THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET - - - CHICAGO, ILL.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - - Six dollars per annum in advance

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SATURDAY, DECEMBER 10, 1921

THE BLOOD AND ANTIPYRETIC DRUG ACTION

Antipyretic drugs are so commonly used in the practice of medicine today that their mode of action ought to be well established in every detail. It must be admitted, however, that the pharmacology of this group of potent substances is by no means completely unraveled. The most probable types of deportment of the antipyretics can be sketched in general outline. Two regulative factors, heat production and heat dissipation, in the body need to be taken into consideration. As both of these are under nervous control, the functions of the nervous tissues and centers in relation to body temperature must also be included in any scheme of interpretation. The demonstration of the presumable existence of heat-regulating centers in the body soon directed attention to the possibility that antipyretics are effective in lowering temperature by their action on these thermogenic centers. Before long it further became apparent, however, that the pharmacodynamics of the temperature-depressing compounds is not confined to these centers. Certain substances can act directly so as to influence heat dissipation or formation independently of any central function of the brain stem. As heat loss is a factor of heat dissipation from the surface of the body, the rate of loss of heat and its regulation will depend chiefly on variations in the circulation through the skin and the activity of the sweat glands. Some of the drugs in the so-called antipyrin group of antipyretics can depress the vasomotor tone, thus leading to marked vasodilatation, particularly in the skin.

More specific details of the possible antipyretic action of drugs have been furnished in recent years by Barbour and his pupils at the Yale University School of Medicine. They rest on the demonstration of the antipyretic action of glucose, the normal sugar of the blood.[1] For example, in the fever produced by injection of colon bacillus vaccine, intravenous injections of glucose are effective in reducing the body temperature of experimental animals, and the antipyretic action is paralleled by a decrease in the blood solids. In other words, the reduction of body temperature is exhibited at a time when the blood becomes diluted with water drawn from the tissues.[2] Normal subjects do not respond in this way. The fact that the antipyretic phase of glucose action is exhibited especially in the febrile and not in the normal state, which is readily explained by the presence of more available water in the tissues in the former condition, led to the hypothesis that the action of antipyretic drugs can be explained along similar lines.

The latest investigations of Barbour and Herrmann[3] at Yale confirm the assumption. Sodium salicylate, acetylsalicylic acid, antipyrin and quinin all increase the blood sugar concentration in both normal and febrile animals. Thus, after the administration of salicylates the glucose concentration in the whole blood may increase from 25 to 50 per cent. Antipyrin apparently gives a less marked effect than do salicylates, whereas quinin exhibits a greater one. At the same time there occurs, in human as well as experimental animal febrile cases, a notable dilution of the abnormally concentrated blood. This dilution accounts for the decrease in the body temperature.

The newly discovered mobilization of glucose in the blood after administration of antipyretic drugs thus suffices to support the theory of their action. They do not act primarily by decreasing heat production.[4] As Barbour and Herrmann[3] interpret the situation, antipyretics increase the blood sugar concentration. This in fever causes a plethora, extra water being available in the tissues. Plethora promotes the dissipation of the heat by radiation and surface evaporation, for the peripheral blood flow becomes augmented. In health, no plethora occurs—consequently there is no antipyretic effect. The possibility that methods of blood dilution other than that just discussed may be potent in promoting heat dissipation from the body needs to be kept in mind in further considerations of how fever in general may be modified in its course.

1. Barbour, H. G.: The Antipyretic Action of Dextrose, Proc. Soc. Exper. Biol. & Med. **16**: 136, 1919.

DO THE DIFFERENT IMMUNOLOGIC REACTIONS DEPEND ON ONE OR SEVERAL ANTIBODIES?

References to precipitins, agglutinins, opsonins, complement-fixation antibodies, and even anaphylactins, as they are found in medical literature, including even the writings of immunologists, generally carry the assumption that each of these is a distinct and separate entity. Despite this assumption, there has always been some doubt as to their individuality. The view that agglutinins and precipitins are the same thing, causing agglutination of visible cellular antigens and precipitation of

2. Barbour, H. G., and Howard, J. A.: Dextrose Plethora and Its Antipyretic Effect in Coli Fever, Proc. Soc. Exper. Biol. & Med. **17**: 150, 1920.

3. Barbour, H. G., and Herrmann, J. B.: The Relation of the Dextrose and Water Content of the Blood to Antipyretic Drug Action, J. Pharmacol. & Exper. Therap. **18**: 165 (Oct.) 1921.

4. Barbour, H. G.: Antipyretics, III, Acetylsalicylic Acid and Heat Regulation in Fever Cases, Arch. Int. Med. **24**: 624 (Dec.) 1919.

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