jnm/ PRELIMINARY NOTE

Diagnosis of Deep-Vein Thrombosis with Sodium Pertechnetate

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Sodium pertechnetate was used to image venous thrombosis in the legs of 20 patients with clinical signs of deep-vein thrombosis. The rate-of-uptake ratios and the activity ratios at 3 min and 4 hr after the injection were calculated. Venography was used as a standard. Discrimination, as well as agreement with venography, was highest for the ratios obtained 4 hr after injection, in which case there were ten patients with a pathologic activity ratio and with venographic signs of thrombosis in the leg with increased uptake. There were six with a normal activity ratio and no venographic signs of thrombosis, but one patient had a normal ratio and abnormal venography.

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Sodium pertechnetate has been shown to localize in infarcted cerebral tissue (*1*). In the present study we tested the hypothesis that this substance could also show increased uptake in the distribution area of thrombosed peripheral veins. The tracer was used in patients with clinical findings suggestive of deep-venous thrombosis in the legs and the results were compared with those obtained by radiographic venography.

MATERIALS AND METHODS

Twenty patients were studied. As a rule, the scintigraphic investigation was performed 5 days after the onset of symptoms and was followed by venography during the ensuing 5 days.

All patients were studied scintigraphically with 10 mCi of $Na^{99m}TcO_4$ and venographically with the technique described by Nylander (*2*). The activity in a volume of 1–3 ml was injected as a bolus into a brachial vein with the patient in the supine position. During the first 3 min after the administration, sequential scintigrams of the lower legs were recorded at 20-sec intervals using a high-resolution collimator (15,000 parallel holes) and a scintillation camera interfaced to a minicomputer system.* Four hours later, an anterior view of the lower legs was obtained. Each single exposure was completed within 15 min and contained at least 300,000 counts.

The calculation was performed using activity values obtained from regions of interest of a standard rectangular form, as seen in Fig. 1A. Rates of uptake were defined by (A) the steepness of the activity–time curve at the point of inflection, and (B) the amount of activity at 3 min or 4 hr after injection. The rate-of-uptake ratio is the maximal slope for the involved leg divided by that for the normal leg.

After correcting for room background in the 4-hr uptake study, the activity in the leg with clinically suspected thrombus was divided by the activity in the corresponding zone in the other leg. Since the regions were moved laterally over each leg until maximal count values were obtained, the count rates thus measured were quite reproducible and independent of the investigator. The uncertainty of an

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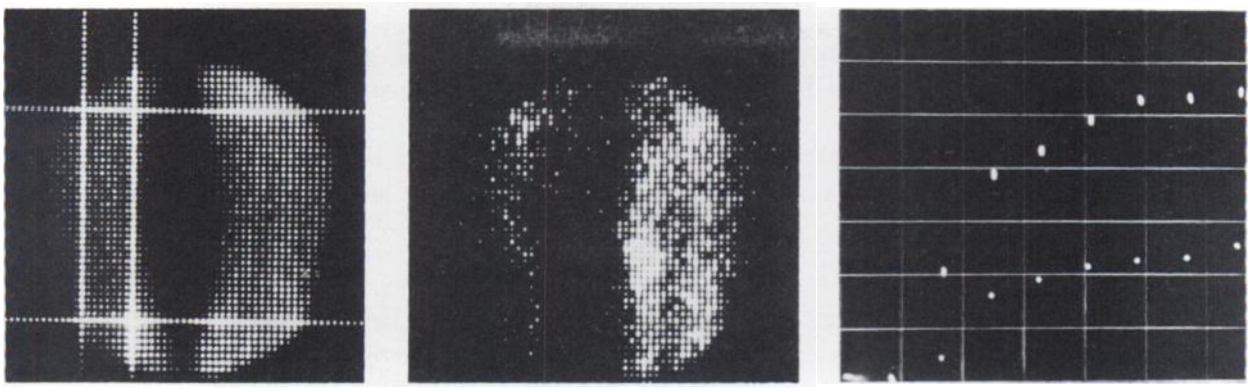

FIG. 1. (A) Venous thrombus in left leg. Moderate activity ratio = 1.62. (B) Image of same patient in third 20-sec interval. Increased, and more rapid, uptake of radioactivity is seen in leg with thrombus. (C) Time–activity curves representing early uptake in lower legs of same patient during first 3 min after administration. Vertical bars indicate uptake of activity in leg with thrombus; dots, in leg without thrombus. Vertical scale in units of 800 cpm. Rate-of-uptake ratio was 2.5. Activity ratio at 3 min was 2.1.

TABLE 1. DATA FOR 20 CASES WITH CLINICALLY SUSPECTED THROMBOSIS

Sex	Age	Rate-of-uptake ratio	Activity ratio		Venography	Main location of thrombus
			3 min after injection	4 hr after injection		
F	92	1.1	1.2	1.22	Pos.	Calf
F	83	1.9	1.6	1.78	Pos.	Entire leg
F	40	0.40	0.76	1.53	Pos.	Calf
F	70	1.1	1.0	1.18	Pos.	Calf
F	56	2.1	1.9	2.64	Pos.	Calf
F	74	2.0	1.4	1.83	Neg.	
F	57	1.3	1.0	1.05	Neg.	
F	65	1.3	0.90	1.04	Neg.	
F	73	0.95	1.1	1.11	Neg.	
F	83	1.1	1.2	1.21	Neg.	
M	56	1.9	1.0	1.51	Pos.	Calf
M	80	1.2	1.3	1.18	Pos.	Thigh
M	62	2.5	2.1	1.62	Pos.	Entire leg
M	76	1.6	1.1	0.98	Pos.	Thigh
M	59	Not performed		1.45	Pos.	Calf
M	76	1.7	1.6	1.66	Pos.	Entire leg
M	72	2.2	1.1	1.07	Neg.	
M	63	1.1	1.2	1.13	Neg.	
M	39	1.9	1.2	0.87	Neg.	
M	69	1.4	1.5	1.25	Neg.	

activity value due to lateral positioning of the region of interest was small compared with the random error (s.d.). The activity ratios were considered abnormal if they exceeded 1.15, while values between 0.87 and 1.15 were considered normal. Pathologic differences are not always visible in a scintigram; hence the need for a digital system.

