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.

investigate the action of subcutaneously injected epinephrin in normal human subjects.

Six young healthy medical students were subjected to subcutaneous epinephrin injections (0.4 cc. of a 1:1000 solution). Before injection the normal systolic and diastolic blood pressure and the heart and respiratory rates were determined. From 10 to 15 minutes following the injection of epinephrin there was a rise in blood pressure of 30 to 50 mm. of Hg., a slight increase in the heart and respiratory rates without any massage. The injected area was blanched, the face pale, there was a slight muscular twitching in the arms and legs; and a thumping, palpitating heart was evident. The subjects felt slight head-ache, throbbing in the head, some nausea, the mouth was dry and there was in some cases subjective sensation of warmth, in others the hands and feet felt cold. Nervousness and general feeling of anxiety were evident in most subjects, whereas one subject appeared to be in a fighting mood.

The injected areas were massaged from 15 minutes to 48 hours following injections. In the course of the 48 hours the area was massaged about 25 times. On the whole, all the symptoms which appeared following epinephrin injection without massage, could be duplicated by massaging the injected area, *for about 48 hours.* They were, however, much less marked, the blood pressure rises for instance being seldom more than from 7 to 15 mm. of Hg. The rise was practically the same when one massaged the area 20 minutes or 20 hours following the injection. One subject developed constipation following the injection.

Comparing the results obtained in the dog and in man, it is evident that (a) there is a hemodynamic effect following the hypodermic injection of epinephrin in man even without massage, whereas no such effects occurred in the dog. Apparently in man epinephrin is more readily absorbed from the subcutaneous tissues, than in the dog. (b) Both in man and in dog the hypodermic epinephrine depot is not depleted for from 22 to 48 hours and may be utilized to produce hemodynamic effects upon massage. The blood pressure rises following massage are more marked in the dog than in man.