EFFECT OF LEAD POISONING ON CONTRACTIONS OF THE ISOLATED INTESTINE OF WARM-BLOODED ANIMALS PRODUCED BY SOLUTIONS OF LEAD ACETATE

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One of the most marked disturbances of the activity of the digestive apparatus in lead poisoning is the symptom of lead colic. The pathogenesis of this symptom is not yet clear. Many investigators have attributed the tendency towards spasms of the intestine in patients with lead poisoning to lesions of various parts of the nervous apparatus of the intestine [3,4,11,14], and only a few writers have attributed it to the direct action of lead on the muscle [12,13]. However, the results of the investigation by this latter group proved contradictory, especially in relation to the character of the action of lead solution on the tone of the isolated intestine. According to some authors [12,13], lead acetate abolishes the peristaltic waves and increases the tone of a strip of the smooth muscle of the gastrointestinal tract; according to others [3,4], it never produces an increase in the tone of the isolated intestine but, on the contrary, it lowers the tone and weakens the peristaltic waves. Accordingly, several investigators have concluded that the clinical picture of lead colic is independent of the local action of lead on the intestinal muscle and that the relaxation of the isolated intestine is associated with stimulation of the sympathetic nerve endings.

The object of the present investigation, a continuation of previous studies [6,7,9], was to determine the reaction of the isolated intestine of healthy animals and animals with lead poisoning to the local action of lead.

EXPERIMENTAL METHOD

Experiments were carried out on isolated segments of the small intestine of guinea pigs by the usual method. The isolated intestine remained viable for 3-4 h and exhibited its characteristic peristaltic waves. Recordings were made on a stationary kymograph simultaneously from two segments taken from a healthy animal and one with lead poisoning. The degree of relaxation and contraction in response to introduction of solution of lead acetate into the receiver were taken to reflect relaxation and an increase in the tone of the isolated segment, respectively. The amplitude of the contraction was expressed in millimeters. The working concentration of lead acetate in the receiver was 0.02, 0.05, 0.1, 0.25, 0.5, 0.75, 1.0, and 5%. Each successive solution was added to the receiver (capacity 20 ml) after the preceding solution had been rinsed out. To prevent precipitation of the lead salt to the bottom of the receiver, air was bubbled from tubes for aerating the solution. In addition, from time to time the solution in the receiver was mixed by a stream of air from a syringe.

The animals were poisoned with a 5 and 25% solution of lead acetate by mouth in doses of 5 and 25 mg/100 g body weight (groups 1 and 2, respectively). The criteria of poisoning were the changes in body weight and in the blood picture (hemoglobin concentration, numbers of reticulocytes and erythrocytes with basophilic granules). In all the animals, changes in the blood at the time of the experiment demonstrated the development of acute and subacute poisoning. The periods of poisoning in most guinea pigs of group 1 were 1.5-2 months, and in a few animals from 42 to 90 days. In the animals of group 2, the duration of poisoning varied from 9 to 22 days. Altogether, 98 guinea pigs were used in the experiment, made up of 43 healthy animals (series I), 32 poisoned with 5% lead solution (series II), and 23 poisoned with 25% lead acetate solution (series III). For a quantitative analysis, experiments were carried out on 45 male guinea pigs of approximately equal weight, with 15 animals in each series.

Altogether 498 tests were made with different doses of lead acetate, including 24 with a 0.02% solution, 57 with a 0.05% solution, 81 with a 0.1% solution, 92 – 0.25%, 126 – 0.5%, 17 – 0.75%, 87 – 1.0%, and 14 with a 5% solution.

