

Effects of Intravenous Heparin on the Plasma Lipoproteins in Primary Hypercholesteremic Xanthomatosis and Idiopathic Hyperlipemia¹

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The action of heparin on the plasma has been studied in 7 normal subjects, 8 patients with primary hypercholesteremic xanthomatosis and 7 patients with idiopathic hyperlipemia. Electrophoretic analyses in a Tiselius apparatus as well as determinations of the lipids and of the turbidity of the plasma were carried out before and 15 minutes after the intravenous injection of 50 mg of heparin. The results are briefly outlined here; they will be reported in detail elsewhere (1).

In 5 of the 7 normal subjects the electrophoretic pattern revealed no changes after the injection of heparin, while in 2 the size of the β -1 peak decreased to less than half of its normal size. Compensating for this decrease there was in one person an increase in both the α -1 and albumin peaks, and in the other an increase in the α -2 peak. No significant changes occurred in the values for cholesterol, phospholipids, or neutral fat following the injection of heparin.

In primary hypercholesteremic xanthomatosis, in which the values for cholesterol and phospholipids are elevated and the plasma is clear, the fasting electrophoretic pattern showed an abnormally high β -1 peak in all 8 patients. Following the injection of heparin no changes occurred in 2 patients, while in 6 patients the β -1 peak decreased considerably, from an average of 16.8% to 7% of the total protein, a value far below the normal average value of 13% (Fig. 1). Compensating for the decrease in the size of the β -1 peak there was an increase in the size of the α -2 peak in 3 patients; of the albumin peak in 1 patient; and of both the α -2 and albumin peaks in 2 patients. No changes occurred in the amounts of neutral fat or phospholipids; but the elevated cholesterol values decreased slightly in all 8 patients, from an average of 444 mg/100 ml of plasma to 417 mg.

In idiopathic hyperlipemia, in which not only the values for cholesterol and phospholipids but also for neutral fat are elevated and the plasma is creamy, the fasting electrophoretic pattern showed an abnormal elevation of the α -2 peak in 3 patients, and of both the α -2 and β -1 peaks in 3 patients. In the seventh patient the pattern was obscured by the very great turbidity of the plasma. After the injection of heparin the first 6 patients showed a reduction of the previously elevated peaks to normal size and the appearance of a new peak ahead of the albumin peak con-

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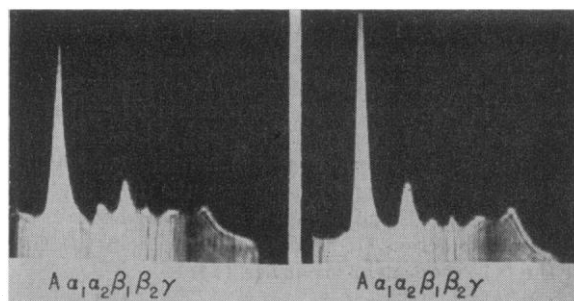


FIG. 1. Electrophoretic patterns in primary hypercholesteremic xanthomatosis. Left, fasting plasma: the β -1 peak is abnormally high. Right, plasma after the injection of heparin: the β -1 peak now is smaller than normal while the α -2 peak has increased in size. (Determinations were carried out in a Perkin-Elmer Tiselius electrophoresis apparatus using as buffer sodium diethylbarbiturate-sodium citrate at pH 8.6 and an ionic strength of 0.1. Field strength: 200 v, 9 ma. Time of run: 55 min.)

taining from 3.7 to 16.9% of the total protein (Fig. 2). In the seventh patient no pre-albumin peak was observed. High speed centrifugation of the plasma at 18,000 revolutions per minute for one hour prior to electrophoretic analysis reduced the size of the pre-albumin peak; and rotation of the plasma with ethyl ether at +5 C. for one hour abolished it. Chemical analyses following the injection of heparin revealed in all 7 patients a decrease in the degree of turbidity and in the amounts of cholesterol and phospholipids; and in 5 patients also a decrease in the amount of neutral fat. The decrease in these values was moderate in the first 6 patients and considerable in the seventh patient (who had shown no pre-albumin peak). With the exception of the latter patient, the average decreases were: cholesterol from 663 mg/100 ml to 576 mg; phospholipids from 658 to 602 mg; and neutral fat from 1812 to 1665 mg. In the seventh patient, heparin was injected on three occasions and caused average decreases as follows: cholesterol from 592 mg/100 ml to 312 mg; phospholipids from 564 to 313 mg, and neutral fat from 4900 to 3049 mg.

