practice [4, 5]. It can be tentatively suggested that the timely correction of the disturbed rheologic properties of the blood after revival from the agonal state by properly oriented pathogenetic treatment is an important component in the prophylaxis of postresuscitation complications.

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ROLE OF ARACHIDONIC ACID IN PLATELET AGGREGATION INDUCED BY *Salmonella typhimurium* ENDOTOXIN

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Much evidence has recently been obtained to show that many functions of platelets are under the controlling influence of arachidonic acid (AA) and its metabolic products — the prostaglandins (PG). Meanwhile many aspects of the mechanism of their action are still unexplained. In particular, the role of PG in changes in platelet function under the influence of endotoxins of the agents of many infectious diseases has not been adequately studied. Yet endotoxinemia in infectious diseases (acute intestinal infections, meningococcal infections, septic states) is an essential factor determining disturbance in the hemostasis system and leading to thrombo-hemorrhagic complications which aggrevate the course of these diseases [3-6].

Endotoxins of Gram-negative bacteria (*Salmonella typhimurium, Neisseria meningitidis*) have been shown to induce aggregation of platelets from normal bood donors. Meanwhile scanning microscopy has revealed morphological changes in platelets reflecting their activation by endotoxins. In this connection data showing that during activation of platelets there is a sharp increase in PG biosynthesis from AA, which is a component of the phospholipids of their membranes, are of considerable interest [9]. These observations indicate that PG play an essential role also in platelet aggregation induced by endotoxin.

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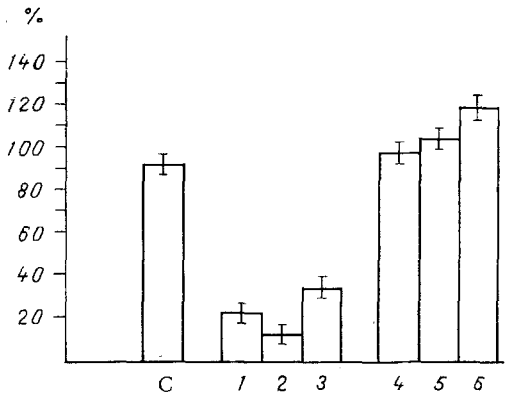

Fig. 1

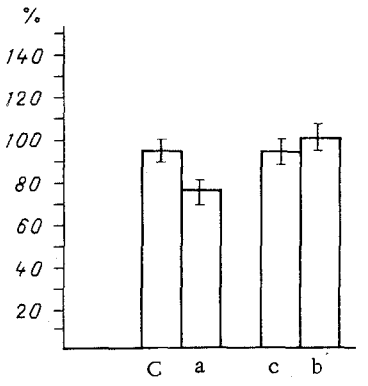

Fig. 2

Fig. 1. Increase in degree of ADP-induced platelet aggregation (in %) on addition of AA (1), endotoxin (2), endotoxin and AA (3), AA and ADP (4), endotoxin and ADP (5), and AA, endotoxin, and ADP (6) to samples of PEP. Here and in Fig. 2: C) degree of platelet aggregation in samples of PEP treated with ADP only.

Fig. 2. Degree of ADP-induced platelet aggregation after incubation of samples of PEP for 60 min with endotoxin (a) and with AA and endotoxin (b).

In the investigation described below the role of AA in platelet aggregation was studied. Changes in the functional properties of the platelets in response to *S. typhimurium* endotoxin and ADP were recorded in the presence and in the absence of the sodium salt of AA.

EXPERIMENTAL METHODS

Experiments were carried out *in vitro* with platelet-enriched plasma (PEP) obtained from blood from normal donors, stabilized with sodium citrate. Platelet aggregation was recorded by the method in [8], using an FÉK-56 photoelectric colorimeter connected to a KSP-4 automatic writer.

The *S. typhimurium* endotoxin used in the experiments was obtained by Boivin's method and its final concentration in the samples of PEP was 0.1 μg/ml; the sodium salt of AA was used in a final concentration of 50 μg/ml and ADP in a concentration of 1 μg/ml.

Altogether 12 samples of PEP were tested. Before the experiments began all samples were studied for platelet function by the test with ADP. This degree of aggregation was taken as 100 in a concrete specimen of PEP. In all experiments 0.7 ml of the PEP sample was treated either successively or simultaneously with endotoxin, the sodium salt of AA, and ADP, each in a volume of 0.1 ml.

There were two series of experiments: in series I the test substances were added to the PEP sample contained in an aggregometer without interrupting the recording; in the experiments of series II samples of PEP were preincubated at room temperature with endotoxin or with a combination of endotoxin and the sodium salt of AA, after which the ability of the platelets to aggregate under the influence of ADP was recorded.

The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The degree of platelet aggregation induced by the sodium salt of AA was much less than when the reaction was induced by ADP, namely 27 ± 2.2% ($P < 0.05$; Fig. 1, 1). Addition of ADP led to a higher degree of aggregation than with ADP alone: the degree of aggregation was 107.2 ± 3.0% ($P < 0.01$; Fig. 1, 4).

The degree of platelet aggregation under the influence of endotoxin was significantly lower than with the sodium salt of AA (Fig. 1, 2), namely 14 ± 2.3% of the initial level of platelet function. Addition of ADP, just as with the sodium salt of AA, led to a value considerably higher than the initial level (Fig. 1, 5). The degree of platelet aggregation under these circumstances was 116 ± 3.5%).

Simultaneous addition of endotoxin and the sodium salt of AA to samples of PEP increased the aggregating power of the endotoxin threefold (Fig. 1, 3). On subsequent addition of ADP the degree of platelet aggregation was 130 ± 5.6%, which differed significantly from the original platelet activity (Fig. 1, 6).

The results of the experiments of series I thus demonstrated the distinct stimulating effect of the sodium salt of AA on the reaction of platelet aggregation induced both by endotoxin and by ADP.

After incubation of the PEP samples with endotoxin there was a significant decrease in the degree of aggregation induced by ADP. It amounted to 80 ± 4.0% (Fig. 2a). After incubation for the same period with endotoxin, but combined with the sodium salt of AA, the platelets retained the same aggregating power as initially (Fig. 2b). Consequently, just as in the experiments of series I, AA had a stimulating effect on the aggregating properties of the platelets.

The stimulating effect of AA on endotoxin-induced platelet aggregation requires further study. Meanwhile the results so far obtained suggest that the addition of the substrate for PG biosynthesis (AA) to samples of PEP from normal blood donors probably leads to a change in the PG level. Activation of platelets by thrombin, collagen, or ADP is known to lead to the liberation of AA from membrane phospholipids under the influence of phospholipase. Platelet lipoxygenase and cyclo-oxygenase transform AA into PG, which stimulate (PG_2, PGH_2, thromboxane A_2) or inhibit (PGE_1, PGD_2) the aggregating properties of platelets [1, 2, 9].

The results of the present investigations are evidence that the degree of platelet aggregation induced by endotoxin is increased in the presence of AA, probably because of its role in PG biosynthesis.

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