly reduces the lag between the time that blood is withdrawn and the time that it leaves the tip of the catheter.

The results reported here, showing detection of hemorrhage at a bleeding rate of 0.1 cc/min, are in general agreement with the experimental literature evaluating gastrointestinal hemorrhage. Alavi and colleagues (*1*) reported visualization of bleeding rates of 0.05 to 0.1 cc/min using Tc-99m sulfur colloid. Winzelberg et al. (*2*), using Tc-99m-labeled red blood cells, detected hemorrhage in patients with transfusion requirements of 500 ml/day (0.35 cc/min [= 490 cc/day]). Utilizing labeled red blood cells in a rabbit model of GI bleeding, Winzelberg et al. (*3*) detected a total bleeding volume of 2 cc (1% of blood volume).

Winzelberg (*3*) made an attempt to estimate the smallest volume of blood that could be visualized, assuming a particular specific activity. Multiplying the smallest detectable volume seen by the μCi/cc of blood injected into the colon, the total detectable activity was estimated at between 1.3 and 1.9 μCi. Our results (Table 2) indicate that 2.1 μCi was the lowest activity that we could recognize in the simulated pulmonary hemorrhage. The amount ranged from 2.1 to 8.5 μCi in different dogs.

This wide range probably relates to the distribution and location of each bleeding site. Intrabronchial bleeding that had diffused over a larger space and was located deeper within the chest was more difficult to detect. A more concentrated and peripheral bleeding site was easier to image.

Technetium-99m sulfur colloid has been used successfully to detect venous hemorrhage not seen at angiography (*4,5*). The major advantages of this agent are its ready availability and rapid blood clearance, which facilitate visualization of an area of increased activity, except near the liver or spleen. Labeled red cells (*2,6*) have proven useful in chronic or intermittent bleeding and have been used to detect vascular tumors (*6*) and in hemorrhage in the extremities (*11*). In Denmark, Tc-99m-labeled albumin has been used successfully (*7,8*).

Agents that label the blood pool have the advantage of continued accumulation of activity at the bleeding site even hours after intravenous injection. Serial imaging can then be used to detect a bleeding site. These agents, however, have some disadvantages. The labeling technique requires time, a luxury often not permitted with an acutely hemorrhaging patient. With technetium-labeled red cells, the patient must be pretreated with perchlorate and should be maintained on nasogastric suction to prevent gastric technetium from passing into the intestine (*2*). Also, blood-pool images have high background activity that varies from organ to organ and makes detection of a small area of bleeding more difficult.

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