Fractionation of the plasma proteins according to a modification of Cohn's method 10 (2) revealed that the elevations of the β -1 peak in xanthomatosis and

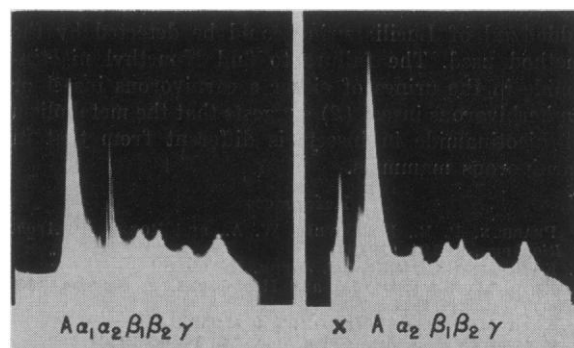


FIG. 2. Electrophoretic patterns in idiopathic hyperlipemia. Left, fasting plasma: the α -2 peak is abnormally high. Right, plasma after the injection of heparin: the α -2 peak is reduced to normal size, and a new peak, marked x, has appeared in front of the albumin peak.

of the α -2 and β -1 peaks in hyperlipemia were caused by a lipoprotein with the solubility characteristics of β -1 lipoprotein. There are two possible reasons for the increase in the speed of electrophoretic migration of the β -1 lipoprotein after the intravenous injection of heparin: either combination with heparin (which has a high negative charge) increases the negative net charge of the β -1 lipoprotein molecules, or heparin by its lipolytic action (3) causes a decrease in the size of the β -1 lipoprotein molecules (4).

References

1. LEVER, W. F., SMITH, P. A. J., and HURLEY, N. A. *J. Invest. Dermatol.* To be published.
2. LEVER, W. F., et al. *J. Clin. Invest.*, **30**, 99 (1951).
3. SHORE, B., NICHOLS, A. V., and FREEMAN, N. K. *Proc. Soc. Exptl. Biol. Med.*, **83**, 216 (1953).
4. HERBST, F., and HURLEY, N. A. To be published.

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The Metabolism of Niacin in Insects¹

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A number of studies have demonstrated species differences in the metabolism of niacin. In carnivorous mammals the principal end product, as evidenced by urinary excretion, is N¹-methyl nicotinamide (NMN). In contrast, species of herbivora do not excrete appreciable amounts of NMN (1).

The present author has reported that the urinary excretion of NMN could not be detected following the subcutaneous injection of nicotinamide in the herbivorous insect, *Bombyx mori* (2). The urine analyses were done by the author's method (3, 4). The methylation of nicotinamide has not yet been demonstrated in other insects.

Hence the methylation of nicotinamide was looked for in the carnivorous insect, *Lucilia caesar*, L. which had been fed with fish protein in the larval stage. The urine of the last pupal stage before emergence was examined for NMN by paper chromatography (4), using a urea butyl alcohol solvent (5) and Dragendorff's reagent (6). No NMN was found in the urine. Control experiments indicated that 10 μ g of NMN added/ml of *Lucilia* urine could be detected by the method used. The failure to find N-methyl nicotinamide in the urines of either a carnivorous insect or an herbivorous insect (2) suggests that the metabolism of nicotinamide in insects is different from that in carnivorous mammals.

References

1. PEARSON, P. B., PERLZWEIG, W. A., and ROSEN, F. *Arch. Biochem.*, **9**, 191 (1949).
2. KATO, M. *J. Sericult. Sci. Japan*. In press.
3. KATO, M., SHIMIZU, H., and HAMAMURA, Y. *Science*, **116**, 3017 (1952).
4. KATO, M. *Science (Japan)*, **23**, 9 (1953).
5. CARTER, C. E. *J. Am. Chem. Soc.*, **72**, 1466 (1950).
6. KARIYONE, T., and HASHIMOTO, Y. *Nature*, **163**, 739 (1951).

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A Discontinuous Paper Drive

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A discontinuous paper drive for use with paper ionophoresis strips containing radioactive samples has been designed and built similar to that shown in Fig. 1. The apparatus pulls 3.5-cm-wide strips of paper

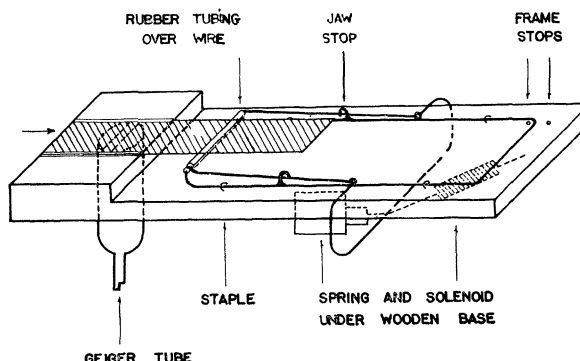


FIG. 1. Drawing of discontinuous paper drive.

over a thin window Geiger tube but could be used on various widths of paper. Construction of the paper drive was from clothes hanger wire, rubber tubing, nails, one solenoid, one spring, and 1/2-in. plywood. The wire jaw runs through loops in the wire frame and connects to the solenoid. The solenoid opens the jaws against the jaw stops and moves the frame backward. Then, the spring closes the jaws on the paper and moves the frame and paper any desired distance up to 1.5 cm, depending on where the frame stops are placed.

In use the solenoid is connected to a scaler such that any predetermined count will activate the solenoid. A pen, which makes a mark on a constant speed paper tape so that the exact cross section containing activity can be determined, is also connected in parallel.

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Survival of Irradiated Rats in Parabiosis with Hypophysectomized Partners¹

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Brecher and Cronkite (1) first demonstrated that postirradiation parabiosis is a means of altering the effect of a lethal dose of x-irradiation to rats. Their results have been confirmed and extended during the

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