ON THE SENSITIVITY, RESISTANCE AND TOLERANCE
OF RATS OF VARIOUS AGES TO TETANUS TOXIN

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In evaluating the differences between lethal doses of bacterial toxins for animals of different ages, many author:
apply concepts of sensitivity, resistance and tolerance that differ in meaning and in physiological content.

Thus, D. F. Pletsityi [4] reported that newborn mice do not contract local or systemic tetanus, easily withstand
doses of tetanus toxin which are lethal for adults, and thus, in comparison with the latter, are characterized by a
higher resistance or stability. L. I. Tank [11], on the other hand, established that newborn mice do contract tetanus;
the absolute lethal dose of tetanus toxin for them is almost three times greater than the analogous dose for adults.
The author sometimes designates this difference as greater tolerance, and other times as less sensitivity.

In the investigations of our laboratory, attention was drawn to the necessity for differentiating the threshold
doses of toxin in animals of differing ages, including the doses that first cause local tetanus, and those at which
one observed the transition to systemic tetanus and death of the animals [1, 2, 5].

In analyzing the action of a series of pharmacological substances, we concluded that it was necessary to differ-
entiate in the use of the terms, "sensitivity," "resistance," and "tolerance" for evaluating the reactions of the ani-
mals of different ages [6-9].

The purpose of this work was to determine the sensitivity, resistance, and tolerance of rats of different ages to
tetanus toxin.

EXPERIMENTAL METHODS

Tetanus toxin, diluted in physiological saline, was injected subcutaneously into the left posterior extremity,
using a volume of from 0.025 to 0.05 ml, and doses ranging from threshold to the absolute lethal level. Each dose,
expressed in micrograms per gram of body weight, was injected into rats of known age (each group contained 5-10
animals). The experiment included newborn rats, rats that were 3-8 days old, 4-6 weeks old, and adult animals.
Observations were not only carried out on the clinical symptoms of local and systemic tetanus, but also for changes
in temperature, respiration, ECG and body weight.

EXPERIMENTAL RESULTS

Considering that the concept of "sensitivity," in the physiological sense, is close to that of "excitability" or
"stimulation threshold," we proposed to use the minimum dose causing initial symptoms of local tetanus as the criter
for sensitivity.

The investigations showed that the threshold dose of tetanus toxin for newborn rats is almost 8 times greater
than for adults, and for rats 3-8 days old the dose is almost 5 times greater than for adults. Only beginning with
the fourth week of age does the threshold dose of tetanus toxin approximate that for adult rats (see table).

Our data not only permitted us to evaluate the difference in threshold doses, but also to construct curves for
the individual sensitivity, which reflect the variation in the threshold doses for different individuals of two age groups:
for rats 3-8 days old and for 4 week old rats (Fig. 1). The curve for the individual sensitivity of the rats in the 4 week old age group (A) was situated more to the left, in the limits of the lower doses, than the curve for the 3-8 day old rats (A1). Thus, both newborn rats and those 3-8 days old are characterized by less sensitivity to tetanus toxin than 4 week old rats.

Doses of Tetanus Toxin for Rats of Different Ages (in micrograms per gram of body weight)

<table>
<thead>
<tr>
<th>Age</th>
<th>Threshold</th>
<th>DMT</th>
<th>DL&lt;sub&gt;100&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>0.0066</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-8 days</td>
<td>0.004</td>
<td>0.02</td>
<td>0.09</td>
</tr>
<tr>
<td>4 weeks</td>
<td>0.00034</td>
<td>0.009</td>
<td>0.03</td>
</tr>
<tr>
<td>Adult</td>
<td>0.00085</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Fig. 1. Curves of the individual sensitivity (A, A1), curves of the variation in resistance—tolerance (B, B1), curves of the variation in tolerance—lethality (C, C1), in rats of different ages. Abscissa — doses of tetanus toxin (in micrograms per gram of body weight, expressed logarithmically); ordinate — reaction of the sensitivity, resistance and tolerance type (in percents).

As the criterion of resistance to tetanus toxin, we used the width of the dosage range in which the animals of differing ages maintained the homeostatic state (despite marked manifestation of local tetanus) as reflected in a series of vegetative indices and in the closeness to normal of posture and mobility. For the rats in the early age groups, the indices of normal growth and development also served as essential criteria for appraising resistance. In previous investigations it was shown that the signs of local tetanus in adult rats and rats over 3 weeks of age, when injected with tetanus toxin,