Etherization or other operations or both might also lead to this anemia. In 8 rats, using such operations as laparotomy and castration or crushing the testicle, removal of one or both adrenals, removal of the frontal lobes of the brain, no significant anemia followed the operation. In 4 of these animals splenectomized from 11 to 13 days after operation severe anemia promptly followed the splenectomy.

In 2 cases thus far we have injected blood from a rat of the infected stock into Wistar rats. Splenectomy of these rats led to the development of a typical fatal anemia in both cases, showing the transmission of the virus.

Our findings further emphasize the great importance of the spleen as a dominant part of the defensive mechanism of the body against latent infections. In addition, we feel that the demonstration of *Bartonella* infections among rats in this country necessitates careful elimination of such infected animals from experiments involving a study of nutrition and particularly from all experiments in which splenectomized animals are used.

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Circulatory Reactions to Ergotamine and Effect Upon Them Produced by Adrenalectomy and the Blood pH.

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According to the observations of Rothlin,[1] Dale and Spiro,[2] and Schegg,[3] ergotamine tartrate in doses not exceeding 1.0 mg. per kilo given intravenously to cats and dogs produces a rise of blood pressure. Rothlin reported that very small doses also produced a slight fall of blood pressure in cats, but he ignored this observation in a later communication.[4] His blood pressure tracings showed that the pressor effect was not of exactly the same type. Some showed a persistent elevation of blood pressure while others showed a steep rise followed soon after by a prompt fall. But in all cases there was reversal of action of adrenalin when given soon after the administration of ergotamine.

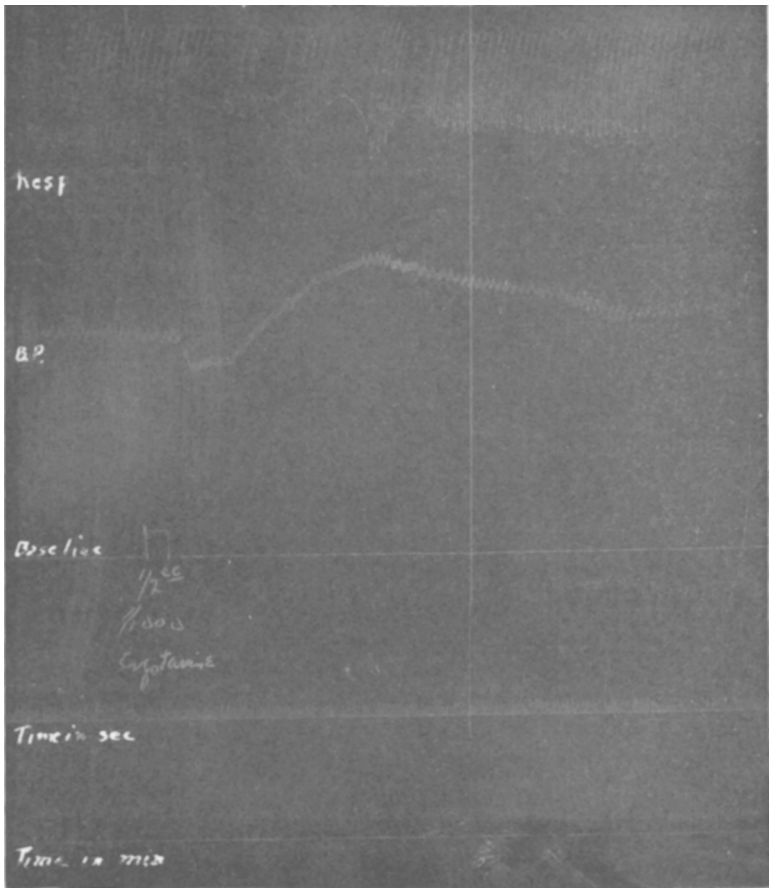
In reinvestigating the action of this alkaloid we were impressed by the difference in the response of the circulation, under the same experimental conditions. Elevation occurred in some cats and depression was observed in others after the same doses of ergotamine, whatever the anesthetic, whether urethane or ether. The administration of adrenalin given by vein always produced a fall of blood pressure after the first or second doses of ergotamine. After repeated injection of ergotamine, adrenalin usually produced a slight rise of blood pressure, that is, reversal of effect was absent.

The depressor action of ergotamine was very severe and occurred in a large percentage of cases in some groups of experiments. As this bore a striking resemblance to the effect produced by adrenalin given after ergotamine, it occurred to us that the function of the suprarenals might be a causative factor in the production of the depressor action of ergotamine. Removal of both adrenals confirmed our suspicion. In no case did a fall of blood pressure occur after ergotamine, such as was observed with the adrenals intact. There was elevation of blood pressure in more than 50% and no effect in the rest of the experiments. The negative results were probably due to trauma produced by excessive manipulation and exposure of the abdominal viscera in the course of the operation for the removal of the adrenals, which was made by the abdominal route. The fall of blood pressure observed after intravenous injections of ergotamine was apparently caused, therefore, by adrenalin present in the circulation.

