TABLE I.
Action of Botulinum Filtrate upon Milk—4 to 1 Mixture.

cc. given	1	1/10	1/100	1/1000	1/5000
NaCl Solution and Filtrate (Mixed after incubation)	+	—	—	—	—
Milk and Filtrate (Mixed after incubation)	+	+	—	—	—
Milk and Filtrate Mixed (Incubated 4 days at 37° C.)	+	+	+	+	—

This result has been obtained again and again and we feel that these results together with certain other observations lend support to the view that the toxin may be produced extracellularly by the action of the enzymes of the organism on certain protein substrates. Similar results have been obtained with purified casein solutions in place of skimmed milk, and likewise when the filtrate is incubated with a suspension of sterile yeast cells. On the other hand, we have not succeeded in demonstrating a comparable increase in toxin when the filtrate is allowed to act upon peptone, ash-free gelatin, extract of fresh beef (in concentrations used in bacteriological media), and trypsin digested milk. While the trypsin digested milk yielded a greater increase in toxicity than the other substances which are listed as giving negative results, the increase was not comparable to that obtained from normal skimmed milk. This is suggestive.

That the increased toxicity obtained by the action of botulinum filtrate upon skimmed milk is due to an increase in the specific toxin is indicated by the fact that this toxicity was completely counteracted by a type A antitoxin procured from a biological supply house.

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Chronic Barbital Poisoning in the Rabbit.

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Clinically chronic barbital poisoning has been observed repeatedly. On the other hand no observations upon the effects of repeated injections of this drug upon animals seem to have been reported. The desirability of comparing similarities of symptoms in man and in laboratory animals is obvious.

At the start of a 12 week period rabbits were injected daily with a dose of 0.03 gm. of soluble barbital which was gradually increased to reach 0.15 gm. at the end of the period.

At the end of the 12 week period there were no appreciable changes in weight, heart and respiratory rates, appearance of the skin and hair coat, in the amount and character of stools, whereas the urine output seemed to be slightly diminished. There was undoubtedly a marked vasodilatation in the animals as evidenced by the congestion of the ears. At the end of the period the blood sugar level was found to be normal.

The most outstanding effects produced were upon the central nervous system. There was a marked increase of irritability and restlessness. They developed a very peculiar disturbance in gait. The movements of the fore limbs were quite normal. The hind limbs, however, showed a very decided backward thrust, such as one might expect were the rabbits attempting forceful movements on a very slippery surface. In this connection it should be recalled that in chronic barbital poisoning in human subjects one frequently sees cerebellar ataxy. The motor phenomena described above resemble the "rebound" seen in man.

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The Effect of Subcutaneously Injected Epinephrin in Normal Human Subjects.

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The conditions under which subcutaneously injected epinephrin gives a pressor effect in the dog, have been studied by Luckhardt and Koppányi,[1] who found that, when the site of injection has been massaged, there was a rise in blood pressure of from 15 to 180 mm. of Hg. following each massage. Lilienthal[2] used this method in the treatment of asthma and shock in man and obtained pressor responses upon massaging the injected area, for nearly 48 hours following the injection of 0.3 cc. of epinephrin 1:1000. The blood pressure elevations he obtained were comparatively slight (7 to 10 mm. of Hg.). In view of these observations it seemed desirable to

[1] Luckhardt and Koppányi, *Am. J. Physiol.*, 1927, lxxxi, 436.

[2] Lilienthal, *J. Am. Med. Assn.*, 1928, xc, 1192.