tentials can be often isolated in succession over a distance of 1–2 mm.

These electrodes have also been used to study action potentials in rat muscle *in situ* (*10*). In normal muscle at rest, no electrical activity was detected. In chronically denervated muscle, shown by conventional electrodes to be fibrillating, spontaneous potentials were recorded. Most commonly these were diphasic spikes (Fig. 2), the large initial deflection being positive, and they recurred in totally irregular rhythm at a rate averaging about 6/sec.

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Modification of the Distribution and Excretion of Radioisotopes by Chelating Agents[1]

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When the sodium salt and calcium chelate of ethylenediamine tetraacetic acid (EDTA) are administered intravenously to man, an equivalent amount of calcium is rapidly excreted by the kidneys (*1, 2*). Lead-EDTA and yttrium EDTA have been demonstrated to leave the body quite rapidly when injected intravenously (*3, 4*). Furthermore, when carbon^{14}-labeled EDTA is injected into animals, 99% is excreted in 48 hr (*5*). It was, therefore, rather unexpected to find in the course of our work on the distribution and excretion of lanthanum (*6*) in man, that less than 10% of the lanthanum is excreted through the kidneys when lanthanum-EDTA is intravenously administered, and it was decided to investigate this effect further.

A tracer dose of 200 μc lanthanum^{140} as the EDTA complex was injected intravenously. The patient was catheterized to facilitate accurate urine collections. Urine and blood samples were collected at frequent intervals until the activity was no longer measurable. After 48 hr, the urinary excretion of lanthanum^{140} had become negligible. However, only about 5% of the injected lanthanum^{140} dose had been excreted up to that time, as indicated in the lower curve of Fig. 1.

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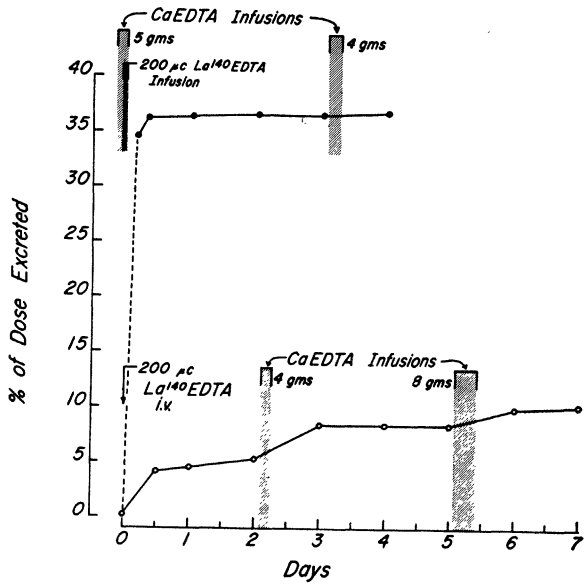

FIG. 1. Effect of calcium-EDTA upon the cumulative urinary excretion of lanthanum^{140}-EDTA. The upper graph illustrates the effect of preceding and *simultaneous* administration, and the lower graph that of *subsequent* infusions of calcium-EDTA.

At this time, 4 g of calcium-EDTA in 500 ml of a 5% solution of glucose in water were infused in 3 hr. Immediately after the start of the infusion, the rate of urinary excretion of the lanthanum^{140} rose by a factor of approximately 100, as shown in Fig. 2. By the 5th day, urinary excretion had again become negligible, and a 7-hr infusion of 8 g of calcium-EDTA in 1000

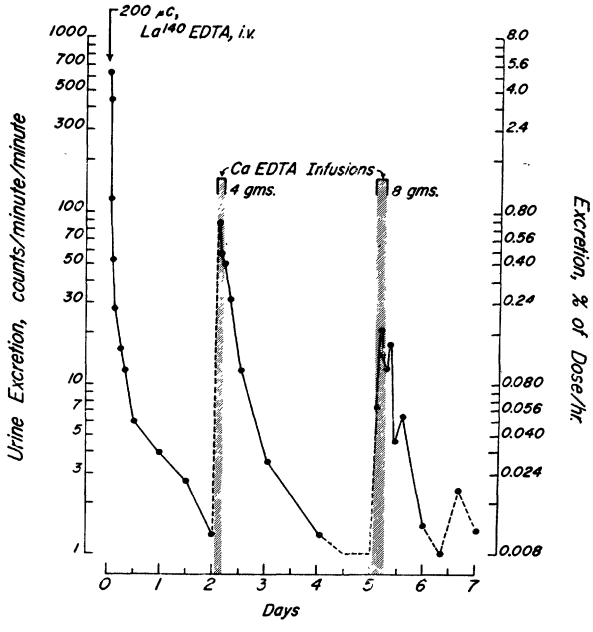

FIG. 2. Influence of calcium-EDTA upon the rate of urinary excretion of lanthanum^{140}-EDTA, expressed in terms of measured radioactivity and of the proportion of the total dose excreted per hour.

ml glucose solution was given. As Fig. 2 shows, the urinary excretion of lanthanum^{140} rose rapidly once more. The short half-life of lanthanum^{140} (40.4 hr) resulted in low counting rates and large statistical errors so that the irregular shape of the excretion curve after the last infusion has no true significance.

