STUDIES IN THE ETIOLOGY OF ACUTE APPENDICITIS*

THE SIGNIFICANCE OF THE STRUCTURE AND FUNCTION OF THE VERMIFORM APPENDIX IN THE GENESIS OF APPENDICITIS

A PRELIMINARY REPORT

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THE observations of the nineteenth century stressed mechanical causes as responsible agents in the genesis of inflammations of the vermiform appendix. Convincing evidence and substantial proof, however, were lacking to establish mechanical causes as the chief etiologic agency of appendiceal suppurations. Speculation and armchair philosophizing created a considerable literature of "paper experimentation" concerning the origins of this disease in which complete sight was lost of the pathologic observations of our medical ancestors and new factors of latitude, longitude, diet and habits of life came to occupy, in the medical mind, a significant rôle in the causation of the disease. The confusion over admixture of fact and speculation has grown until what is speculation and what is fact is scarcely longer discernible.

The cogency of the vigorous declarations of Professor Aschoff, who has come to believe that acute suppurative appendicitis is essentially a specific bacterial disease (not unlike gonorrhea in its specificity) due to the entercoccus Type B (Gundel), has won many converts for the idea that appendicitis is infectious in origin.

The significance of the observations made by Volz, Matterstock and Fitz with reference to the obstructive factor, however, cannot be lightly dismissed or set aside. The surgeon, conscious of the paucity of specific infections in the alimentary canal and its appendages and impressed with the unfavorable anatomic arrangement for satisfactory function presented by the long narrow diverticular-like vermiform appendix, does not readily abandon the notion that obstruction is an important item in originating the disease.

Purpose of the Present Study.—This study was undertaken with the consideration of investigating the minute anatomy of the vermiform appendix of man, to determine whether the obstructive features of acute suppurative appendicitis found an accordant explanation in the behavior of this appendage. In a previous study many of the numerous theories and hypotheses relating to the origins of appendicitis were discussed at length. An attempt was also made to evaluate the likely significance of the factors of infection and obstruction. It was pointed out also that in the severe forms of the disease in man (perforative and gangrenous appendicitis) a demonstrable obstruction, often

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a fecalith, was usually present. Subsequently the presence of a mechanism exhibiting resistance to outflow from the lumen of the vermiform appendix and interfering with satisfactory evacuation of its content was described.[26] This latter finding suggested the necessity of a more extended exploration of the anatomic and functional features of the vermiform appendix.

Plan of This Study.—(I) It is proposed first to examine the nature of the appendicocecal union in man and to note: (1) The manner in which the appendix meets the cecum; (2) the nature of the appendiceal orifice; (3) the presence of mucosal folds overlying the orifice and their nature; and finally (4) the disposition of the muscle fibers at the site of appendicocecal union.

(II) It is proposed further to elucidate the nature of the resistance offered to intraluminal perfusion of the vermiform appendix by noting its order of magnitude in acute, interval and normal appendixes at the time of appendicectomy.

(III) (1) An opportunity to study this behavior of the appendix over longer intervals of time was afforded in sixteen patients with appendicostomies. Fifteen of these were made coincidentally during colostomy for malignant disease of the colon or rectum; the other was effected at the same time that a permanent ileostomy opening was made in a case with ulcerative colitis.

(2) The appendicostomy opening was cannulated to determine whether fluid was secreted by the appendix.

(3) The effect of various drugs upon the resistance to luminal outflow was also determined in several instances.

(4) In a few others, organisms obtained from the exudate of acute suppurative appendicitis were transferred to the lumen of appendicostomy openings.

(5) In others a lead birdshot No. 9 (one-ninth inch or 2.79 Mm. in diameter) was inserted into the lumen of the appendicostomy.

(6) In a few instances in which the exteriorized portion of the appendix was long, segments were cut off and studied histologically after the maintenance of increased intraluminal pressure for several hours.

(IV) In the excised appendix after appendicectomy, the resistance to luminal outflow was again noted; in addition, by suspending segments of the appendix in an oxygenated and temperature controlled water bath attached to a muscle lever, the contractions of both the circular and longitudinal muscle coats of the appendix could be studied. The effects of certain drugs upon the activity of the appendix were better studied in this medium than in patients with appendicostomies.

