

of 3 experiments and 350  $\mu$ g in the fourth.

**Discussion.** The cardiac action of 3-acetyl-strophanthidin has been shown to be a positive inotropic one in the dog heart-lung preparation. This confirms the positive inotropic response of the cat papillary muscle found by Greiner and Reilly(3), and indicates that the therapeutic action of the drug in man is similar to that of digitalis. Apparently, the cold-blooded turtle heart used in the experiments of Wedd and Blair(2) reacts in a different manner to different cardiac drugs than does the warm-blooded mammalian heart.

The experiments reported here are not sufficient in number to permit any quantitative comparison of the activity of ouabain and 3-acetyl-strophanthidin, but the results indicate that the two drugs have approximately the same therapeutic and toxic potencies. This would agree with the comparative toxicity of the two substances as measured by the cat lethal dose assay. The mean (geometric) cat

lethal dose is 0.116 mg/kg for ouabain(6) and 0.1866 mg/kg for 3-acetyl-strophanthidin(7).

**Summary.** In the failing heart-lung preparation of the dog, 3-acetyl-strophanthidin has been found to produce a positive inotropic effect comparable to that produced by ouabain.

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### Esophagitis in Dogs Following Operations Employed in the Treatment of Mega-Esophagus.\* (20566)

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The most severe complication resulting from the operative treatment of mega-esophagus, esophageal dystonia, or cardiospasm is chronic esophagitis. Indeed, this may become more disabling than the original condition which the operation was designed to correct. This study was devised to determine, in dogs, the incidence of esophagitis following the two standard surgical procedures for the treatment of mega-esophagus which have been most popular in recent years. These are the Heller operation and the Wendel operation, which are described in detail below.

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**Materials and methods.** Mongrel dogs weighing 8 to 16 kg were used in this study. Pentobarbital sodium was administered intravenously in a dosage of 30 mg per kg of body weight for anesthesia, and a mechanical respirator was used during surgery. The esophagogastric junction was exposed through an incision in the 10th left intercostal space, and where necessary the stomach and pyloro-duodenal junction could be delivered easily into the chest by enlarging the esophageal hiatus. The Heller operation consists of an extramucous myotomy of the esophagogastric junction. In this study, the myotomy was made by incising the muscularis of the distal 4 to 5 cm of the esophagus and proximal 4 cm of the stomach longitudinally down to the submucosa with a sharp knife. Care was taken to leave no muscle fibers undivided. The Wendel procedure consists of a longi-

TABLE I. Esophagitis in Dogs Attending Performance of Heller and Wendel Operations on the Esophagogastric Junction. Degree of esophagitis as revealed by esophagoscopy, graded 0-4. Results are listed in 4 wk intervals.

| Dog No.                                                           | Weeks |     |      |       |       |       |       |       |                             |
|-------------------------------------------------------------------|-------|-----|------|-------|-------|-------|-------|-------|-----------------------------|
|                                                                   | 0-4   | 5-8 | 9-12 | 13-16 | 17-20 | 21-24 | 25-28 | 29-32 | 33-36                       |
| Group 1. Heller operation                                         |       |     |      |       |       |       |       |       |                             |
| 1                                                                 | 0     |     |      | 0     | 1     | 1     |       | 1     | 1                           |
| 2                                                                 | 0     |     | 0    | 0     | 1     | 1     | 1     | 1     | 1                           |
| 3                                                                 | 0     | 0   | 1    | 0     | 0     | 0     | 0     | 0     | 0                           |
| 4                                                                 | 0     | 1   | 0    | 1     | 0     |       |       |       |                             |
| 5                                                                 | 0     | 1   | 1    | 1     |       |       |       |       |                             |
| 6                                                                 |       | 0   | 0    | 0     | 0     | 1     | 0     | 0     |                             |
| Group 2. Wendel operation                                         |       |     |      |       |       |       |       |       |                             |
| 1                                                                 |       | 1   | 2    | 2     |       | 3     | 3     | 3     | 3                           |
| 2                                                                 |       | 1   | 1    | 2     | 2     | 2     | 3     | 3     | 3                           |
| 3                                                                 | 1     | 1   | 2    | 3     | 3     |       |       |       |                             |
| 4                                                                 | 1     | 1   | 2    | 3     | 3     |       |       |       |                             |
| Group 3. Heller operation + histamine                             |       |     |      |       |       |       |       |       |                             |
| 1                                                                 |       | 2-3 | 3    | 3     | 3     | 3     | 4     |       | (EP)*                       |
| 2                                                                 |       | 1   | 2    | 2     | 3     | 2     | 2     |       |                             |
| 3                                                                 |       | 2   | 2    | 3     | 3     |       | 3     | 3     |                             |
| 4                                                                 |       | 1   | 1    | 1     | 1     | 1     | 1     | 1     |                             |
| Group 4. Wendel operation + histamine                             |       |     |      |       |       |       |       |       |                             |
| 1                                                                 | 1     | 2   | 2    | 3     |       |       |       |       |                             |
| 2                                                                 | 3     | 3   | 3    | 4     |       | (EP)* |       |       |                             |
| 3                                                                 | 1     | 2   | 2    | 3     | 3     | 3     | 3     | 3     |                             |
| 4                                                                 | 1     | 2   | 2    | 3     | 3     | 3     | 3     | 3     |                             |
| Group 5. Wendel operation and vagotomy + histamine                |       |     |      |       |       |       |       |       |                             |
| 1                                                                 | 1     | 2   | 3    | 3     | 3     | 3     | 3     | 3     |                             |
| 2                                                                 | 0     | 3   | 3    | 3     |       |       |       |       |                             |
| 3                                                                 | 0     | 1   | 2    | 2     |       |       |       |       |                             |
| Group 6. Wendel operation, vagotomy, and pyloroplasty + histamine |       |     |      |       |       |       |       |       |                             |
| 1                                                                 | 0     | 0   | 0    | 1     |       |       |       |       |                             |
| 2                                                                 | 0     | 0   | 0    | 0     |       |       |       |       |                             |
| 3                                                                 | 0     | 0   | 0    | 0     |       |       |       |       |                             |
| 4                                                                 | 0     | 1   | 0    | 0     |       |       |       |       |                             |
| 5                                                                 | 0     | 1   | 1    | 3     |       |       |       |       | (Isolated esophageal ulcer) |

