

CHOLESTEROL EXCRETION BY THE INTESTINE IN ANIMALS OF SPECIES DIFFERING IN THEIR RESISTANCE TO EXOGENOUS CHOLESTEROL

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The cholesterol concentration in the contents of the small intestine is higher in dogs and rats than in rabbits. In experimentally induced disturbances of cholesterol metabolism the ability of the small intestine to excrete cholesterol is also greater in dogs than in rabbits, and increased excretion of cholesterol is observed in dogs in the earlier period of development of the pathological changes. The results suggest that the species-specific resistance of animals to exogenous cholesterol is linked, along with other factors, with the ability of the small intestine to excrete varied amounts of cholesterol.

Dogs and rats are animals in which the prolonged administration of a high cholesterol diet produces no appreciable changes in the blood cholesterol concentration. In rabbits, however, the addition of cholesterol to the diet rapidly leads to alimentary hypercholesteremia followed by the development of atherosclerosis [1, 2, 4, 9, 10]. The problem of which mechanisms determine the resistance of omnivorous animals to an excess of cholesterol has not been solved. All that is known is that these animals produce large quantities of heparin, an activator of lipoprotein lipase [11], their digestive juices are rich in enzymes of lipid breakdown, and most of the excess cholesterol is converted by the liver into bile acids [1-3, 5].

Previous investigations showed [6-8] that the intensity of the hypercholesteremia and subsequent atherosclerotic changes in dogs with disturbances of cholesterol metabolism depends on the intensity of cholesterol excretion by the small intestine.

It was therefore decided to compare the ability of the small intestine to excrete cholesterol in animals of species with different resistance to exogenous cholesterol.

EXPERIMENTAL METHOD

Experiments were carried out on six dogs, 70 rabbits, and 105 rats.

The total cholesterol and cholic acid concentrations in the bile and intestinal contents and the cholesterol concentration in the blood were determined.

These parameters in the acute experiments were determined in the contents of the small intestine obtained immediately after the animals were killed. In addition, the cholic acid concentration was studied in bile taken from the gall bladder of the dogs and rabbits. In the chronic experiments on dogs cholesterol and cholic acid were determined in the periodic secretion from a fistula into the proximal portion of the small intestine and in bile taken from a fistula of the gall bladder, while in rabbits they were determined in secretion from a duodenal fistula.

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EXPERIMENTAL RESULTS

The results of the acute experiments showed that the cholesterol concentration in the contents of the small intestine of dogs and rats was much higher than in rabbits (102 ± 2 , 146 ± 13 , and 19 ± 3 mg %, respectively). The cholesterol concentration in the bile also was higher in dogs (40 ± 5 mg %) than in rabbits (23 ± 3 mg %). The cholic acid concentration in the bile also was much higher in dogs (3050 ± 88 mg %) than in rabbits. The concentration of cholic acid in the intestinal contents of the rats also was higher than in rabbits (1386 ± 56 and 188 ± 16 mg %, respectively).

The chronic experiments on dogs and rabbits showed that both under normal conditions and in disturbances of cholesterol metabolism the ability of the small intestine of these animals to excrete cholesterol differed. Under normal conditions the cholesterol concentration in the periodic intestinal secretion of the dogs was 56 ± 3 mg % and of the rabbits 15 ± 4 mg %.

Keeping the rabbits on a diet enriched with cholesterol (1 g/kg) for 7 days led to the development of moderate hypercholesteremia (194 ± 4 mg % compared with the normal 62 ± 6 mg %); the excretion of cholesterol with the bile also was increased (63 ± 1 mg %, normal 23 ± 3 mg %). The excretion of cholesterol with the intestinal secretion was unchanged. Keeping the rabbits on a similar diet for 30 days led to considerable hypercholesteremia of the animals (435 ± 4 mg %), the excretion of cholesterol with their bile rose to 78 ± 15 mg %, and the excretion of cholic acid with the bile also was increased (to 759 ± 106 mg % from the normal 616 ± 116 mg %). Under these conditions the excretion of cholesterol with the intestinal secretion also was increased (65 ± 8 mg % from the normal of 19 ± 3 mg %).

Previous investigations [6-8] showed that feeding dogs for a long period on a high intake of pure cholesterol did not lead to disturbances of their cholesterol metabolism; no hypercholesteremia was observed. No changes in the excretion of cholesterol by the intestine likewise were found. In healthy animals most excess cholesterol is destroyed and excreted as bile acids [3, 5]. In the present experiments, a single administration of cholesterol in doses of up to 30 g to dogs was followed by increased excretion of cholic acid with the bile (up to 6200 mg %) with no appreciable changes in the excretion of cholesterol by the intestine.

A diet including cholesterol and with the addition of 6-methylthiouracil (1.5 g) and vitamin D₂ (500 i.u.), led to a disturbance of cholesterol metabolism in dogs, accompanied by persistent hypercholesteremia. Even the administration of only a single dose of these substances led to an increase in the excretion of cholesterol and cholic acid with the bile (71 ± 9 and 4040 ± 116 mg %, respectively) and a considerable increase in the excretion of cholesterol with the intestinal contents (198 ± 25 mg % compared with the normal 43 ± 2 mg %).

It is interesting to note that both the short-term and long-term administration of a high-cholesterol diet to rabbits combined with amphetamine, which accelerates the development of atherosclerosis, were accompanied by a less marked increase in the excretion of cholesterol with the bile and intestinal contents and by a higher hypercholesteremia.

The ability of the small intestine to excrete cholesterol is thus greater in dogs than in rabbits both under normal conditions and when cholesterol metabolism is disturbed. In the latter case the excretion of cholesterol is increased in dogs at an earlier stage than in rabbits.

The results suggest that the species-specific resistance of animals to exogenous cholesterol, together with other factors, is linked with the ability of the small intestine to excrete a varied amount of cholesterol.

LITERATURE CITED

1. N. Ya. Anichkov, in: *Atherosclerosis and Myocardial Infarction* [in Russian], Moscow (1959), p. 68.
2. M. V. Bavina et al., *Kardiologiya*, No. 11, 36 (1970).
3. G. P. Iroshnikova, *Pat. Fiziol.*, No. 5, 57 (1965).
4. S. M. Leites, *Biokhimiya*, No. 8, 283 (1943).
5. S. M. Leites and S. Ya. Karliner, *Byull. Éksperim. Biol. i Med.*, **15**, No. 3, 47 (1943).
6. M. S. Martsevich, L. A. Shekun, and E. D. Klimenko, in: *The Physiology and Pathology of the Cardiovascular System* [in Russian], Moscow (1965), p. 111.
7. M. S. Martsevich, in: *Atherosclerosis and Coronary Insufficiency* [in Russian], Kazan' (1966), p. 33.
8. M. S. Martsevich, in: *Activity of the Digestive System and Its Regulation Under Normal and Pathological Conditions* [in Russian], Moscow (1969), p. 119.

9. Yu. T. Pushkar', The Effect of Choline and Certain Neurotropic Drugs (Phenobarbital and Amphetamine) on the Development of Experimental Atherosclerosis, Author's Abstract of Candidate's Dissertation, Moscow (1954).
10. T. A. Sinitsina, Experimental Atherosclerosis of the Coronary Arteries [in Russian], Leningrad (1964).
11. N. T. Shutova, in: Current Problems in Pathological Physiology [in Russian], Moscow (1969), p. 189.