When lanthanum^{140} was injected as the chloride instead of the EDTA, less than 5% of the injected dose was excreted through the kidneys over a period of 48 hr. However, subsequent calcium-EDTA infusions were equally effective in enhancing urinary excretion of lanthanum^{140}.

Although the response to calcium-EDTA infusions in promoting lanthanum^{140} excretion is quite definite, the *total* amount of lanthanum^{140} excreted is only of the order of 10–15%. It was found that shortening the time interval between injection of lanthanum^{140} as lanthanum-EDTA or lanthanum chloride and the subsequent infusion of calcium-EDTA increased the total lanthanum^{140} urinary excretion. In an effort to further enhance lanthanum excretion, calcium-EDTA was administered *simultaneously* with, and in part, even prior to the lanthanum^{140} EDTA infusion.

A "priming" dose of 3 g of calcium-EDTA in 300 ml glucose solution was infused in 2.5 hr and was followed by a 1.5-hr infusion containing 2 g of calcium-EDTA and 200 μc lanthanum^{140}-EDTA. The immediate urinary excretion of lanthanum^{140} was found to be rapid. Approximately 37% of the total activity was eliminated in the first day, about 30% being excreted in the first 4 hr as may be seen in the upper curve of Fig. 1.

These results are in qualitative agreement with decontamination studies using iron^{59} and yttrium^{91} (*7, 8*). From the above results, as well as from current distribution studies in animals using lanthanum-EDTA and lanthanum chloride, it seems that the lanthanum in the lanthanum-EDTA complex can be replaced in significant amounts by physiological competitors such as calcium. Experiments with calcium^{45} as a tracer indicate that the calcium bound to EDTA is capable of prompt exchange with the calcium depots of the body (*2*). Therefore, it seems reasonable to assume that calcium exchanges also with lanthanum^{140}. The somewhat stronger bond formed by lanthanum with EDTA at physiological pH values does not rule out the possibility of calcium exchange by virtue of the law of mass action. Such an effect has not been reported for the lead-EDTA and yttrium-EDTA complexes, probably because of the greater affinity of these metals for the chelating agent.

The renewed excretion of lanthanum^{140} following the infusion of calcium-EDTA may be explained by the exchange of lanthanum^{140} for calcium; lanthanum which has been deposited in the bones and other tissues may thus once again form lanthanum-EDTA and be excreted. The equal effectiveness of calcium-EDTA infusions in promoting excretion of lanthanum following lanthanum chloride as well as lanthanum-EDTA injections would seem to support this hypothesis. When large amounts of calcium-EDTA and tracer amounts of lanthanum-EDTA are infused simultaneously, the increased amount of EDTA available for combination with lanthanum reduces the possibility of lanthanum remaining in ionic form and consequently the kidneys excrete more lanthanum in form of lanthanum-EDTA. Yet, even under these conditions, only 40% of the lanthanum is excreted and it would appear that, in addition, some irreversible binding or absorption of lanthanum occurs in the organism.

The fact that the effectiveness of lanthanum-removal by this chelating agent (EDTA) decreases with time, suggests its use as an investigative tool. Metals with different chelating tendency and affinities to body constituents (extra- or intracellular) will be removable in varying quantities, depending upon the specific properties, relative strengths, amounts, and time of administration of the complexing agents employed. That is, a given chelating agent will be effective only until the metal becomes physically or chemically unavailable. Furthermore, the prompt removal by chelating agents of excess radioisotopes subsequent to their administration in therapeutic doses suggests itself as a general method of changing the relative distribution, radiation efficiency and biological half-life of such isotopes. The use of chelating agents may thus permit the administration of isotopes of longer "physical" half-life to humans than has previously been considered safe.

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Colloidal-Size Silica in Sediments

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For many years students of sedimentation have questioned the role of colloidal silica in sediments. Most workers believe that dissolved silica is transported and precipitated in colloidal form. Very little is known about the amount of silica which is precipitated as a colloid. A recent study by Roy (*1*) indicates that silica in natural waters is in true solution, probably as an SiO_3^{2-} ion. In light of this study by Roy, the problem of chemical silica in sediments should be re-evaluated.

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