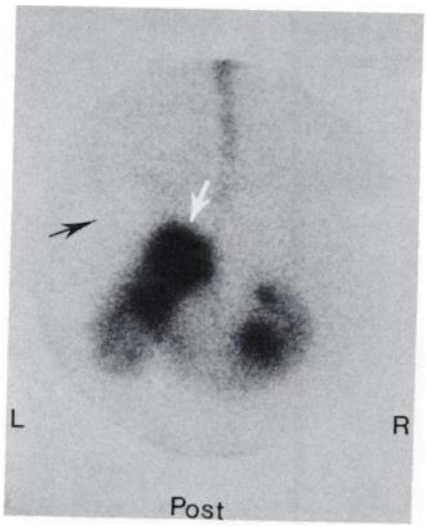

FIG. 3. Posterior scintigram after oral administration of Tc-99m DTPA to illustrate separation of stomach (white arrow) from photon-deficient area of perisplenic hematoma (black arrow).

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FOOTNOTE

*Mallinckrodt/Nuclear.

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Detection of Prethrombotic or Thrombotic States

The detection of prethrombotic or thrombotic states by laboratory methods has long been neglected. Von Kaulla and von Kaulla (*1*) have described a panel of procedures that evaluate various pertinent coagulation parameters and provide information useful for both diagnosis and treatment. The panel requires performance by well trained technicians, thus removing it from most laboratory situations. However, two tests within the capability of a routine clinical laboratory may provide useful information as to thrombin generation (a reflection of both the speed and amount of thrombin formed in plasma, and thus, by inference, extent of clotting) and loss of protective mechanisms that interfere with clotting. The first of these tests is the modified ethanol gelation test, and the second is the functional serum antithrombin assay (*1,2*). In the presence of active clotting, the ethanol gelation test is positive and the serum antithrombin III levels are depressed. Resolution is correlated with a return to normal levels. Heparin does not interfere with the assays.

Radionuclide techniques for thrombus detection offer the advantage of localization of thrombus formation, much as contrast venography does, but are severely limited by confinement to use in the lower extremities. Clots occur in many other areas. Tow (*3*) has well summarized the approaches using radionuclide techniques.

Caretta et al. (*4*) notes variable correlation of radionuclide findings with clinical results of anticoagulant therapy. This is not surprising in that such techniques ignore temporal patterns and physiologic bases of clot formation and dissolution. This limits the utility of the procedure.

Nuclear medicine is a discipline that merges laboratory, imaging, and physiologic approaches in delineating regional and global function for diagnostic purposes and in planning or implementing therapy. A limitation of focus of the discipline of nuclear medicine, as suggested by current approaches to thrombus detection, is self-defeating.

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A Qualitative Method for Determining the Level of Oxidant in a Solution of [^{99m}Tc] Pertechnetate

The presence of trace levels of oxidants in various sources of pertechnetate has often been blamed for the inability of some kit radiopharmaceuticals to bind the added technetium-99m adequately. Some years ago, many manufacturers of molybdenum-99–technetium-99m generators used trace levels of hydrogen peroxide or sodium hypochlorite (*1*) in the eluant to ensure that all the technetium would be in the form of pertechnetate and would therefore be

