EFFECTS OF DISODIUM CROMOGLYCATE AND
ANTIHISTAMINES IN ACUTE SERUM SICKNESS
OF RABBITS

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An increase of the vascular permeability induced by the release of vasoactive
amines from platelets seems necessary for the deposition of immune
complexes in acute serum sickness of rabbits. Direct evidence has been
obtained that this mechanism is triggered by IgE-sensitised basophils.

We have previously shown in acute serum sickness of rabbits that a
reduction in basophil count occurs 48 hours before the onset of proteinuria
and appears to be a prerequisite for the production of the kidney lesion.

Recently it has been suggested that the use of disodium Cromoglycate or
antihistamines prevents the development of glomerulonephritis.

The aim of this work is to prove the therapeutic effect of disodium
Cromoglycate in association with various antihistamines in acute serum
sickness of rabbits.

Material and Methods

Acute serum sickness was induced in inbred white rabbits weighing between
1.5 and 2.5kg by a single intravenous injection of bovine serum albumin
(BSA) labelled with $^{125}$I, at a dose of 250mg/kg/body weight. To enhance
the incidence of disease, 10mg/kg of BSA in Freund's complete adjuvant were
subcutaneously injected three days before the large dose of BSA.

Levels of $^{125}$I BSA, total leucocytes, basophils and proteinuria were
determined daily. Circulating immune complexes were assayed by measuring
the amount of $^{125}$I–BSA precipitated from plasma by 50% ammonium
sulphate at 4°C.

Disodium Cromoglycate was administered from the day before the low
dose of BSA and antihistamines from the third day after the large dose of
BSA.

Schedules of treatment employed are shown in Table I.

Some rabbits were injected again with BSA after interruption of all
drugs.
TABLE I  Schedules of Treatment Employed

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatments</th>
<th>Doses/Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Disodium Cromoglycate</td>
<td>5mg/kg/day</td>
</tr>
<tr>
<td>B</td>
<td>Disodium Cromoglycate</td>
<td>50mg/kg/day</td>
</tr>
<tr>
<td>C</td>
<td>Hydroxyzine</td>
<td>30mg/kg/day</td>
</tr>
<tr>
<td>D</td>
<td>D-Chlorpheniramine</td>
<td>0.30mg/kg/day</td>
</tr>
<tr>
<td>E</td>
<td>Mequitazine</td>
<td>2mg/kg/day</td>
</tr>
<tr>
<td>F</td>
<td>Azatadine</td>
<td>0.375mg/kg/day</td>
</tr>
</tbody>
</table>

Disodium Cromoglycate was administered daily in five SC injections
Antihistamines were administered daily in three SC injections

The kidneys were studied by light microscopy, immunofluorescence and in some cases with electron microscopy.

Results

The percentage of rabbits with glomerulonephritis in all groups, the maximal amount of immune complexes, basophils count reduction and proteinuria are shown in Table II.

TABLE II  Maximal amount of IC, BCR and proteinuria in rabbits with glomerulonephritis

<table>
<thead>
<tr>
<th>Rabbits with glomerulonephritis</th>
<th>Maximal Levels of IC†</th>
<th>Maximal BCR*</th>
<th>Maximal Proteinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>No/Total</td>
<td>Percentage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>10/12</td>
<td>83</td>
<td>50 ± 4.5 *</td>
</tr>
<tr>
<td>Group A</td>
<td>4/5</td>
<td>80</td>
<td>40.25 ± 11</td>
</tr>
<tr>
<td>Group B</td>
<td>4/9</td>
<td>45</td>
<td>48.45 ± 8.53</td>
</tr>
<tr>
<td>Group C</td>
<td>3/5</td>
<td>60</td>
<td>42.66 ± 11</td>
</tr>
<tr>
<td>Group D</td>
<td>2/4</td>
<td>50</td>
<td>52.5 ± 0.70</td>
</tr>
<tr>
<td>Group E</td>
<td>3/5</td>
<td>60</td>
<td>41.83 ± 4.80</td>
</tr>
<tr>
<td>Group F</td>
<td>2/5</td>
<td>40</td>
<td>47.0 ± 5.65</td>
</tr>
</tbody>
</table>

Reinduction
Acute serum sickness 3**/12  25  61.0 ± 8.55  148 ± 38
P<0.005  ***  P<0.005

†IC : Immune complexes; expressed as percent of total daily plasma radioactivity
*BCR : Basophil count reduction; expressed as percent of the mean individual values during the predisease period
*Mean ± standard deviation
‡Student’s t test : n.s., not significant, as compared with controls
** Other three died of anaphylactic shock when reinjected
*** Compared with maximal BCR in primary induction

Comments

All treated animals except those receiving low doses of disodium Cromoglycate developed a lower percentage of glomerulonephritis than controls.

Rabbits with glomerulonephritis in all groups presented no differences as
compared with controls neither in intensity of proteinuria, in basophils count, nor in the histological examination.

When antihistamines and high doses of disodium Cromoglycate were given, results were similar to those obtained with disodium cromoglycate alone. Some rabbits injected again with a large dose of BSA developed glomerulonephritis and the reduction of the circulating basophil count was more remarkable than in the first injection. This fact in addition to the sudden death of other animals in anaphylactic shock, supports the hypothesis of the participation of the IgE-basophil system in acute serum sickness.

Conclusions

The participation of IgE-basophil system in acute serum sickness is confirmed.

Disodium Cromoglycate prevents the development of glomerulonephritis in some rabbits and has no effect in others.

The association of antihistamines has no additional protective value.

Other drugs capable of inhibiting the basophil degranulation and antagonising permeability increasing agents are needed.

References

3 Kniker, WT and Wagner, MS (1975). In Abstracts of free communications. VIth International Congress of Nephrology, Firenze, 418