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IN VIVO TRANSFER OF RADIOSELENIUM, Se^{75}, ACROSS THE PERICARDIUM OF DOGS*

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Whereas the exact significance of trace elements is currently indeterminable, there is little doubt that proper assessment of their physiologic importance can not be effected until more is known of their behavior in living systems. For these reasons we have begun studies of biokinetic aspects of selenium. This report is concerned with some aspects of the *in vivo* transfer of Se^{75} across the pericardial membrane of dogs.

Material and Methods

Radioselenium, Se^{75}, (T ½ = 127 days) was obtained from Oak Ridge National Laboratories as H_2SeO_3 in hydrochloric acid and neutralized with sodium hydroxide. Gamma ray spectrometric and physical decay studies confirmed the identity of the isotope.

Mongrel dogs weighing 9–20 kgm were used. Anesthesia was initially effected with intravenous pentobarbital (30 mgm/kgm) and maintained when necessary with supplementary doses of pentobarbital administered by the same route. After insertion of a tracheotomy tube, respiration was assisted with a Harvard respirator. An indwelling polyethylene catheter was placed in the femoral vein to obtain serial samples of whole blood. The pericardium was exposed through a thoracic incision, a small soft polyethylene catheter inserted into the pericardial cavity and the tip advanced to the dorsal surface of the heart. After removal of indigenous pericardial fluid, the catheter was fixed in place with a leak proof purse string sutures, and fifty cubic centimeters of physiologic saline containing approximately 0.3 microcuries of Se^{75} and 0.00105 mgm of selenium were introduced into the pericardial sac. The surgical incision was closed immediately. Serial samples of the pericardial fluid were aspirated at 3, 5, 10, and 30 minutes, thereafter at 30 minute intervals for a total of 240 minutes. Samples of venous blood were obtained at 30, 60, 120, 180, and 240 minutes. During the course of the first experiment both pericardial and venous samples were obtained more frequently during the first hours but showed so little change that the latter schedule cited above was followed in all subsequent studies. At the end of the experiment all residual pericardial fluid was collected. Selected tissues were removed, washed with normal saline solution, blotted dry and weighed.

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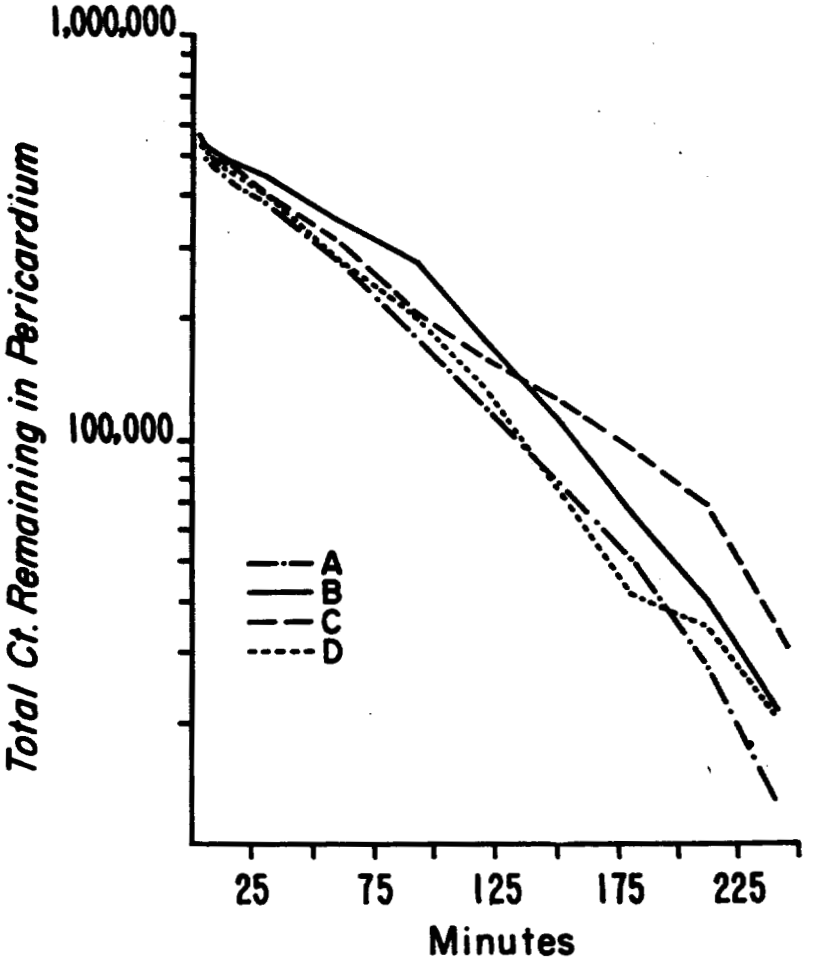