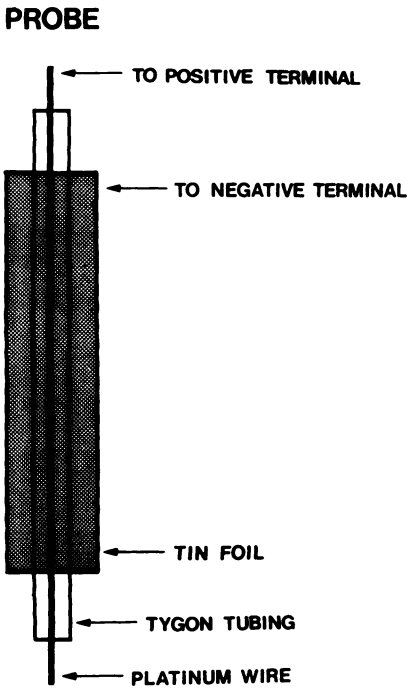

FIG. 1. *Construction of bimetallic probe.*

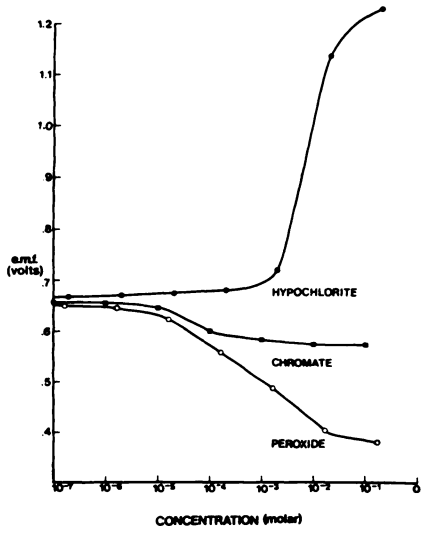

FIG. 2. *Voltages generated by bimetallic probe as a function of oxidant concentration in pertechnetate solution. Sensitivity and repeatability of individual determinations are primarily a function of accuracy and readability of voltmeter.*

eluted. More recently Boyd (*2*) has suggested the use of chromate. With the advent of radiopharmaceutical kits, the presence of oxidants in the pertechnetate solutions became a problem, and today many manufacturers try to avoid or minimize the use of oxidants. However, Tofe and Francis (*3*) reported the determination of oxidant levels of up to 38 ppm in generator eluant. Moreover, much of the "instant pertechnetate" is separated from the parent molybdenum by means of methyl-ethyl-ketone extraction incorporating the use of an oxidant, normally hydrogen peroxide. Any excess hydrogen peroxide should be destroyed in the evaporation of the methyl ethyl ketone. The possibility does exist, however, that this destruction may not always be complete. Thus the ability of pertechnetate to be bound in radiopharmaceutical kits may vary considerably both from one supplier to another and from one individual batch to another.

We have developed a test that permits rapid determination of the level of oxidant present in the pertechnetate, with only 0.1 ml of the pertechnetate solution. This test is capable of easily detecting oxidant levels of 10^{-4} *M*, while typical radiopharmaceutical kits use at least 2×10^{-3} m*M* of reductant or 1 mg of stannous chloride. New England Nuclear glucoheptonate has only 0.1 mg of stannous chloride, and Proctor and Gamble's Osteoscan has only 0.16 mg. Thus, the level of detection of oxidant is more than an order of magnitude lower than that which would neutralize the reductant if 10 ml of eluate were used in the kit (most kits call for a maximum volume of 8 ml or less).

The equipment needed is:

1. 1 voltmeter with an accuracy of ±0.01 V in the 0–1.0 volt range and at least 100,000 Ω/V input impedance;
2. 1 ultrasonic bath;
3. 1 short piece of pure tin;
4. 1 piece of tygon tubing; and
5. 1 short piece of platinum wire.

The platinum wire is inserted into the tygon tubing with both ends extending beyond the tubing. The piece of tin is wrapped around the tubing, as in Fig. 1, care being taken to ensure that the platinum wire and the tin do not touch. In this way a compact bimetallic probe is formed. The test is conducted as follows: 0.1 ml of the eluate is added to 0.1 ml of 0.056 *N* sodium pyrophosphate in a 10- × 75-mm culture tube. One end of the bimetallic probe is inserted into the solution, immersing both metals, while the free end is connected across the terminals of the voltmeter, the platinum wire to the positive terminal and the tin foil to the negative. The culture tube containing the probe is then placed in the ultrasonic bath and the voltage between the metal electrodes read. Figure 2 shows the observed voltages as a function of concentration of hydrogen peroxide, chromate, or hypochlorite.

