C reductase activity by aged kidney homogenates may be related to changes in permeability of the mitochondrial membrane for the substrate or other intermediates. An essentially similar suggestion has been made by Chance and Hagibara(6) who found that succinate linked pyridine nucleotide reduction in aged mitochondria may be enhanced by additions of ATP. On the other hand, the aging effect is also consistent with the possibility that a second form of the enzyme may be liberated similar to that found in the lactic dehydrogenase family of isozymes(7). Many other hypotheses may be suggested, but it is not possible at this time to offer an explanation for the aging effect, and clarification of this phenomenon must await further study.

Summary. The succinic cytochrome C reductase activity of rabbit kidney and liver homogenates is significantly greater in homogenates aged for 48 hours at 4°C than when freshly prepared. Enzyme activities are greater for freshly prepared kidney and liver homogenates in fed animals than in animals starved for 10 days, but the activity in aged preparations for tissues of fed or starved animals is not significantly different. These data suggest the need for caution in comparison of enzyme activities of tissues from animals in different physiological states.

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Interference with Fecal Excretion of Zn^{65} by Cadmium.* (27854)

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Although cadmium has long been known as a toxic element, recent interest has been aroused in its destructive effects on the testis (1-3). The damaging effects on this organ have been shown to be due to competition with zinc, since testicular destruction by cadmium can be prevented(1), at least temporarily(2), by simultaneous administration of large doses of zinc. Interference with zinc metabolism in this organ was also confirmed by a permanent decrease in the capacity of this organ to take up administered Zn^{65}(4,5). The Zn^{65} concentrating capacity of another organ, the dorsolateral prostate, a gland particularly rich in zinc(6), was also depressed by the presence of cadmium(4). This depression was shown to be by a 2-fold mechanism; one by virtue of cadmium damage to Leydig cells resulting in prostatic atrophy and lowered Zn^{65} uptake, the other by means of a direct competition between cadmium and zinc at the dorsolateral prostate level. That there was no direct morphological damage by cadmium on the dorsolateral prostate was shown by normal appearing cells in cadmium-treated castrates maintained on testosterone. Zn^{65} uptake studies in these animals showed, however, that altered Zn^{65} uptake can occur even in the face of normal histology(4). Although the doses of cadmium which produce acute destruction of testis do not evoke obvious morphologic damage to liver, kidney or pancreas(3), it was of interest to determine whether, nevertheless,

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there may be a functional derangement in the capacity of these organs to take up Zn^{65}.

Materials and methods. Zn^{65} uptake in rats previously treated with cadmium. Two groups, each consisting of 7 mature, male Wistar rats (350-400 g), were used in these studies. One group received a single subcutaneous injection of $CdCl_2$ (0.03 mM/kg). The other group, injected with physiological saline, served as controls. Four months later both groups were injected intracardially with approximately 0.01 μc/g of Zn^{65}.† They were sacrificed 24 hours later for Zn^{65} uptake determinations in liver, pancreas, kidney and skeletal muscle. Tissues were dissected, dried at 110°C, weighed and counted in a large well-type scintillation detector. Similar studies were conducted in which the cadmium was administered 1 week prior to, 1 day prior to, or at the same time as the Zn^{65}.

Zn^{65} uptake in rats subsequently challenged with cadmium. Four groups, each consisting of 7 mature, male Wistar rats (350-400 g), were used in these studies. All 4 groups were injected intracardially with approximately 0.01 μc/g of Zn^{65}. Twenty-four hours later, 2 of the groups received intracardial injections of $CdCl_2$ (0.018 mM/kg). The other 2 groups, serving as controls, received intracardial injections of physiological saline. One of the cadmium groups and one of the control groups were sacrificed 5 hours following the cadmium or saline injection. The other cadmium and control groups were sacrificed 48 hours following injection. Samples of liver were dissected, dried, weighed and counted as described in the previous section.

Fecal excretion of Zn^{65} in rats subsequently challenged with cadmium. Fourteen mature, male Wistar rats (350-400 g) were injected intracardially with approximately 0.01 μc/g of Zn^{65}. Fecal excretions were collected daily. Four days after the Zn^{65} injection, half of the rats were administered $CdCl_2$ (0.03 mM/kg) by the subcutaneous route.

† Zn^{65} was purchased from Union Carbide Nuclear Co. as $Zn^{65}Cl_2$ in HCl solution with a specific activity of approximately 500 mc/g. The solution was diluted with physiological saline containing sufficient NaOH to neutralize some of the acid present compatible with solubility.