Of interest also is the effect of repetition of the dose. The action was practically uniform whatever the effect of the first injection, a second dose of ergotamine usually producing a slow and persistent rise of blood pressure. Occasionally the third dose would have the same effect as the preceding injection, but sometimes it was less active. If still more of the drug was administered, no change in the circulation was observed, thus corroborating the results obtained by Rothlin in experiments on cats and dogs.

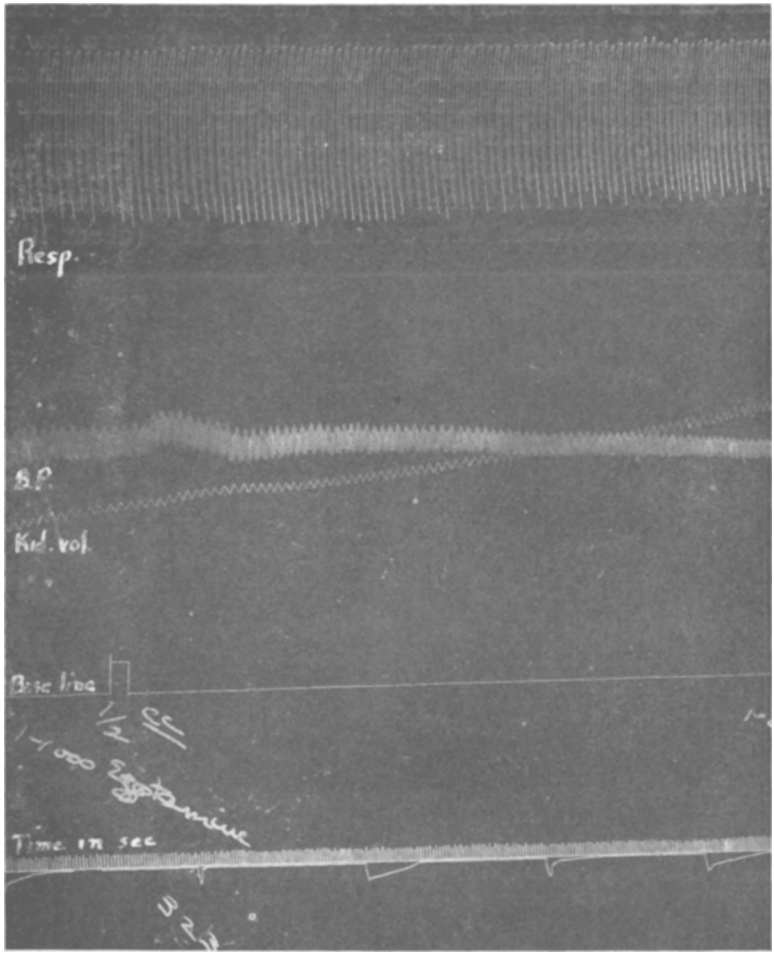
On account of the changes in the reactions of the heart and circulation to drugs produced by alteration in the pH of the blood, as shown by investigations in this laboratory on caffein,[5] cocaine,[6] mercury,[7] the effect of this factor on ergotamine was also studied. Six experiments were carried out on cats, under urethane anesthesia, to which 1% HCl was given intravenously until there was evidence of increased H ion concentration of the blood. The pH of the blood was determined colorimetrically in 4 experiments, and was found to be reduced by 0.1 to 0.2. In 2 experiments in which

the same amounts of acid were given as in the other 4, the pH was not determined, but there was increased respiration and fall of blood pressure with slowing of the heart. In all of these experiments the same effect was produced by the injection of ergotamine, namely, a fall of blood pressure, varying in extent from a few millimeters to about 30 mm. of Hg. When sodium carbonate in sufficient amounts was given intravenously to 6 cats under urethane anesthesia, ergotamine always produced a rise of blood pressure. In one of the experiments this amounted to 15%; in another to 40%; in a third blood pressure rose 33%. In the remaining 3 the increase of blood pressure varied from a few to 9 mm. Hg. (about 10%).



EXP. 14. (C. S. H.) Cat, weight 1.4 kilos. Urethane anesthesia. Seven cc. of 5% sodium carbonate injected intravenously 3 minutes before ergotamine. (Reduced one half.)

In all cases the effect lasted several minutes and was followed by reversal of adrenalin action when this was given after ergotamine, whether the pH was increased or diminished.



EXP. 20. (C. S. H.) Cat, female, weight 2.3 kilos. Urethane anesthesia. 18 cc. 1% HCl injected intravenously shortly before ergotamine. (Reduced one half.)

[1] Rothlin, *Arch. Int. Pharmacol. et Ther.*, 1923, xxii, 459.

[2] Dale and Spiro, *Arch. Exp. Path. and Phar.*, 1922, xcv, 337.

[3] Schegg, *Z. f. Exp. Med.*, 1925, xlv, 368.

[4] Rothlin, *Klin. Wochnschr.*, 4 Jahrg. 30.

[5] Salant, W., and Nadler, J. E., *Am. J. Physiol.*, 1926, lxxviii, 308.

[6] Salant, W., and Nadler, J. E., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 765.

[7] Salant, W., and Nadler, J. E., *J. Lab. and Clin. Med.*, 1927, xiii, 117.