FIG. 1. Time course of changes over a four hour period in total Se^{75} remaining within the pericardium of four dogs. These curves were derived after correction for volume aspirated for sampling and for that volume transferred out of the pericardial cavity. In the latter instance the rate of spontaneous volume change was assumed to be constant throughout the experiment.

Blood samples were collected with heparin (0.1 mgm/5cc) as the anticoagulant. After centrifugation the plasma was removed for counting. Erythrocytes were washed three times with normal saline before counting. Pericardial fluid and urine were counted as obtained. Tissues were digested with concentrated nitric acid and heating, excess nitrates being driven off with formic acid according to the method of Sheppard and Martin (1). All counting was done with a scintillation detector, using methods previously described (2).

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Results

The time course of change in concentration of total Se^{75} in the pericardial fluid in four dogs is presented in Figure 1. These curves were calculated after correction for the volume of fluid aspirated for sampling and for that volume transferred out of the pericardial cavity. In the latter instance the rate of spontaneous volume change was assumed to be constant throughout the experiment. The calculations in Table 1 were made under the same circumstances. In Figure 2 is

TABLE 1

Dog	Se^{75} transfer (Part/min)*	Fluid lost by Diffusion (cc)
A	.0042	17.5
B	.0041	27.0
C	.0035	28.0
D	.0041	25.0

* Part of initial amount in pericardial cavity transferring per minute.

plotted the actual time course of change in Se^{75} concentration per cubic centimeter of pericardial fluid. It must be noted, however, that these plots represent the summation of several simultaneously operating processes. These include the normal exchange of presumably isotonic fluid and its solutes and water between the circulating blood and the pericardial cavity, the production of an inflammatory exudate by the slightly traumatized pericardium caused by the surgery and the small indwelling sampling catheter, and the direct combination of Se^{75} with the tissues of the heart including the pericardium. There may have been increasing toxic damage of the pericardial membrane by selenium.

Table 2 summarizes the results of selected tissue assay for Se^{75}. It will be seen that traces of the isotope were found in several organs. However, all counts are rather low. This is largely related to the low dose of isotope administration. Nevertheless, one can conclude that the topical application of selenium to the heart and pericardium under the circumstances of these experiments does not result in cardiac tissue binding to a striking degree, nor even to that found for cadmium (3).

