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Note

A previously unreported phase transition in cholesterol at 37°C and its possible significance in arteriosclerosis

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A previously unreported phase transition in anhydrous cholesterol at 37°C was discovered by DTA. A subsequent study by DSC confirmed the existence of this phase transition, and indicated that $\Delta H = 0.66$ kcal mole^{-1} and $\Delta S = 2.1$ cal °K^{-1} mole^{-1}. The transition may have biophysical significance.

The cholesterol used for these studies was "purified" material obtained from Fisher Scientific Company. The purity, estimated by DSC, was found to be 99.7%. In the DTA study, a 2.0 mg sample was employed, and in the DSC study, a 21.760 mg sample. In both cases, the studies were conducted in air at normal atmospheric pressure, glass beads were used as the reference material, and chromel–alumel thermocouples were employed. The DTA and DSC instruments were standard equipment manufactured by Du Pont.

The close proximity of the temperature of this phase transition to normal human body temperature has interesting biophysical implications. For one thing, the etiology of arteriosclerosis could be attributed to the departure of a person's body temperature from 37°C, resulting in the presence of the undesirable one of the two phases. If some important biophysical property of the undesirable phase (such as solubility in blood serum, or ease of precipitation) is significantly different from the same property in the desirable phase, the incidence of arteriosclerosis might well be correlated with the body temperature of the individual. At a recent conference, Steim[1] reported that the membranes of many organisms undergo a thermotropic change of state around 40°C, which can be studied by DSC. These findings indicate that the transition found in anhydrous cholesterol at 37°C by the present study probably also occurs in the chlosteric deposits found in the cells of living animals. If this hypothesis is valid, and body temperature is indeed a factor in the development of arteriosclerosis, then drugs that affect body temperature could be used to induce or retard arteriosclerosis.

Fortunately, some data are available which make it possible to correlate the incidence of naturally occurring arteriosclerosis in certain animals as a function of their normal body temperatures. The incidence of naturally occurring arteriosclerosis in various mammals, birds, and reptiles is summarized at length in a review article

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TABLE I

DATA RELATING BODY TEMPERATURE TO INCIDENCE OF NATURALLY OCCURRING ARTERIOSCLEROSIS

Species	*Normal body temperature, (°C)*	*Subject to naturally occurring arteriosclerosis (Ref. 2)*
Man	37[a]	Yes
Chickens	40–42[a], 41.7	Yes
Iguanas	26	No
Snakes	26	No
Turtles	26	No
Monkeys	38	Yes
Rabbits	39.6[a], 39.4, 39.6	Yes
Rats	35.8–37.6[a], 38.2, 38.0	Yes
Mice	35.2, 37.8	No
Dogs	39[a], 38.9	Yes
Cats	37.2–39.0[a], 38.6	Yes
Elephants	35.9–36.7[a]	Yes
Horses	38[a], 37.8	Yes
Swine	38–39.6[a]	Yes
Cows	38[a], 38–39[a], 38.5	Yes
Sheep	38[a], 39.1	Yes
Goats	40[a]	Yes
Pigeons	42–43[a]	Yes

[a]From Ref. 3. Other figures obtained from Ref. 4.

by Lindsay and Chaikoff[2], and the normal body temperatures of these species are given in the literature[3,4]. Referring to Table I, we can see that the higher-temperature form of cholesterol is the phase implicated in the disease. That is, species whose body temperatures are below 37°C (mice, chameleons, iguanas, snakes, and turtles) are not subject to naturally occurring arteriosclerosis, and those whose body temperatures are above 37°C (chickens, pigeons, monkeys, rabbits, rats, dogs, cats, horses, swine, cows, sheep, and goats) are subject to the disease. The elephant appears to be an exception, but not many autopsies have been performed on elephants.

Although it is difficult to draw with certainty a conclusion such as this about a disease as complex and mysterious as arteriosclerosis, the correlation does appear to be sufficiently valid to warrant a well-planned investigation with animals.

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