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Body Metabolism and the Induction of Blood Clotting.

H. NECHELES, C. A. MILLS AND MAO-KENG CHU.

From the Departments of Physiology and Medicine, Peking Union Medical College.

It was shown in a previous communication[1] that protein ingestion causes a decrease of the clotting time in man and dogs, while fat and carbohydrate have little influence. Further work[2] showed that these changes in clotting time are closely accompanied by changes in metabolism—as the metabolic rate increases the clotting time shortens. Ingestion of food with little or no specific dynamic action has practically no effect on the clotting time. Amino-acids have the same effect as proteins.

The question arose as to whether every increase in metabolic rate, no matter how produced, would shorten the clotting time; also whether the clotting time could be shortened without an accompanying increase in metabolism; and finally what caused the decreased clotting time. We suspected that the platelets were responsible, so their behavior was studied.

The experiments were carried out on one of us (C. A. M.) and on dogs. One dog was tracheotomized, the wound permitted to heal thoroughly and a Trendeenburg tampon-cannula used at the time of metabolism study. A Benedict-Knipping[3] closed circuit metabolism apparatus was employed for the determinations.

Blood was drawn from a vein with a paraffined needle and syringe and placed in a paraffined tube at 25° C. Every 2 minutes a sample of the blood was removed by a paraffined pipette and a smear quickly made on a glass slide. This smear was stained with

[1] Mills, C. A., and Necheles, H., *Chinese J. Physiol.*, 1928, ii, 19.

[2] Necheles, H., and Mills, C. A., *Chinese J. Physiol.*, 1928, ii, 25.

[3] Knipping, H. W., *Z. Physiol. Chem.*, 1925, cxlv, 154.

Wright's stain and the speed of platelet clumping and disintegration observed.

The metabolic rate of man and dog was increased by feeding protein. The specific dynamic action was accompanied by a shortened clotting time, while complete clumping of the platelets occurred about the same time as the first appearance of clot in the tube. Glycocoll feeding gave the same changes in the dog as did protein. Fat and carbohydrate feeding with the dog, and carbohydrate and fat-carbohydrate meals with man, gave insignificant changes in the metabolism, clotting time and platelet clumping. The metabolic rate in the dog was next raised by feeding dried thyroid extract. When the metabolism was thus raised to +30%, no change could be detected in the blood clotting or platelet clumping. The metabolic rate was next markedly increased in both man and dog by vigorous exercise, and this was always found to cause a marked quickening of both clotting and platelet clumping. Injections of adrenalin into dogs gave results similar to those following vigorous exercise.

To shorten the clotting time without affecting the metabolic rate, tissue fibrinogen was injected into the dog. Two hours later the clotting time had been reduced by 80% and the platelet clumping correspondingly quickened. There was found no change in the metabolic rate, so this coagulent affects the coagulability by a mechanism independent of basal metabolism.

In vitro experiments with amino acids and different protein metabolites failed to show an accelerating effect of any of them on blood clotting, when used in physiological concentrations. Adrenalin effect *in vitro* is now being tested.

We have here demonstrated that not every increase in metabolic rate is accompanied by a quickened clotting of the blood and platelet clumping, and also that not every decrease in the clotting time is accompanied by an increased metabolic rate.

Metabolic changes which we commonly think to be associated with increased adrenal secretion always seem to be accompanied by quickened clotting.

Apparently the platelet clumping and disintegration are responsible for the time of onset of the clotting process. We are now studying the influence of adrenalin on platelets and platelet-free plasma *in vitro*.