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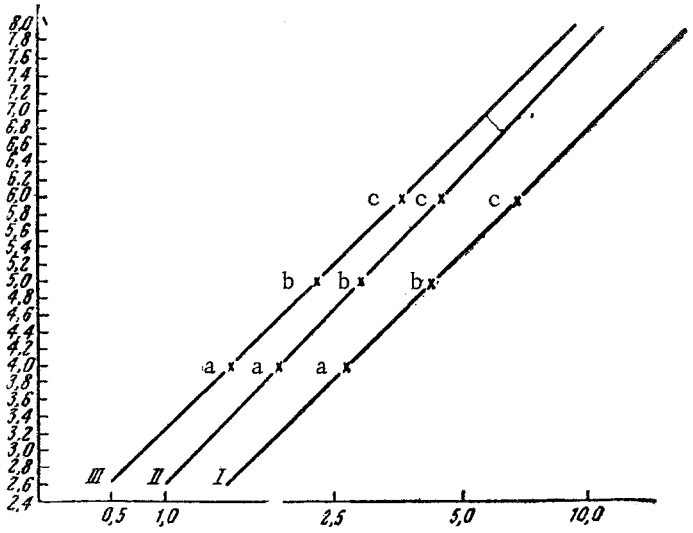

Graph of relationship between doses and effects produced by them (in probit by the method of Litchfield and Wilcoxon): I) healthy animals; II) poisoned with 5% lead solution; III) poisoned with 25% solution; a) ED_{16}; b) ED_{50}; c) ED_{84}.

The quantitative analysis of the experimental data was carried out by the method of Litchfield and Wilcoxon, based on the study of the relationship between the logarithms of the experimentally tested doses and probits corresponding to the observed effects [2]. By this method, graphs can be plotted reflecting the relationship between the doses and the effects they produced, the mean effective dose (ED_{50}) and the standard error of this mean can be determined and, finally, the pharmacological activity can be compared.

EXPERIMENTAL INVESTIGATION

The experiments showed that the action of lead acetate solutions on the isolated segment of intestine, whether from the healthy animals or from animals with lead poisoning, caused an increase in its tone, changing into a state of contracture when the concentration of the lead acetate was increased. This contracture was reversible if the concentration of lead acetate was low (0.25 and 0.5% solution). When more concentrated solutions of lead acetate were applied to the isolated intestine, the intestinal contractions reached a considerable amplitude, and the pen of the myograph rose 60-70 mm above the isoelectric line. In these experiments, the contracture was irreversible, despite vigorous rinsing for a long period (30 min).

The experimental results were used to plot graphs of the relationship between the doses and the effect they produced (see figure). The figure shows that a considerable difference was present between the reactions of the isolated intestine of the healthy animals and the animals with lead poisoning to the local action of lead acetate solution. Whereas ED_{50} for the healthy guinea pigs was 4.2 g/liter, for those poisoned with 5% lead solution it was 2.8 g/liter, and for those poisoned with a 25% solution of the lead salt – 2.2 g/liter. Consequently, the dose of lead acetate producing an effect in 50% of the experimental animals was much lower than the equivalent dose for the control group. Similar relationships were observed when the values of ED_{16} and ED_{84} were compared; these also confirmed that in the poisoned animals, the contracture of the isolated intestine developed at lower concentrations of lead acetate than in the controls.

So far as the difference between the results in the two groups of poisoned rats is concerned, as the material described shows, the greatest changes were observed in the group of animals poisoned with 25% lead acetate solution. The differences between the results of all three series of experiments were statistically significant. Comparison of the data for the experiments of series I and II showed that PR = 1.50, and fPR = 1.47, so that PR > fPR; for comparison of the experiments of series I and III, PR = 1.91 and fPR = 1.47, so that PR > fPR when P = 0.05.

Hence, the reaction of the isolated intestine to the action of the concentrated solutions investigated was shown by an increase in the tone of its smooth muscle, changing into a contracture. In animals preliminarily poisoned with lead acetate, a contracture of the isolated intestine developed at lower concentrations of lead acetate than in healthy animals. Evidently, lead poisoning creates a special predisposition to spasms of the intestine of contracture type, and this in turn may lead to disturbances of the motor function of the intestine.

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