sibility of preventing greying of hair by substances other than vitamins. Studies of this nature on black rats of a pure bred strain are in progress.

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Toxicity of Pantothenic Acid.

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Pantothenic acid, first discovered as a growth factor for yeast,[1] has been established as a member of the vitamin B complex.[2] The vitamin was recently identified[3, 4] as *N*-(α,γ-dihydroxy-β, β-dimethylbutyryl)-β'-alanine and has been synthesized.[5]

In continuation of our studies of the toxicology of the vitamins of the B complex,[6, 7] the following investigation of the toxicity of pantothenic acid was carried out on animals maintained on completely adequate diets. Synthetic dextrorotatory calcium pantothenate was used in all experiments. Calcium pantothenate is readily water-soluble and almost neutral in reaction, the pH of a 10% solution being approximately 8.

Local effects of calcium pantothenate were studied by instillation into the eye and by subcutaneous injection. Instillation of 0.5 cc of a 10% solution into the conjunctival sac of 3 rabbits did not produce any irritation. Likewise no irritation, inflammation or abscess formation was observed in 4 rabbits following the subcutaneous injection of 1.0 cc of a 10% solution. The infiltration of the subcutaneous tissues subsided about as rapidly as following a control injection of 10 cc of saline.

Acute toxicity was studied in mice, rats, dogs, and monkeys. In mice and rats the L.D. 50 was determined following oral, subcu-

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TABLE I.
Acute Toxicity of Calcium Pantothenate L.D. 50 (g per kg body wt).

	Oral	Subcutan.	Intraper.	Intrav.
Mice	10.0	2.7	0.92	0.91
Rats	No deaths at 10.0	3.4	0.82	—

taneous, intraperitoneal and intravenous injection, 10 animals being used for each dose level. Table I summarizes the results obtained from a total of 180 mice and 110 rats.

All 10 rats dosed with 10 g of calcium pantothenate per kg, when administered by mouth, survived without showing toxic symptoms. Lethal doses in mice and rats produced prostration and respiratory failure. Death occurred within one hour following intravenous or intraperitoneal injection and within 2 hours following oral or subcutaneous administration. No late deaths were observed.

A dose of 1 g of calcium pantothenate per kg was fed to each of 5 dogs and to 1 monkey. No toxic symptoms were observed in these animals. After 2 weeks the monkey and one dog were sacrificed; gross examination of the organs failed to show any pathologic changes.

Chronic toxicity was studied in rats, dogs, and monkeys. Two groups of 20 young rats, 10 males and 10 females, were fed 50 mg and 200 mg respectively of calcium pantothenate per rat per day over a period of 120 days. The animals developed normally, their growth rate did not differ significantly from that of the control group.

A group of 6 adult dogs was fed 50 mg of calcium pantothenate daily over a period of 100 days, and 4 monkeys of 2.5 to 4 kg body weight received 1 g of calcium pantothenate by mouth daily over the same period of time. Both dogs and monkeys failed to show any toxic symptoms, and their weights remained constant.

Our findings, which will be extended later by histological examinations, demonstrate that calcium pantothenate is, like other members of the vitamin B complex, a substance of extremely low toxicity. Excessively large doses (0.8 g to 10 g per kg, depending on the mode of administration) were found to produce death due to respiratory failure in mice and rats. Prolonged feeding of sublethal doses failed to produce toxic manifestations, indicating that an excess of pantothenic acid is either rapidly destroyed or excreted. Studies on this problem are now in progress.