(V) The retention of foreign material by the appendix has been further studied by spectrographic studies upon the intraluminal content of the appendix in patients who had previously ingested barium.

(VI) The results noted in the above experiments (Group III, item 2) suggested the necessity for investigating whether fluid was secreted or absorbed in the cecal appendages of other animals.

(VII) Determination of the volume of the lumen of the vermiform appendix of man has been made to ascertain what intraluminal increase in volumetric content and tension may occur without perforation.

This broad study of the problem of appendicitis cannot be related in detail in this paper. Several additional expositions will be necessary to recount all the evidence with a bearing upon the problem which has been gleaned from the study. It is proposed only to state briefly here what has been done and what the results are.

I. The Nature of the Appendicocecal Union.—*The Material:* Through the cordial coöperation of the Department of Pathology of the University of Minnesota, an ample postmortem material was obtained.* Over 800 specimens of the human proximal colon, including the cecum, vermiform appendix, and terminal ileum, became available to us. Many of these specimens were received in the fresh state, one to 24 hours after death. The usual mode of dealing with these specimens was to fill the lumen of the specimen with 4 per cent formalin solution (both ends of the gut being tied). It was then placed in a tank containing similar fluid. This method of fixation, it was felt, eliminated contraction phenomena to some extent. Specimens which had been injured or exhibited unusual contraction were excluded from the study. In a number of instances, the specimen was filled with gelatin in the fluid state to show the internal topography of the ileocecal valve, the cecal pouch and the appendicocecal union. Casts of the appendix and cecum were made also in a number of instances by filling the preparation with melted Wood's metal. A few air dried specimens were also studied.

(1) *How the Appendix Meets the Cecum.*—In 1885, in his Hunterian Lectures, Treves studied the external form of the appendicocecal union and established four general types. Berry and Jacobshagen have employed the grouping of Treves. The Type I cecum of Treves is the smooth embryonic funnel shaped organ with the appendix at the apex and true center of the most distal portion of the cecum. The Type II cecum is similar to Type I except that the cecum is sacculated evenly on both sides and there is not, as in Type I, a gradual fusion of the lumina of appendix and cecum, but on the contrary, a sudden transition from the one into the other. Type III shows an increased sacculation of the lateral half of the cecum, thus forcing the site of appendicocecal union far mesiad to the left toward the ileocecal valve and away from the apparent apex of the cecum. The Type IV cecum of Treves is characterized by an even greater lateral sacculation in which the medial wall of the cecum practically disappears and the base of the appendix in consequence comes to lie near the termination of the ileum. In this type, the appendixes are commonly adherent to the ileum.

A summary of our findings in a study of 262 cases is to be found in Table I. It is to be noted that all the fetal specimens fell in Group I. The majority of the specimens during the first year of life (from both term fetus

* The authors desire particularly to acknowledge the great assistance lent them by Dr. J. F. Noble, pathologist to Ancker Hospital, Saint Paul, and by Dr. N. F. Lufkin, pathologist to the Minneapolis General Hospital.

to the second year) fell also into Group I. In the older age groups (11 to 84 years), the majority fell into Group III.

TABLE I

CLASSIFICATION OF CECUMS

Age	Number	Treves' Type I	Treves' Type II	Treves' Type III	Treves' Type IV
Fetal	63	63	—	—	—
Term—1 yr.	25	20	—	5	—
1–10 yrs.	12	5	—	6	1
11–20 yrs.	7	1	—	5	1
21–30 yrs.	9	1	—	8	—
31–40 yrs.	16	1	1	13	1
41–50 yrs.	33	3	1	26	3
51–60 yrs.	37	7	1	27	2
61–70 yrs.	33	2	2	25	4
71–80 yrs.	23	2	—	18	3
81–84 yrs.	4	—	—	4	—
Total	262	105 (40.1)	5 (1.9)	137 (52.3)	15 (5.7)
Fetal	63	63 (100.0)			
Term—84 yrs.	199	42 (21.1)	5 (2.5)	137 (68.9)	15 (7.5)
Term—10 yrs.	37	25 (67.6)		11 (29.7)	1 (2.7)
11–84 yrs.	162	17 (10.5)	5 (3.1)	126 (77.8)	14 (8.6)
Treves	100	(2.0)	(3.0)	(90.0)	(5.0)
Berry	100	(10.0)	(6.0)	(80.0)	(4.0)

