lactic effect is not surprising.

At present we have no explanation for the marked difference in the results obtained with Lot 1 and Lots 2 and 3 which presumably were prepared by the same method. Possibly some unrecognized variation in the method of preparation led to the production of the unknown antihypertensive constituent in Lot 1. Unfortunately further studies with Lot 1 can not be conducted since the supply is exhausted.

The relationship of the antihypertensive substance in Lot 1 to that reported by Grollman and Harrison[16] in fish liver oils is, of course, problematical. The vitamin A concentrate which they reported as showing some therapeutic effect in hypertensive rats was the same as Lot 2 which proved inactive in our hypertensive dogs.

We are of the opinion that an exhaustive search for the antihypertensive agent of Lot 1 is well-warranted, since it was effective by mouth and apparently in small amounts.

This report should discourage the use of vitamin A concentrates in the treatment of human hypertension, unfortunately stimulated by our preliminary report.

[16] Grollman, A., and Harrison, T. R., PROC. SOC. EXP. BIOL. AND MED., 1943, **52**, 162.

Conclusions. 1. One lot of a vitamin A concentrate dissolved in sesame oil produced striking reductions in the blood pressures of renal hypertensive dogs when administered by mouth in a dosage of 200,000 units daily for 3 months followed by 400,000 units daily for 3 months.

2. Second and third lots of the concentrate dissolved in sesame oil and fish liver oil respectively, a purified vitamin A alcohol in sesame oil, and a fourth lot of the concentrate dissolved in fish liver oil and subjected to heat inactivation of the vitamin A, as well as sesame oil, were all without antihypertensive effect. Likewise the second lot of the concentrate showed no prophylactic effect in experimental renal hypertension.

3. No toxic effects were observed in the dogs.

4. Obviously the antihypertensive effect of the first lot of the concentrate was not due to vitamin A but to some unknown constituent not present in the second and third lots.

5. Since this antihypertensive substance was effective by mouth and apparently in small amounts, further work leading to its reproduction and identification is highly desirable.

14227

Supra-Diaphragmatic Section of the Vagus Nerves in Treatment of Duodenal Ulcer.*

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Much of the experimental work on the pathogenesis of gastroduodenal ulcer that has appeared in recent years is in harmony with the concept that the cause of these ulcers is the corrosive action of the gastric juice. It has been adequately demonstrated that pure gastric juice can destroy and digest living tissues including the wall of the stomach itself, producing in this case a defect which appears to be identical with the lesion encountered in man.[1] Under normal conditions, the gastric wall is not digested away apparently because it is not exposed to pure gastric juice. Food, which in the normal individual is the stimulus for the formation of gastric juice, is also the chief factor which protects the tissues against

* This work has been aided by a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

[1] Dragstedt, L. R., *Arch. Surg.*, 1942, **44**, 438.

its corrosive activity. Pancreatic juice, gastric and intestinal mucus, duodenal juice and bile (probably in the order named) constitute an additional mechanism which protects the duodenal and, to a certain extent, also the gastric and the jejunal mucosa. When excessive volumes of normal gastric juice are continuously secreted in experimental animals, this defensive neutralizing mechanism is overcome, and ulcer is produced. Wangensteen and his associates[2] have produced ulcers in many experimental animals by the implantation of pellets of histamine mixed with beeswax into the muscles or beneath the skin. The gradual liberation of histamine provoked a long continued secretion of gastric juice. Most ulcer patients display an excessive secretion of gastric juice in response to the stimulus of food, histamine, or alcohol. A considerable number secrete large amounts of gastric juice when there is no obvious stimulant, as at night when the stomach has been previously emptied of food by lavage. The cause of this abnormal secretion is unknown. Presumably it might be due to the continuous formation of histamine-like substances in the body or to the constant excessive activity of the gastric secretory fibers in the vagus nerves. It was to secure information on this latter possibility that the present work was done.

Supra-diaphragmatic section of the vagus nerves was performed on 2 patients with duodenal ulcer. The left side of the chest was opened after removing the eighth rib. The lower esophagus was mobilized for a distance of about 10 cm. Vagus fibers were readily identified, separated from the esophagus by blunt finger dissection and collected in two main bundles. Segments of these nerves, 3 to 4 cm in length were excised, the ends ligated, and the pleura closed. The chest was closed without drainage.