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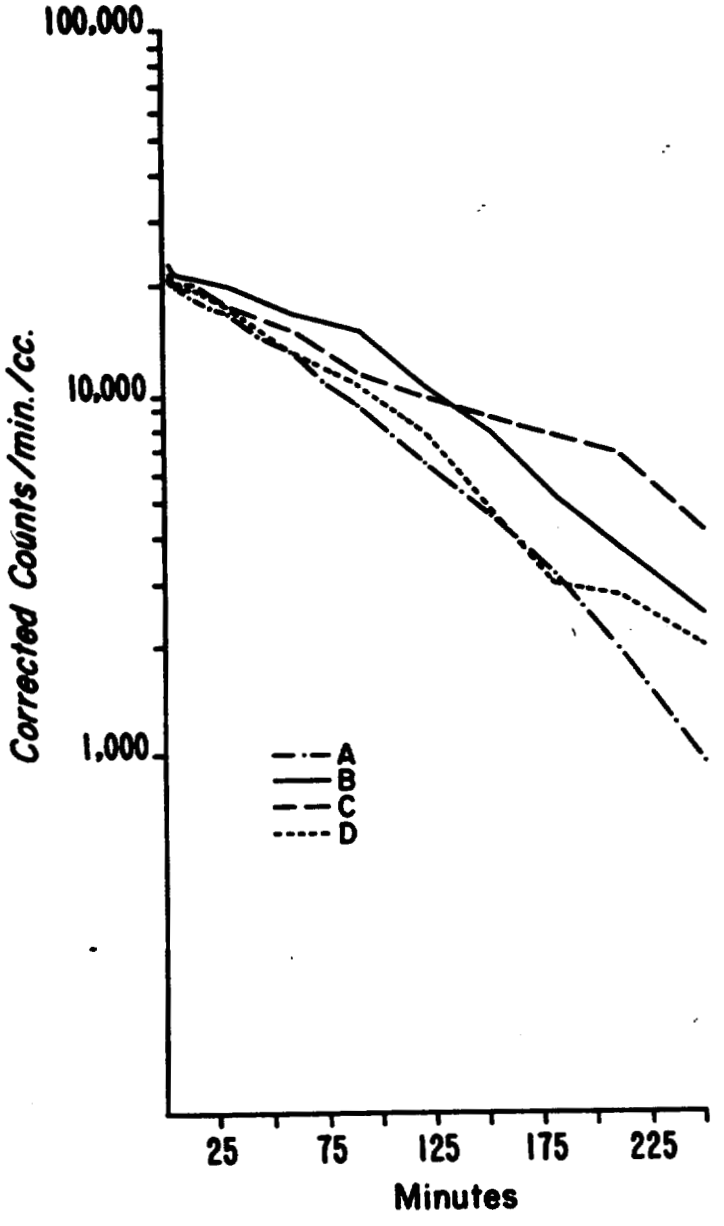

FIG. 2. Time course of changes in Se^{75} concentration per cubic centimeter of pericardial instillate in four dogs. The observation period was four hours.

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TABLE II

Se^{75} content of selected organs expressed in counts per minute per gram of tissue

	A	B	C	D
Liver	-	-	990	589
Spleen	-	-	314	237
Kidney	-	-	138	143
Pancreas	-	-	391	138
Rt. auricle	-	0	198	116
Lt. auricle	-	0	297	649
Rt. ventricle	-	0	220	391
Lt. ventricle	-	0	297	237
Septum	-	0	424	204
Pericardium	-	0	396	127

Serial studies of whole blood, plasma and erythrocytes indicated that the isotope was detected in the blood thirty minutes after the beginning of the experiment and that a low level of radioactivity persisted throughout the observation period in plasma and erythrocytes. Urine obtained at the conclusion of the experiment was assayed in one dog and found to contain a trace of Se^{75}.

Discussion

Previous investigations in our laboratories have utilized these techniques in studies of the kinetics of transfer of Mg^{28} and Cd^{115M} (3), as well as those of Rb^{86}, K^{39}, Na^{24}, Na^{23}, Cl^{36} and Cl^{35} (4) across the pericardium of the dog. In every instance considerable information was obtained relative to the biokinetic behavior of these elements. Probably of even more basic importance is the information obtained concerning the behavior of membranes generally. The single layer of serosal cells which comprise the pericardium is well suited for such studies and simple to employ but still complex to understand.

Small doses of selenium were used in this investigation since it was considered that the use of trace amounts of a trace substance would more closely reflect the physiologic state. The behavior of Se^{75} is described in this current study. It is entirely in keeping with other studies with this isotope conducted in our own laboratories (5, 6) and adds

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knowledge of those elements of borderline significance. Probably the most interesting observation of this experiment is the ubiquitous distribution of administered Se^{75}. It is evident that metabolic mechanisms exist which make it possible for the organism to handle selenium. These mechanisms are little known and understood.

Summary

Measurements of the rate of transfer of Se^{75} across the pericardium of the dog indicated a rather complete removal of this substance from the pericardial instillate over a period of four hours. Trace amounts of the element were demonstrated in the plasma, erythrocytes and selected organs of the dog.

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