TABLE I. Zn^{65} Uptake in Tissues of Rats Injected 4 Months Previously with Cadmium.

	Zn^{65} uptake in % administered dose/g tissue*	
	Saline control	Cadmium-treated
Liver	2.35 ± .109	6.17 ± .312
Pancreas	2.02 ± .179	2.68 ± .157
Kidney	1.13 ± .069	2.07 ± .077
Skeletal muscle	.41 ± .019	.38 ± .031

* Mean ± S.E.M. are shown.

The remaining animals served as controls. In both groups, fecal excretions were collected daily for 3 more days. Some of the rats were terminated 1 week and some 6 weeks later for determination of Zn^{65} uptake levels in liver, kidney and pancreas.

Zn^{65} retention in mice previously treated with cadmium. Two groups, each consisting of 16 mature, albino mice (8 males and 8 females, weighing 30-40 g), were used in these studies. The first group served as controls and were injected subcutaneously with approximately 0.1 μc/g of Zn^{65}. The second group received a subcutaneous injection of $CdCl_2$ (0.03 mM/kg) 3 days prior to the Zn^{65} injection. One, 2, 3 and 7 days following the Zn^{65} injection, 4 control mice and 4 cadmium-treated mice (2 males and 2 females in each case) were sacrificed. The whole liver, whole kidneys and a sample of pancreas were dissected, weighed and counted as described above. The remainder of the mouse carcass was chopped and placed in three 20-ml capacity tubes for counting. Similar studies were conducted in which the cadmium was administered at the same time and 2 days following Zn^{65}.

Results. Zn^{65} uptake in rats previously treated with cadmium. Table I shows the 24-hour Zn^{65} uptake of liver, kidney, pancreas and skeletal muscle in rats which had received a single subcutaneous injection of $CdCl_2$ (0.03 mM/kg) 4 months previously. In comparison with the controls, Zn^{65} uptake values in cadmium-treated rats were 162% greater in liver ($P<<0.01$), 83% greater in kidney ($P<<0.01$) and 33% greater in pancreas ($P<0.02$). There was no significant change in 24-hour Zn^{65} uptake of skeletal muscle as a result of the cadmium injection. Similarly increased Zn^{65} uptake values were

TABLE II. Zn^{65} Uptake in Rat Liver 5 and 48 Hours Following Challenge with Cadmium.

	Zn^{65} uptake in % administered dose/g liver*	
	Saline control	Cadmium-treated
5 Hr post-saline or post cadmium	3.54 ± .191	2.75 ± .220
48 Hr *idem.*	1.74 ± .093	3.08 ± .220

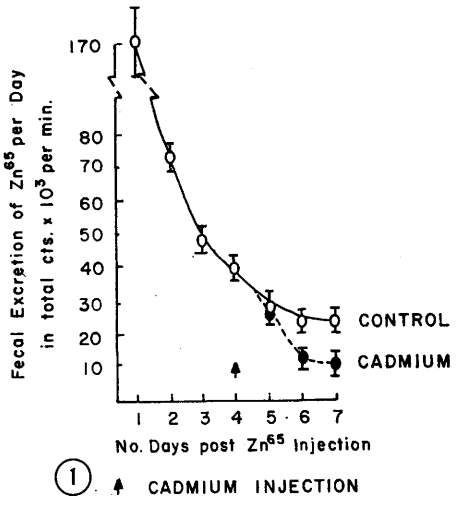
* Mean ± S.E.M. are shown.

observed in liver, kidney and pancreas of all rats injected with cadmium, whether injected 1 week, 1 day or even at the same time as the Zn^{65}.

Zn^{65} uptake in rats subsequently challenged with cadmium. Table II shows that 5 hours after challenge with cadmium (administered intracardially) Zn^{65} uptake in liver was diminished approximately 22% ($P<0.02$) below control levels. However, by 48 hours following cadmium, a reversal had occurred; and Zn^{65} levels in liver were 77% greater ($P<<0.01$) than the values noted in the controls. The results presented in this and the previous section indicate that cadmium, whether administered by the vascular or subcutaneous route, either before or after Zn^{65}, ultimately causes an increased retention of Zn^{65} in the liver.

