The investigations into the relationship between the adrenal cortex and the properdin level have revealed the following:
1. Under the effect of a stress the properdin level decreases.
2. Adrenalectomy considerably decreases the properdin level.
3. On examining the effect of the various cortical hormones, the following facts could be established: the deep fall of the properdin level in the untreated group is lessened by prednisolone and increased by DOCA, whereas it is completely counteracted by aldosterone and cortisol displaying mineralo- and glycocorticoid properties. In the case of normal adrenal function, the properdin level is decreased by cortisone DOCA and prednisolone treatments, but it hardly changes under the effect of aldosterone.
4. By a regular zymosan treatment the amount of properdin, after a transitional increase of the level, can be completely exhausted. The adrenal gland has probably something to do with it, although the exact nature of its function has not yet been clarified.
5. In adrenalectomized and zymosan-treated rats, after the temporary maintenance of the initial level, the exhaustion sets in earlier.

Ever since Pillemer's\textsuperscript{16} discovery, properdin has been discussed in a growing number of papers devoted partly to its biochemistry, partly to its role in certain pathological processes. Properdin is a constituent of the normal serum, a protein found by Pillemer\textsuperscript{17} in his electrophoretic experiments to be bound to gamma 1, and by Scheiffarth\textsuperscript{18} in immuno-electrophoresis to be bound to beta globulin. Its quantity in the serum varies according to species. It requires Mg\textsuperscript{++} and the complement C'3 for its action. It protects the organism against certain bacteria and viruses, and inhibits the growth of these bacteria \textit{in vitro}. It lyses the pathological red blood cells. The properdin system is an important, aspecific protective means of the organism.

Since, on the basis of Selye's\textsuperscript{19} investigations and his stress conception, the hypophysis—adrenal system is regarded as the defence regulator of the
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organism, the question arises how the activity of the adrenal cortex is related to the properdin level and whether there is any connection between stress and properdin level. In this respect little information can be obtained from the literature.

In humans Hinz\textsuperscript{14}) observed no change in the properdin level after adrenalectomy, surgical interventions or steroid treatment. A pronounced decrease in the properdin level was observed by Benson\textsuperscript{1}) after splenectomy and by Fumarola\textsuperscript{13}) after carcinosis, infarct, operation necroses, etc.

By using cortisone Soloviev\textsuperscript{20}) could inhibit the activity of the properdin system.

By administering echinacin, an extract from Echinacea purpurea having a stressor effect, Büsing\textsuperscript{8}) could achieve a considerable increase of the properdin level after a transitional decrease.

Frank, Fine and Pillemer\textsuperscript{10}) observed a sudden fall of the properdin and complement levels in hemorrhagic shock. Fischer, Brückner, Fritzschke and Becker\textsuperscript{9}) observed the decrease of the amount of properdin and complement in every state which Hoff\textsuperscript{15}) referred to as “vegetative Gesamtumschaltung”. Since this is regularly concomitant with the increase of fibrinolysin and with the liberation of heparin, Fischer and co-workers ascribe the decrease of properdin hypothetically to these phenomena. The danger of infection, increased after X-irradiation and stress states, is traced back also by Fritzschke\textsuperscript{11}) to the liberation of heparin and to the subsequent decrease in the properdin level.

In our animal experiments we endeavored to approach the influence of the adrenal cortex and of the properdin level upon each other\textsuperscript{2-7}).

Attempts were made to answer the following questions:

I. What is the effect of the adrenocortical hormones upon the properdin level a) in intact and b) in adrenalectomized organisms?

II. What is the effect of zymosan treatment upon the adrenal cortex?

METHODS

For the experiments white male rats were chosen, weighing 100 to 150 g. Each group comprised ten animals. All animals were kept on the same diet during the experiments.

a) The bilateral adrenalectomy was performed in one session, under ether narcosis, through the lumbar incision.

b) Blood samples were taken on every third day, at an identical time of the day in each group, from starving animals by amputating part of their tails under ether narcosis. The amount of blood on every occasion was 1 ml.

c) The pseudo-operation consisted of the following: through the lumbar incision the kidneys were removed, then replaced, without removing the adrenal
d) Treatments:
- Zymosan: 20 gamma/animal daily, s.c.
- Prednisolone: 1 mg/animal daily, s.c.
- DOCA 1 mg/animal daily, i.m.
- Aldosterone: 0.1 mg/animal daily, water solution, s.c.
- Cortisone: 5 mg/animal daily, suspension, i.m.

e) The properdin was determined by Schultze's method.

f) Statistical evaluation according to the T test.

For the computations we relied on the properdin values obtained on the 3rd and 6th days.

Groups investigated:
1. Untreated control group
2. Prednisolone-treated group
3. DOCA-treated group
4. Cortisone-treated group
5. Aldosterone-treated group
6. Zymosan-treated group

Every group contained two subgroups: a) intact and b) adrenalectomized

RESULTS

Fig. 1 shows the effect of the adrenocortical hormones upon the properdin
level in animals with intact adrenal gland on and in those adrenalectomized. The curves represent the mean of ten values.

In the intact animals of the untreated control group the properdin level rises above the initial value after a slight temporary fall. In the untreated adrenalectomized animals the level shows a sudden fall.

In the intact animals of the prednisolone-treated group the properdin level shows a slight but constant decrease.

After DOCA treatment there is a marked decrease in the properdin level in both subgroups a and b; yet even more pronounced in the adrenalectomized rats.