The first patient was a male, age 51, who was first seen in December, 1938. He had been operated upon for perforated duodenal ulcer in 1930. He remained well until 1938, when he again developed epigastric distress, relieved by food and alkalies. X-rays showed a crater in the duodenum and blood appeared in the stools Medical management was carried out with partial success until December, 1942, when the symptoms again recurred. At this time he was found to secrete large volumes of highly acid gastric juice at night. A small rubber tube was introduced through the nose into the stomach. At 9:00 P.M. the stomach was emptied and continuous suction maintained to collect the gastric secretion for the following 12 hours. Sleep was not interfered with. Aspirations were carried out 13 times usually with a rest period of one or 2 days between tests. An average of 1160 cc of gastric juice was obtained, the minimum being 800 and the maximum 1600 cc. The pH of the juice varied between 1.19 and 2.98 with most of the samples between 1.45 and 1.70. Section of the vagus nerves was performed January 18, 1943, and following the operation aspiration was carried out 9 times. The volume of secretion obtained fell to an average of 310 cc, the minimum being 162 and the maximum 615 cc. The pH varied between 2.0 and 6.7 with most of the samples between 2.36 and 3.20. In April 2 aspirations were made yielding 162 and 375 cc with a pH of 3.2 and 6.3 respectively. The ulcer symptoms have been relieved and no disturbance in swallowing has appeared.

The second patient was also a male, age forty, who was first seen in March, 1940. A non-stenosing duodenal ulcer was diagnosed by the symptomatology, x-ray findings, and direct visualization of the crater by the gastroscope. A massive hemorrhage occurred in June, 1942. In February, 1943, aspiration of the 12 hour gastric content at night was carried out 6 times. The volume of gastric juice obtained varied between 990 and 1700 cc with an average of 1450 cc. The pH of the secretion varied between 1.11 and 1.40. Section of vagus nerves was done on February 22, 1943. In March, aspiration of the night secretion was carried out 6 times, the volume secured varying between 150 and 750 cc with an average of 510 cc. The pH varied between 1.5 and 3.9. In April, 1943, 3 aspirations were made, the amounts secured being 550,

[2] Walpole, S. H., Varco, R. L., Code, C. F., and Wangensteen, O. H., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 619.

350, and 300 cc and the pH 3.9. This patient also has been relieved of his epigastric distress and has experienced no difficulty in eating.

The data obtained from these 2 patients indicates that the excessive night secretion of gastric juice in ulcer patients is probably neurogenic in origin and may be markedly reduced by supra-diaphragmatic section of the vagus nerves. Although both of these patients appear to have been benefitted by the operation, it is obvious that the period of observation is too short and the number of patients too small to warrant recommendation of this procedure at this time for the treatment of duodenal ulcer.

14228 P

Evaluation of the Ratio of Aortic Rigidity to Peripheral Resistance.

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The expressiveness of pulse rate and blood pressure measurements may be enhanced by introducing the values obtained into the formula described below. This formula helps to differentiate between the effects which conditions in different parts of the cardiovascular system produce upon the blood pressure by offering a number which expresses the ratio of aortic rigidity (or capacity) to the peripheral resistance.

Various investigators (most recently Apéria[1]) in the field of vascular dynamics (comprehensively reviewed by Wezler and Böger[2]) have evaluated the E and W functions, and the E/W ratio. E is the volume-elasticity coefficient and is a measure of the rigidity (or capacity) of the aorta and other large arteries (*windkessel*) and W is a measure of the peripheral resistance. (These symbols are adopted from Wezler and Böger). The evaluations of this ratio published hitherto have been based on data obtained by technics which are not readily available in most laboratories and clinics, as for instance measurements of cardiac output. It is the purpose of this note to point out that the E/W ratio is independent of the stroke volume of the heart, and that this ratio may be determined from heart rate and blood pressure measurements alone.

Development of the Formula. E (volume-elasticity coefficient) is defined as $\frac{\Delta P}{\Delta V}$, where ΔP is the pulse pressure, and ΔV is the change in volume of the *windkessel* corresponding to the given ΔP. Wezler and Böger have equated ΔV to $\frac{V_s}{2}$, where V_s is the stroke volume of the heart. E then becomes $\frac{\Delta P}{\frac{1}{2}V_s}$. In absolute units, E has the dimensions $\frac{\text{dynes}}{\text{cm}^5}$.

W (peripheral resistance) is defined as $\frac{P_m{}^*}{V_s \cdot r/60}$, where P_m is the mean arterial pressure, V_s is the stroke volume as before, and r is the heart rate per minute. The denominator of the ratio is the second-volume of the heart. In absolute units, W has the dimensions $\frac{\text{dynes} \cdot \text{seconds}}{\text{cm}^5}$.

The ratio E/W therefore is equal to $\frac{\Delta P}{\frac{1}{2}V_s} \div \frac{P_m}{V_s \cdot r/60}$, which simplifies to $\frac{r \cdot \Delta P}{30 P_m}$. It should be noticed that V_s cancels out. The constant (30) depends upon the use of Wezler

1 Apéria, A., *Acta Physiologica Scandinavica*, 1941, **2**, 64.

2 Wezler, K., and Böger, A., *Ergeb. Physiol.*, 1939, **41**, 292.

* The venous pressure theoretically should be subtracted from P_m in the numerator of the ratio, but ordinarily may be neglected because of its small magnitude compared with P_m.