Due to good counting statistics the standard deviation of the ratio never exceeded 0.01.

RESULTS

Table 1 lists the rate-of-uptake ratios and the activity ratios at 3 min after injection, as well as the ratios for the 4-hr uptake study. Generally there is more rapid accumulation in the thrombosed leg, especially when the entire leg is involved. Figure 1 illustrates a case with a thrombus in the left leg. For this patient the activity ratio is moderate. Figures 1B and 1C show faster and earlier increased uptake of radioactivity in the thrombosed leg of the same patient.

Table 2 gives the results of the 4-hr uptake study compared with those obtained with venography, and shows that ten patients with abnormal activity ratios had venographic evidence of thrombosis. In this group the ratios ranged from 1.18 to 2.64. The range was 0.87–1.13 in the group of six patients with nor-

TABLE 2. CORRELATION OF ACTIVITY RATIO WITH VENOGRAPHY (FIGURES GIVE NUMBERS OF PATIENTS)

	Venography		
Activity ratio	Postive	Negative	Total
>1.15	10	3	13
<1.15	1	6	7
Total	11	9	20

mal activity ratios and without venographic signs of thrombosis. There were three patients who had no venographic evidence of thrombosis but activity ratios that ranged from 1.21 to 1.83. Finally, there was one patient with an activity ratio of 0.98 in whom venography revealed a thrombus.

DISCUSSION

This work was undertaken to evaluate the influence, if any, on the activity ratio of significant amounts of sodium pertechnetate present as impurities in ^{99m}Tc-labeled streptokinase (*3*). For practical reasons, therefore, only the lower legs were viewed. The results suggest that sodium pertechnetate tends to localize in the distribution area of thrombosed veins.

The study of each patient consisted of two phases: one concerning accumulation during the first 3 min after injection, the other measuring uptake at 4 hr. When the rate-of-uptake ratio was 1.2 or greater, it was considered pathologic. This was the case in seven of the ten patients with a venographically proven thrombus. The activity ratio 3 min after injection was considered pathologic if it was 1.2 or greater. This was the case in six of ten patients. In only five patients were both parameters pathologic and consistent with the detection of thrombosis. Dilated vessels and passive venous congestion may be factors that contribute to rapid and early increased uptake of radioactivity in the thrombotic leg. Finding increased uptake 4 hr after injection, however, is an indication of thrombosis superior to the findings of faster and early increased uptake. In 16 of 20 patients the results of the scintigraphic study at 4 hr were in agreement with those of venography (see Table 2). Binomial sampling theory (*4*) gives $p < 0.05$.

The method does not seem to be specific, since there were three false pathologic results as checked by venography. This suggests limitations similar to those of comparable methods—fibrinogen tagged with radioactive iodine, for example, gives increased uptake in conditions such as healing fractures, hematomas, and arthritis (*5*). Two patients outside the present study, one with osteitis in the foot and the other with gangrene in the leg, were also classed as pathologic when studied with sodium pertechnetate.

There were six patients with normal results for both scintigraphy and venography. Four of the six met two of the following clinical criteria indicative of deep-vein thrombosis: local edema, pain, and raised skin temperature. This is of interest since the above-mentioned lack of specificity otherwise would seem to deny the clinical usefulness of the method. In only one patient did scintigraphy fail to detect a thrombus shown by venography to be in the femoral vein; this was probably because in this series only the lower legs were viewed.

In the group of patients judged normal both by activity ratio and venography, the mean activity ratio was 1.04 and was thus slightly increased, presumably due to various nonthrombotic processes in the leg in which a thrombus was suspected. Alternatively small thrombi may have been overlooked at venography in this group as well as in the group with pathologic uptake and negative venography. However, although there seems to be some risk of overlooking small thrombi in the soleus sinusoids or in the superficial venous system (*6*), radiographic venography is generally regarded as reliable and is a standard reference method.

Admittedly the number of patients in the present study is small. If our findings are reproducible in a larger-scale investigation, however, sodium pertechnetate may find a place in screening for deep-vein thrombosis.

The solutions to the theoretic problems encountered during the search for ideal agents for radioactive detection of thrombi have hitherto been met by preparing labeled substances from involved constituents in the processes of thrombus formation and degradation. A successful example in the former category is fibrinogen labeled with radioactive iodine (*5*). Less is known about the clinical value of exponents in the latter category, such as ^{99m}Tc-labeled urokinase (*7*) and streptokinase (*8*). The assumption underlying the exploration of these substances seems to be that they specifically participate either in structuring or dissolving thrombi.

In contrast, sodium pertechnetate is not known to take part in these processes, and the factors promoting activity uptake in an area of thrombosis are unknown. This uptake cannot reasonably be attributed to properties unique to sodium pertechnetate. Thus, increased uptake of ^{99m}Tc-tripolyphosphate in the thrombosed leg has recently been reported (*9*). Accordingly, it may be pertinent to raise the question of whether the alleged biochemical specificity of the

hitherto used radiopharmaceuticals is a prerequisite in the radioactive demonstration of thrombi.

FOOTNOTE

* Intertechnique, Ciné-200.

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