In the aldosterone-treated animals no essential difference could be detected; the properdin level in both subgroups runs parallel to that of the untreated control animals.

Under the effect of cortisone treatment the properdin level of the intact animals shows a gradual decrease which is significantly greater than that of the prednisolone-treated animals, its effect being almost as strong as that of DOCA. On the other hand, the properdin level of the adrenalectomized rats in this group displayed hardly any change. Its curve is similar to that of the aldosterone-treated ones.

The effect of zymosan treatment is shown in Fig. 2: in the intact rats the properdin level rises considerably for two weeks and drops suddenly to zero on the third week. The adrenalectomized animals show no changes in the properdin level during the first nine or so days but between the 9th and 15th days it suddenly drops to zero.
DISCUSSION

After adrenalectomy the properdin level drops significantly lower on the third day than in the control group: it falls to the 1/6 of its initial value.

We tried to find out whether and to what extent this was due to the operational trauma and to the cessation of the adrenal activity.

For this purpose the influence of a pseudo-operation upon the properdin level was examined.

The fall of the properdin level in the pseudo-operated group significantly differed from that in the adrenalectomized group; accordingly (cf. Fig. 2), the fall in the properdin level caused by far less marked than that caused by adrenalectomy. It may then be concluded that the great fall in the properdin level is attributable to adrenalectomy.

On examining the role of the glycocorticoids, it can be seen that in prednisolone-treated animals with intact adrenal cortex the properdin level gradually decreases. This differs significantly from that of the untreated animals. After adrenalectomy we have a different picture: here the curve does not fall as deep as in the untreated control group on the third day (a significant difference), and shows a significantly higher rise on the sixth. Hence it seems that in animals with intact adrenal glands the prednisolone treatment decreases the properdin level whereas after adrenalectomy it gradually increases it, i.e. it has a beneficial effect.

The properdin level in the DOCA-treated intact rats is significantly lower than in the controls or even in the prednisolone-treated animals; after adrenalectomy this effect is even more pronounced; the value falls to zero and the animals die. Since the DOCA-treated animals are known to endure adrenalectomy better than the untreated ones, it may be presumed that the taking of blood on every third day constitutes a series of stresses for the animal and that the DOCA treatment weakens their resistance to the stresses. Under the effect of mineralo- and glycocorticoids the properdin level was thus found to behave quite differently. It is interesting to note that aldosterone, which is in the first place a mineral corticoid but has glycocorticoid properties, hardly affected the properdin level. No essential difference could be noticed between the intact and the adrenalectomized rats in this group on the third day, where otherwise the values after adrenalectomy were the lowest. It may be concluded that after adrenalectomy, when only the externally administered corticosteroids are active, this effect can clearly be evaluated.

Aldosterone and cortisone, the hormones having mineralo- and glycocorticoid properties, can be regarded as the best substituents for adrenal activity. This is valid also for the properdin level. If, however, the adrenal gland is intact, probably on account of the active adrenal gland in the organism, the situation is less clear. In such cases, as with prednisolone and DOCA but at variance
with aldosterone, the effect of cortisone is unfavorable. It may be concluded that aldosterone, owing to the proportion of its mineralo- and glycocorticoid properties, is the most effective hormone for immunity, at least as far as properdin is concerned. The properdin curve of animals subjected to a regular zymosan treatment shows the changes occurring after a single dose of zymosan. This lasts up to the 12th day when it begins to fall, attaining zero on the 21st day. This indicates that by a regular zymosan treatment the amount of properdin in the organism can be exhausted. Zymosan in large doses is known to bind a quantity of properdin whereas in small doses it enhances properdin production.
It seems, however, that the regular administration of zymosan fails to stimulate properdin production which gradually decreases to zero. The production and utilization of properdin are influenced by many factors which probably have not been entirely clarified so far. Since, however, we were concerned with the relation of properdin to the adrenal gland, we examined the state of the latter when the properdin completely vanished. The histological examination showed signs of hypertrophy in the control animals (Figs. 3–6). In addition to the
symptoms of hypertrophy covering mainly the zona glomerulosa, the adrenal glands of zymosan-treated animals showed blood serous imbibitions, i.e. the histological picture of acute adrenocortical insufficiency. As a supplementary experiment, in addition to the groups listed above, ten intact animals were zymosan-treated for twenty-one days. Blood was taken from them only on the 21st day. The samples showed that the properdin level had fallen to zero by that day and the "acute collapse" of their adrenal glands could be demonstrated. Hence, this effect is independent of the aspecific stress series (taking of blood samples) and is related to the fall of the properdin level to zero under the effect of zymosan.

In the adrenalectomized animals of the zymosan-treated group, the properdin level remained practically unaltered: neither did the properdin level fall in the rats after adrenalectomy, nor did it rise as it would have done in the intact zymosan-treated subgroup. On the 9th day following adrenalectomy the properdin level started to decrease and fall to zero on the 15th. Hence the zymosan treatment could maintain the properdin level at the initial value even after adrenalectomy; yet on the 12th day the fall occurred sooner than in the adrenalectomized untreated subgroup.

The fact that on adrenalectomy the properdin level falls, as well as the fact that the amount of properdin in the adrenalectomized animal can be exhausted much sooner than in the intact ones, proves the existence of some connection between the adrenal cortex and the properdin system. Our experiments conducted so far have not yet revealed the nature of this connection, but further investigations into this problem are in course.

References
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