EFFECT OF ANTI-INFLAMMATORY AGENTS ON HEAT PRODUCTION IN RED BLOOD CELLS

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The effect of the principal anti-inflammatory drugs in current use (prednisolone, acetylsalicylic acid, rheopyrine, chloroquine, and indomethacin) on the thermal effect of human peripheral red blood cells was studied. Only chloroquine was found to inhibit this effect significantly. This fact indicates that chloroquine inhibits energy production during glycolysis and this can be regarded as one of the factors in the therapeutic action of this substance.

KEY WORDS: anti-inflammatory agents; therapeutic action of chloroquine; glycolysis; thermal effect of red blood cells.

An important aspect of the mechanism of the therapeutic action of anti-inflammatory agents is their restrictive effect on the supply of energy for inflammation [1, 2]. The use of experimental models very far removed from physiological conditions has demonstrated inhibition of ATP generation through the uncoupling of oxidative phosphorylation by salicylates, indomethacin, and pyrazolone preparations [2-4]. Inhibition of glycolysis by salicylates and corticosteroids has also been described [5, 6]. Attention is accordingly directed to the identical sensitivity of partial reactions of oxidative and glycolytic phosphorylation to particular uncoupling agents, including drugs [1, 7]. No special investigations into the action of anti-inflammatory agents on processes adequately reflecting the energy yields of glycolysis have hitherto been undertaken.

This paper describes a comparative study of the effect of all the principal current anti-inflammatory agents on heat production in human blood, a function of glycolysis taking place in the red blood cells.

EXPERIMENTAL METHOD

Kinetic investigations were carried out on the LKB (Sweden) continuous-flow microcalorimeter. The donor's blood was pumped through the mixing chamber at a rate of $1.47 \cdot 10^{-2}$ ml/sec. The thermal effect (Q) per red cell was calculated by the equation

$$Q = \frac{W}{V \cdot N},$$

where W is the thermal power in the chamber; V the rate of flow of the component; and N the number of red cells per ml. The thermal power was determined by a calibration curve obtained by passing an electric current of known magnitude.

The following anti-inflammatory drugs were studied: prednisolone, acetylsalicylic acid (aspirin), rheopyrine, chloroquine, and indomethacin. In their degree of purity all satisfied the demands of the USSR State Pharmacopoeia. The concentrations of the drugs in the experiments corresponded to therapeutic doses (10^{-2} and 10^{-3} M).

Blood taken from a vein into a tube containing heparin was divided into two parts. One part was the control, and the drug to be studied was added to the other. Measurements were made at 25°C 4 h after the

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blood was taken; in the meantime the blood was kept at 4°C. Immediately before the measurement blood was diluted 1:1 with Eagle's medium.

EXPERIMENTAL RESULTS

Of the anti-inflammatory agents studied only chloroquine was found to actively influence heat production in the blood. The mean thermal effect of intact blood was $5.05 \cdot 10^{-13}$ cal/sec/RBC; that of blood treated with chloroquine was $1.26 \cdot 10^{-13}$ cal/sec/RBC. The differences were statistically significant ($P < 0.05$). Treatment of the blood with prednisolone, aspirin, rheopyrine, and indomethacin did not alter the thermal effect.

Chloroquine thus inhibits energy production during glycolysis. This property of chloroquine, in conjunction with general views on inflammation as an endoergic process [1, 2], can be regarded as one of the factors in its therapeutic effect.

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