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Effect of Chromium, Cadmium and Lead on Serum Cholesterol of Rats. (27358)

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Curran showed that chromium compounds considerably enhanced hepatic synthesis of cholesterol and fatty acids by rat liver, both *in vitro* and *in vivo*(1). Therefore, it appeared rewarding to determine what effect small amounts of chromium and 2 accumulating metals, cadmium and lead, given over the long term, might have on circulating levels of total cholesterol in rats on a regime rigidly restricted as to contact with these trace metals.

Method. Eighty weanling male rats of the Long-Evans strain were bred in quarters remotely situated on a hilltop and especially constructed so as to avoid environmental contact with these and other metals. The diet was composed of whole seed rye flour (60%), powdered skim milk (30%), corn oil (9%) and sodium chloride (1%), with added vitamins and ferrous sulfate (0.01%)(2). Food contained no detectable cadmium(3), 0.2 μg/g of lead(4), and 0.1 μg/g of chromium (5). Cages were made of acrylic resin, covers of stainless steel, water bottles of polyethylene. Laboratory air from near a forest was filtered through electrostatic precipitators to avoid airborne lead and cadmium, found in snow contaminated by automobile exhausts(3,4). Environmental temperature approximated 24°C. Food and water were repeatedly analyzed for trace metals by microanalytical chemical methods(3,4,5).

Soft water from a forest spring was passed through a polyresin water softener and through both a bulk and a laboratory deionizer and contained no detectable metal. To it was added 5 essential trace metals in amounts approximating those contained in commercial laboratory diets: Zinc 50 ppm., copper 10 ppm., manganese 10 ppm., cobalt 1 ppm., and molybdenum 1 ppm. as the chlorides, acetates or molybdates. To each group of 20 rats, 4 to a cage, was given 5 ppm. of metal as lead acetate, cadmium chloride or chromic acetate in their drinking water, one group of 20 serving as control. Animals remained on this regimen for 10 months or longer and were subjected to no controllable stresses, all being handled alike.

Blood was obtained from the tails of pairs of animals and serum cholesterol measured by the method of Abell *et al.*(6) in duplicate. Hepatic cholesterol was measured by the same method after acetone-alcohol extraction in male animals aged 307 to 372 days dying spontaneously.

Results. Mean serum cholesterol levels are shown in Table I. Significant alterations from the controls ($p<0.01$) occurred in those given lead and cadmium, but in a direction opposite to what might be expected, *i.e.*, by depression. The level for the lead-fed animals was significantly lower than that of the animals given chromium ($p \pm 0.01$), but did not differ statistically from that of the cadmium group. Nor did the cadmium and chromium groups so differ.

Analyses of livers for metals by microanalytic chemical methods(3,4,5) revealed no detectable cadmium in the controls or lead-fed groups, while in those taking cadmium concentrations approximated 1.7 μg/g wet tissue. Lead concentrations were 0-0.33 μg/g in the control, 0-0.49 μg/g in the cadmium-fed and 2.0-3.1 μg/g in the lead-fed

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TABLE I. Effect of Cadmium, Chromium, and Lead on Serum Cholesterol of Male Rats (mg/100 ml).

	Control	Cadmium	Chromium	Lead
No. of animals	20	20	20	20
Mean (mg/100 ml)	101.7	76.1	90.5	71.3
Range	82.5–128.6	54.6–102.5	61.8–115.3	54.0–87.7
Stand. dev.	±14.2	±14.8	±16.6	±13.2
Stand. error of mean	± 4.5	± 4.7	± 5.2	± 4.2
p (control)	—	<.01	N.S.	<.01
p (cadmium)	—	—	N.S. (<.1)	N.S.
p (chromium)	—	—	—	±.01
Duration of exp. (mo)	12	12	10	10

N.S. = Not significant.

groups. Chromium concentrations were 0-0.2 μg/g in the controls, 0.15-0.37 μg/g in the lead-fed, and 0.18-0.27 μg/g in the cadmium-fed groups. No chromium-fed animals died in the first year of the experiment.

Hepatic cholesterol concentrations were measured in pairs of male animals matched for age and dying spontaneously. No animals were killed as they are part of a larger experiment involving life-time studies. No obvious changes were evident. Controls averaged 335 mg/100 g, cadmium-fed 333 mg/100 g and lead-fed 325 mg/100 g tissue (wet weight).

Discussion. We cannot explain the lowering of serum cholesterol in male rats by small amounts of lead and cadmium in drinking water. Both of these metals accumulate in mammalian tissues; hepatic and renal concentrations in these rats approximated those present in young adult human beings in the United States(3,4). To our knowledge, no influence on synthesis or catabolism of cholesterol by these metals has been demonstrated. Chromium, on the other hand, might be expected to have some effect(1); none was demonstrable. Hepatic deposition of excesses was not shown. The mechanisms involved are obscure.

Summary. Male rats on a diet and environment controlled as to trace metals were given 5 ppm. cadmium, chromium and lead in drinking water for 10 to 12 months. Lead and cadmium appeared to lower serum cholesterol levels significantly; chromium was without demonstrable effect. Hepatic levels were apparently unchanged.

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Comparison of Serum Cholesterol Esters in Gerbil and Rat. (27359)

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The findings of Swell *et al.*(1) and Sinclair (2) suggest that a deficiency of arachidonic acid may be an important factor in the etiology of atherosclerosis. Swell(1) reported various serum-cholesterol-ester fatty acid (CEFA) patterns for 8 species, which did not appear to be related to dietary intake of fatty acids. The data suggested an inverse correlation between susceptibility to atherosclerosis of these species and content of arachidonic