\* EP = Esophageal perforation.

tudinal incision through all layers of the esophagogastric junction which is closed transversely. In this study, the incision extended from 4 cm above to 4 cm below the esophagogastric junction. It was closed transversely in 2 layers—an inner mucosal stitch of continuous 000 plain catgut and an outer row of interrupted 0000 silk. After both procedures, the left crus of the diaphragm was carefully resutured to esophagus with a few interrupted silk sutures.

The animals were allowed to recover for 2 to 4 weeks following operation, and then esophagoscopy was performed every 2 to 3 weeks to assess the condition of their esophagi. Six groups of animals were studied. Group 1 animals had the Heller procedure alone, and Group 2 the Wendel operation alone. Groups 3 and 4 were similar to Groups 1 and 2 with the addition of daily intramuscular injections

of 30 mg of histamine-base in beeswax. The dogs in Group 5 had a Wendel operation and in addition, a bilateral supradiaphragmatic vagotomy; and those in Group 6 had a Wendel operation, a vagotomy, and a Heineke-Mikulicz pyloroplasty. The animals in both Groups 5 and 6 were given daily injections of histamine-in-beeswax.

**Results.** The results are shown in Table I. When, at esophagoscopy, esophagitis was observed to follow these operative procedures, the process was found usually to be limited to the distal third of the esophagus; however, in some of the more severe cases, changes were present throughout the entire esophagus. The degree of esophagitis was graded on the basis of 0 to 4.

0—normal

1—mild esophagitis (slight to moderate hyperemia)

- 2—moderate esophagitis (more hyperemia, early linear erosions)
- 3—severe esophagitis (marked hyperemia, linear erosions which bleed easily, erosions covered by exudate)
- 4—esophageal perforation.

Of the dogs in Group 1 subjected to the Heller operation and not receiving histamine, none developed severe esophagitis. Contrast this with Group 2, in which all dogs developed severe esophagitis following the Wendel operation. The marked difference in the incidence of esophagitis between these 2 groups is probably the result of the difference in the degree of regurgitation of gastric juice into the lower esophagus. Some reflux of gastric juice was noted at esophagoscopy in dogs from both groups; however, this finding was more marked and more constant in the Wendel dogs.

Histamine-in-beeswax injections were given to produce a constant stimulus for the secretion of a large volume of highly acid gastric juice. It was believed that this would intensify any esophagitis following these operations inasmuch as regurgitation of acid peptic juice is the cause of esophagitis in these circumstances. In Groups 3 and 4, administration of histamine resulted in a severe degree of esophagitis in dogs with both the Heller and Wendel operations. One dog from each of these groups died following perforation of an esophageal ulcer.

The Wendel operation was chosen to test the effectiveness of vagotomy and pyloroplasty in preventing esophagitis because of the high incidence of severe esophagitis when the animals received histamine injections. In Group 5, vagotomy alone failed to prevent the development of severe esophagitis in dogs with the Wendel operation subjected to histamine stimulation. On the other hand in Group 6, vagotomy and pyloroplasty together were found to be effective in preventing esophagitis under the same circumstances. However, one of the animals in Group 6 did develop a small isolated esophageal ulcer on the posterior wall just above the esophagogastric junction with little or no evidence of esophagitis anywhere else in the distal esophagus. This ulcer was probably caused by constant exposure to the

acid peptic secretion from a fold of gastric mucosa pulled upward in the transverse closure of the Wendel operation. It has previously been demonstrated that transplantation of a bit of fundic mucosa 1 cm in diameter pedicled on a source of blood supply into the wall of the esophagus is regularly followed by the development of a peptic ulcer in the esophageal mucosa in juxtaposition to the transplant.

The dogs of Group 6 in which a vagotomy and pyloroplasty were done, in addition to the Wendel procedure, remained in good condition and maintained their weight well. In contrast, the dogs in Group 5, a similar group in which a vagotomy was done but pyloroplasty was omitted fared badly. They all lost weight rapidly and soon became emaciated and died. The immediate cause of death was often pneumonia, but in many, cachexia was the only post mortem finding. In fact, many dogs were operated upon in this particular group before the 3 survivors for the experiment could be maintained alive throughout an adequate period of observation.

*Summary.* 1. Dogs subjected to the Wendel operation for mega-esophagus developed severe esophagitis, whereas dogs with the Heller operation did not. 2. Daily injections of histamine resulted in severe esophagitis in dogs with both the Heller and Wendel operations. 3. Vagotomy alone did not prevent development of esophagitis following the Wendel procedure when the animals received histamine. 4. Vagotomy and pyloroplasty together were effective in preventing esophagitis in dogs with the Wendel procedure receiving histamine injections.

*ADDENDUM.* Since this paper was submitted for publication, two new groups have been added. In Group 7, a Wendel operation and pyloroplasty were done, the dogs being given histamine; 4 of 5 such dogs developed severe esophagitis and one dog had no esophagitis. A 6th dog receiving no histamine developed a moderate esophagitis within 2 weeks following operation. In Group 8, a Heller operation, vagotomy, and pyloroplasty were done. The dogs also were given histamine; none of the 4 dogs developed esophagitis.

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