TABLE 1. BINDING EFFICIENCIES OBTAINED USING NEW ENGLAND NUCLEAR POLYPHOSPHATE AND GLUCOHEPTONATE KITS WITH PERTECHNETATE OF VARIOUS VOLTAGE VALUES

	Binding Efficiencies	
Voltage value	Polyphosphate	Glucoheptonate
0.600	43.5	1.1
0.625	84.7	13.6
0.640	99.0	98.6
0.670	99.6	92.2
0.675	99.0	22.4
0.700	98.6	14.8
0.740	95.0	0.6

Table 1 shows the binding efficiencies obtained using pertechnetate solutions that had been treated with traces of hydrogen peroxide or sodium hypochlorite to give various voltage readings coupled with New England Nuclear polyphosphate and glucoheptonate kits. In each case, half the maximum volume of pertechnetate recommended was used. It is evident from these data that a voltage outside the range of 0.64–0.67 V indicates an oxidant level that might interfere with radiopharmaceutical labeling, and the pertechnetate should not be used in conjunction with radiopharmaceutical kits.

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Sterilization of Technetium-99m-Labeled Human Serum Albumin by Filtration

Sterilization of technetium-99m radiopharmaceuticals by filtration is a widely used, convenient, and practical technique. One of the most widely used filters for this purpose is the Millipore MF filter with a 0.22-μm pore size. We have found, however, that these Millipore filters suffer from a tendency to chemically absorb a certain amount of human serum albumin (HSA). While this may be unimportant in preparations containing relatively large amounts of human serum albumin (either low-specific-activity or large-quantity preparations) it is very important in small HSA preparations of high specific activity. In this case, a significant amount of the radiopharmaceutical will be retained by the filter, thereby giving a reduced concentration of the product and making necessary a larger injection volume.

TABLE 2. WEIGHT OF ALBUMIN ABSORBED ON MILLIPORE FILTERS

	1st Filter (mg)	2nd Filter (mg)	3rd Filter (mg)
Preparation A			
Calculated weight from radioactivity loss	0.84	0.79	0.81
Experimentally determined weight	0.9	0.8	0.8
Preparation B			
Calculated weight from radioactivity loss	0.72	0.77	0.52
Experimentally determined weight	0.7	0.7	0.5

This phenomenon was investigated using two Tc-99m HSA preparations of different specific activity and two types of sterilizing filters. Preparation A contained 1.4 mg albumin/ml while preparation M contained 0.56 mg albumin/ml, both being prepared using electrolytic labeling with tin electrodes. The sterilizing filters were Millipore MF 0.22 μm, a type prepared from mixed acetate and nitrate esters of cellulose, and Nucleopore 0.2 μm, which is a polycarbonate membrane in which the holes have been produced by an irradiation and etching process. Four milliliters of each Tc-99m HSA solution were passed through a series of three filters of the same type, and the radioactive concentration and percentage of Tc-99m bound to albumin were determined after each filtration. The results recorded in Table 1 show that the Millipore filter removes a relatively large portion of the radioactivity while the Nucleopore filters show no such retention. The radioactive concentration of the solution passing through each filter may be used to calculate the weight of albumin represented by the reduction in radioactive concentration using the equation:

$$\text{Weight of albumin on filter} = \frac{C_o - C_x}{C_o} \times W_o$$

where: C_o = radioactive concentration before filtration; C_x = radioactive concentration after filtration; and W_o = total weight of albumin in preparation before filtration.

Table 2 shows the weight of albumin retained by the Millipore filters, estimated both by the foregoing calculation

TABLE 1. FILTRATION OF TECHNETIUM-99m HUMAN SERUM ALBUMIN

Millipore MF	Conc. before filtration mCi/ml	% Tc bound to albumin	Conc. after 1st filtration mCi/ml	% Tc bound to albumin	Conc. after 2nd filtration mCi/ml	% Tc bound to albumin	Conc. after 3rd filtration mCi/ml	% Tc bound to albumin
Preparation A	3.25	99.5	2.76	99.7	2.30	99.0	1.83	99.3
Preparation B	6.67	98.4	4.53	98.7	2.23	98.7	0.68	98.0
Nucleopore								
Preparation A	3.14	99.4	3.04	99.6	3.03	99.5	3.01	99.4
Preparation B	6.45	98.0	6.34	98.2	6.30	98.1	6.29	98.3