The Influence of Cortisone on Tuberculin Shock in the Guinea Pig

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There have been several reports indicating that cortisone suppresses or "blocks" the tuberculin skin reaction in man and experimental animals.\textsuperscript{1-3} Also it has been shown that ACTH or cortisone inhibits the development of the Arthus phenomenon due to a suppression of antibody formation.\textsuperscript{4} Recently it has been demonstrated that ACTH or cortisone did not prevent histamine effects on sensitized guinea pigs nor did these compounds decrease the mortality from anaphylactic shock in sensitized guinea pigs.\textsuperscript{5,6} This differs from a report that cortisone prevented fatal anaphylactic shock in mice sensitized with horse serum.\textsuperscript{7} Reinmuth and Smith\textsuperscript{8} have demonstrated that ACTH administered to rabbits sensitized to M. tuberculosis and then injected intratracheally with Old Tuberculin had less extensive reactions than untreated controls. When ACTH was withdrawn, a fresh pneumatic consolidation occurred which was less severe than the reactions seen in the controls.

It was thought to be of interest to learn whether or not cortisone modified in any way the classical type of tuberculin shock in tuberculous animals.

\textit{Materials and Methods}: Twenty-four male albino guinea pigs with an average weight of 350 g. were injected intradermally with 0.1 ml. 10 per cent Old Tuberculin and were found to be tuberculin negative. These animals were then inoculated subcutaneously in the groin with 0.1 mg. virulent human tubercle bacilli (H37 Rv) from a young liquid culture (Proskauer and Beck medium).

Twenty-five days after infection these guinea pigs were again tuberculin-tested in the manner described above. All animals were found to react to intradermal injections of Old Tuberculin. On the 27th day after infection, the animals were divided into two groups. Twelve received a daily intramuscular injection of 10 mg.

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cortisone acetate (Merck). Another 12 guinea pigs were injected intramuscularly daily with 0.4 ml. sterile physiological saline. These daily injections of cortisone acetate and saline were continued for five days.

On the fifth day of therapy (32nd day of infection) both groups of animals were injected intraperitoneally with 1.0 ml. concentrated Old Tuberculin. All survivors were autopsied 36 hours later.

A second experiment, employing 16 guinea pigs, was carried out in a similar manner to determine whether or not cortisone merely delayed the occurrence of the tuberculin shock. Instead of sacrificing the animals 36 hours after the intraperitoneal injection of concentrated Old Tuberculin, they were observed for 96 hours after the cortisone was discontinued.

Results: The results of the first experiment are summarized in Table I. All animals exhibited clinical evidence of anaphylaxis. The group that received the daily injections of saline demonstrated a more severe reaction than did the group treated for five days with cortisone acetate. Thirty-six hours after the intraperitoneal injections of concentrated Old Tuberculin, 11 of the 12 guinea pigs of the saline-injected group were dead, whereas only four of the 12 animals in the cortisone-acetate-treated group had died in the same period of time. Autopsy of the animals that died from

<table>
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<tr>
<th>TABLE I</th>
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| Effect of Cortisone on Tuberculin Shock in Guinea Pigs. 
(36 hours after intraperitoneal injection of O.T.) |

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Number Animals</th>
<th>Number Survivors</th>
<th>Per cent Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>H37 Rv Saline (0.4 ml. daily, 5x)</td>
<td>12</td>
<td>1</td>
<td>8.3</td>
</tr>
<tr>
<td>H37 Rv Cortisone Acetate (10 mg. daily, 5x)</td>
<td>12</td>
<td>8</td>
<td>66.6</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>TABLE II</th>
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</table>
| Effect of Cortisone on Tuberculin Shock in Guinea Pigs. 
(Observed for 96 hours after intraperitoneal injection of O.T.) |

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Number Animals</th>
<th>8 hrs.</th>
<th>24 hrs.</th>
<th>48 hrs.</th>
<th>72 hrs.</th>
<th>96 hrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>H37 Rv Saline (0.4 ml. daily, 5x)</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>H37 Rv Cortisone Acetate (10 mg. daily, 5x)</td>
<td>8</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
shock in each group during the 36-hour period revealed active progressive tuberculosis, involving lymph nodes, lung, spleen, and liver. There was marked edema about the face, eyes, and feet. Their peritoneal and thoracic cavities contained a large amount of free fluid, usually quite bloody. The spleens and livers were hemorrhagic and in several cases ruptured. The cutaneous tissue at the site of the intraperitoneal Old Tuberculin injection was hemorrhagic and edematous.

The animals surviving for 36 hours in both groups recovered from the shock and were autopsied. The degree of tuberculosis was comparable to that found in animals which had died of tuberculin shock.

The results of the second experiment are summarized in Table II, where it can be seen again that cortisone afforded some protection against tuberculin shock. There was no significant delay in the development of shock since all of the deaths occurred within 48 hours.

Discussion: Cortisone seems to protect tuberculous guinea pigs from tuberculin type anaphylaxis. Whether the mechanism of action is mediated directly through some interference with antigen-antibody reaction, or whether the suppression of capillary dilatation and acute inflammatory reaction which has been noted with cortisone administration plays the major role, is not clearly understood at this time.

Autopsy studies of the animals which were sacrificed and those which died indicate that protection probably results from inhibition of capillary dilatation and hemorrhagic reaction.

SUMMARY

Cortisone acetate affords partial protection from the classical type of tuberculin shock in tuberculous guinea pigs.

RESUMEN

El acetato de cortisona proporciona un protección parcial contra la forma clásica del choque tuberculinico en los cuyes tuberculosos.

RESUME

La cortisone donne une protection partielle contre le choc classique que réalise la tuberculine chez le cobaye tuberculisé.

REFERENCES


