

It is interesting that the effects of both drugs on 5-HT absorption correspond to their curative activity. Propazepin as an antidepressive drug is less effective than imipramine by $1/3-1/2$.

Zusammenfassung. Propazepin erniedrigt ähnlich wie Imipramin die Serotoninabsorption durch Thrombocyten, in vitro wie auch in vivo. Es besteht eine Korrelation zwischen ihrer Absorptionshemmung und antidepressiven Einwirkung. Diese Substanzen stossen Sero-

tonin nicht aus den Thrombocyten hinaus und beeinflussen die Synthese des endogenen Serotonins nicht. Der aktive Stoff ist wahrscheinlich ein Metabolit.

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Further Evidence of the Existence of Differences in the Mechanism of Immune Cellular Injury of Sheep Erythrocytes and Rat Mast Cells¹

Recent comparative studies on the complement donor activity of sera of various species have revealed striking differences between the in vitro models of immune hemolysis and the rabbit anti-rat γ -globulin/mast-cell system². Further experiments in the mast-cell system have shown that human serum made deficient in the second component of complement (R_2 -serum) has virtually the same donor activity as untreated human serum³, thus indicating that, for immune injury in this system, this step of complement activation might not be necessary. Furthermore, studies with human lipoprotein fractions have demonstrated that α_1 -lipoprotein is a suitable substrate for bee venom phospholipase A to obtain hemolysis, but not for mast-cell lysis³. Moreover, the surface of rat peritoneal mast cells is definitely altered on incubation with rather low concentrations of chymotrypsin, while this does not prove to be so for sheep erythrocytes⁴. These findings indicate that the two cell types behave differently and support the assumption that the mechanism of immune lysis in the above in vitro systems might be different. Recently, K. and U. ROTHER⁵ described a rabbit strain whose serum is deficient in the third component (C'_3) of complement (Freiburg R_3 -Stamm); with this serum, immune hemolysis only occurs in the additional presence of a preparation containing C'_3 . The present study deals with the effect of this serum on the immune reaction in the mast-cell/ARGG system⁶.

Rat peritoneal mast cells were isolated, incubated with purified anti-rat γ -globulin and a 'complement' donor for 10 min at 37°C, centrifuged, and the percentage of total histamine contained in the sediment and supernatant assayed as described previously. Besides C'_3 -deficient rabbit serum, fresh normal rabbit and human sera were used as 'complement' donors.

The results listed in the Table reveal that, in the presence of C'_3 -deficient or normal rabbit serum, virtually the same percentage of histamine is released from rat mast cells during the immune reaction and, under the phase

contrast microscope at 37°C, rat mast cells undergo the same morphological changes with both C'_3 -deficient and normal rabbit serum when antibody is additionally present; these sera, therefore, seem to be equally active in donating 'complement' in the mast-cell/ARGG system. It is known that conversion of pro-enzyme to active C'_1 -esterase and the activity of this enzyme were inhibited by a component naturally occurring in fresh human serum which is non-dialyzable, heat-labile, and unrelated to any of the recognized components of human complement⁷. In the in vitro system under discussion, high concentrations of human serum (20–40%) inhibit the immune reaction and consumption of complement³, and the inhibitory effect is abolished by heat pretreatment (30 min at 56°C). Therefore, it seemed to be of interest to examine, in the presence of C'_3 -deficient or normal rabbit serum as 'complement' donors, the effect of high concentrations of fresh human serum on the process of the immune reaction. These experiments (see Table) show that, in the additional presence of 20% normal human serum in the incubate, the immune reaction is inhibited equally by both C'_3 -deficient and normal rabbit serum. The results therefore strongly indicate that the third component of complement is not necessary to obtain immune cytotoxicity in the in vitro system under discussion; in contrast to this, activation of the first component of complement or a similar esterase seems to be an absolute precondition for this process.

These findings support the existence of profound differences in the biochemical mechanisms leading to immune hemolysis and immune injury in the mast-cell/ARGG system.

Zusammenfassung. Isolierte Rattenmastzellen reagieren auf Zugabe von Antikörper gleichermassen mit Histaminfreisetzung und morphologischen Veränderungen, unabhängig davon, ob als «Komplement»-Donator normales Kaninchenserum oder Serum von Kaninchen zugegeben wird, das kein C'_3 enthält. Dagegen wird die Reaktion mit beiden Kaninchenseren durch hohe Konzentrationen von Humanserum gehemmt.

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% of total histamine released from rat mast cells under various conditions

Mc + ARGG + 7% NRS	70 ($\pm$ 11)
Mc + ARGG + 7% DRS	74 ($\pm$ 8)
Mc + ARGG + 7% NRS + 20% HS	28 ($\pm$ 9)
Mc + ARGG + 7% DRS + 20% HS	24 ($\pm$ 7)

NRS = normal rabbit serum. DRS = C'_3 -deficient rabbit serum. HS = fresh human serum. ARGG = chromatographically purified anti-rat γ -globulin. Mc = isolated rat peritoneal mast cells.

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² R. KELLER, *Int. Arch. Allergy* 24, 255 (1964).

³ R. KELLER, *Int. Arch. Allergy*, in press.

⁴ R. KELLER, unpublished results.

⁵ K. ROTHER and U. ROTHER, *Z. Immunforsch.* 121, 224 (1961).

⁶ C'_3 -deficient rabbit serum was kindly donated by Drs. U. and K. ROTHER.

⁷ J. PENSKE, L. R. LEVY, and I. H. LEPOW, *J. biol. Chem.* 236, 1674 (1961).