

by incubation of a stomach product with beef muscle. It appeared then that our preparation might also resist a temperature of 60°-65°C., although not a boiling temperature.

Consequently, an acid extract was incubated 8 hours, heated at 60°-65°C. for 30 minutes, made 70% alcoholic, and worked up into a product suitable for intramuscular injection. When the equivalent of 75 gm. was administered to a patient over a period of 3 days the reticulocytes rose from 4.5% to 15.9% in 7 days (R.B.C. = 1,400,000 per cu. mm.).

From these experiments it is evident that the incubation of an acid solution of stomach tissue alone produces a substance which is not identical with the active principle of liver (because it is destroyed by boiling) but which is possibly some intermediate product between the original principle in stomach and the heat-stable principle found in liver.

Summary. A water extract of desiccated hog stomach acidified to pH 4.5 is active in the treatment of pernicious anemia. The hematopoietically active substance does not pass through the ultra-filter and is stable toward alkali. Stomach extracts inactivated by heat do not regenerate their hematopoietic activity by treatment with pepsin. An acid extract contains 2 factors, one heat-stable and the other heat-labile, both of which are necessary for the production of a reticulocyte response in a patient with pernicious anemia. An acid extract incubated for 8 hours produces a hematopoietically active substance which is soluble in 70% alcohol and which resists a temperature of 60°-65°C. for 30 minutes, but not a boiling temperature. Incubation in this manner produces a substance which is not so heat-stable as the anti-anemic principle in liver but which may be an intermediate product more heat-stable than the original stomach fractions.

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Response of the Iris to Pitressin and Pitocin.

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Posterior pituitary extract (pituirrin) has been reported¹ to cause a dilatation of the pupil when dropped into the conjunctival sac of

¹ Pollock, W. B., *Brit. J. Ophthalmol.*, 1920, 4, 106.

the normal eye of the rabbit, averaging 0.65 mm. (minimum: 0.25; maximum: 1.5) in 31 of 32 experiments. In one of 32 experiments the pupil was found to contract and stay contracted following the use of pituitrin.

In 8 experiments we have found the posterior pituitary extract prepared by 2 manufacturers (4 experiments with each) to cause a constriction of the pupil of the normal eye of the rabbit amounting to 1.0 mm. in each of the 8 experiments.

The active constituents of the posterior pituitary have been separated into 2 fractions, one possessing vasopressor, the other oxytocic actions.² These fractions are commonly available under the names "pitressin" and "pitocin", respectively. Pitressin in the normal rabbit eye caused a constriction in each of 7 experiments, averaging 2.2 mm. (minimum: 1.5; maximum: 4.0). Pitressin placed in the conjunctival sac following the use of 1% atropin until the light reflex was abolished, caused a constriction of the pupil in each of 9 experiments, averaging 4.9 mm. (minimum: 4.0; maximum: 6.3).

Pitressin placed in the conjunctival sac following pronounced dilatation of the pupil from 4% cocaine caused constriction of 6.5 mm. in each of 2 experiments. Pitressin following ephedrine 3% solution, resulting in dilatation of the pupil averaging 2.0 mm. increased diameter, failed to influence the size of the pupil in each of 4 experiments. Pitressin following epinephrine 1:1,000 solution, resulting in 0.5 mm. dilatation of the pupil, caused constriction of 1.0 and 1.5 mm. in 2 experiments.

Pitocin in the normal rabbit eye caused no change in the size of the pupil in each of 7 experiments. Pitocin in the eye with pupil inactive to light following atropine failed to alter the size of the pupil in each of 3 experiments.

Pitocin (10 unit strength) when mixed with pitressin (10 unit strength) did not appear to influence the degree or duration of pitressin constriction of the normal rabbit pupil (average: 2.6 mm.; minimum: 1 mm.; maximum: 3.1 mm.) in 4 experiments. Pitocin in 3 experiments did not appear to alter the action of pitressin in constricting the pupil dilated with atropine.

All observations were made with uniform artificial light.

² Kamm, O., Aldrich, I. W., Grote, I. W., Rowe, L. W., and Bugbee, E. P., *J. Am. Chem. Soc.*, 1928, **50**, 573