Fecal excretion of Zn^{65} in rats subsequently challenged with cadmium. Since the results above had indicated that following cadmium there was an increased Zn^{65} retention in liver, kidney and pancreas, this raised the question of whether there was any interference with Zn^{65} excretion. The results (Fig. 1) show that there was a decrease in the daily fecal excretion of Zn^{65} which showed a beginning trend by 24 hours following challenge with cadmium. There was a 50% decrease in daily fecal excretion of Zn^{65} on the second ($P<0.001$) and third ($P<<0.01$) day following cadmium injection. Increased Zn^{65} uptake levels in liver, kidney and pancreas were noted in the cadmium-treated rats when they were sacrificed either 1 or 6 weeks later.

Zn^{65} retention in mice previously treated with cadmium. Since there was no significant difference in the values found in males and females, each point on the graph (Fig. 2) represents the mean value for 2 males and 2 females. The results showed that the whole body retention of Zn^{65} in cadmium-treated mice was approximately 15-20% greater than in control mice. The cadmium-treated values were 15% greater ($P<0.01$) on the first, 20% greater ($P<<0.01$) on the second, 21% greater ($P<0.001$) on the third and 17% greater ($P<0.02$) on the seventh day following Zn^{65} injection. The % of administered Zn^{65} retained by the whole liver was greater in cadmium-treated mice than in controls by 97% ($P<0.001$) on the first, 86%



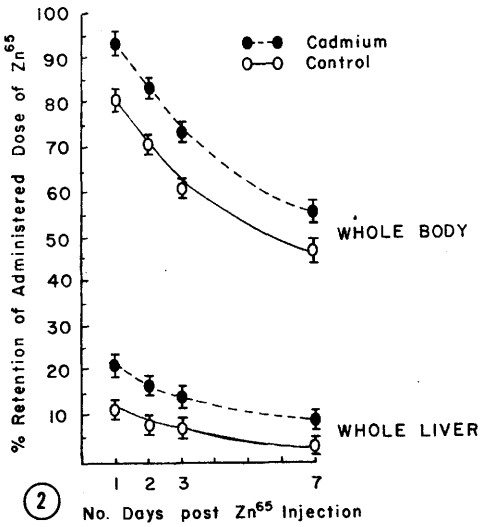


FIG. 1. Fecal excretion of Zn^{65} in rats subsequently challenged with cadmium (mean ± S.E.M. shown).

FIG. 2. Zn^{65} retention in mice previously treated with cadmium (mean ± S.E.M. shown).

($P<0.01$) on the second, 95% ($P<0.001$) on the third and 120% ($P<0.001$) on the seventh day following Zn^{65} injection. Although not shown in the figure, essentially the same type of increased Zn^{65} retention was noted when the cadmium was administered on the same day as the Zn^{65}. When cadmium was administered 2 days following the Zn^{65}, increased Zn^{65} retention in liver and whole body became evident within 24 hours after the cadmium injection. In all of the cadmium-injected mice, there was also increased Zn^{65} retention in kidney and pancreas as noted in studies on the rat.

Discussion. Cotzias, Borg and Selleck(7) have recently reported that cadmium is capable of displacing zinc in certain tissues *in vivo*. In rabbits previously loaded with Zn^{65}, they noted 5 hours following cadmium a slight displacement of Zn^{65} from the small bowel wall and a more marked loss of radioactivity from the liver. They stated their work did not assess the amount of zinc replaced or the functional consequences of this replacement. The studies reported here have indeed confirmed that an initial displacement of Zn^{65} by cadmium does take place in the liver; but, subsequently, there is a marked pile-up of the radioisotope in liver as well as in kidney and pancreas. The results further demonstrated that cadmium caused an actual block in fecal excretion of Zn^{65} and an increased whole body retention of the radioisotope which could, in large part, be accounted for by the increased Zn^{65} levels in liver, kidney and pancreas. These results indicate, then, that one of the functional consequences of the initial displacement of Zn^{65} by cadmium previously reported(7) may be an interference with the normal excretory pathway for zinc.

Summary. The results of this study indicate that cadmium interferes with fecal excretion of Zn^{65}, resulting in an increased retention of radioactive zinc in liver, kidney and pancreas.

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Measles Antibodies in Multiple Sclerosis.* (27855)

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Serologic studies offer a new approach to the problem of pathogenesis of multiple sclerosis (MS) as a possible sequela of measles or measles encephalitis (ME). Although the exact etiology of measles encephalitis is not clear, the pathologic process is characterized by diffuse disseminated demyelinating pathology(1). A demyelinating process is considered characteristic of multiple sclerosis (2-4). In this study measles antibody titers were determined in sera of over 100 patients with MS. Spinal fluid titers were similarly determined in 35 MS patients. The main purpose of this preliminary report is to stimulate further investigation in this important and unsolved problem in medicine.

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