TABLE II

COMPARATIVE SIZE OF 477 APPENDICEAL ORIFICES

Description	Size (Mm.)	Number	Per Cent
Very Large	15 plus	2	0.4
Large	10–15	81	17.0
Medium Large	6–10	12	2.5
Medium	4–6	155	32.6
Medium Small	2–4	7	1.3
Small	0.5–2	210	44.1
Pin Point	0.5	10	2.1
Total		477	100.0

(2) *The Appendiceal Orifice.*—The interior of the cecum in the region of the appendiceal union was studied with the specimen in its usual anatomic position. That portion of the cecal wall including the superior margin of the vermiform process to the inferior lip of the ileocecal valve will be called the superior appendicocecal wall; the inferior portion of the cecum which continues with the inferior appendiceal wall will be designated as the inferior appendicocecal wall.

The appendiceal orifice varies considerably in size and shape as indicated in the accompanying tabulation of 477 orifices (Table II). In sixteen instances no appendiceal lumen could be demonstrated. These specimens will be studied subsequently in greater detail.

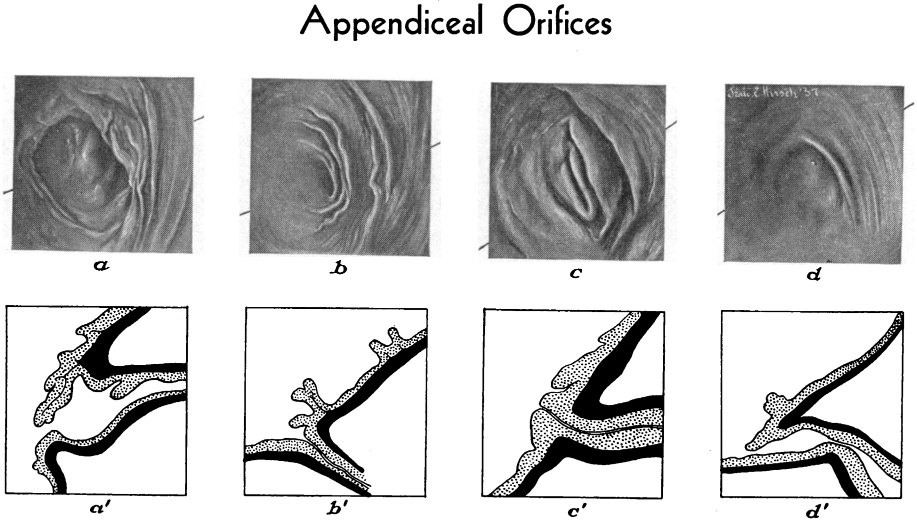

FIG. 1.—Drawings of some of the types of appendical orifices and mucosal folds observed; *a'*, *b'*, *c'*, and *d'* are sketches made from a section cut through the axis of the appendix as indicated by the short lines on the margin. (*a*) Very large round orifice with prominent Gerlach's mucosal fold overlying it (incidence in this series, 0.9 per cent). (*b*) Small crescent-shaped orifice with Gerlach's fold and secondary mucosal fold overlying the appendical opening (41.2 per cent). (*c*) Slit-like appendical orifice with Gerlach's fold and one large secondary mucosal fold (13.6 per cent). (*d*) Pinpoint orifice with persistent mucosal fold with Gerlach's fold overlying it (2.1 per cent).

In Table III the type of orifice has been classified as round, oval, irregular, crescent, and slit like. The size of the orifices has also been correlated and tabulated with its shape.

(3) *Mucosal Folds Overlying the Appendiceal Orifice.*—A mucosal fold overlying the appendiceal orifice was mentioned by Gerlach, in 1847, who described it as an inconstant semilunar fold of mucous membrane guarding the internal appendicocecal orifice. The careful German anatomist, Toldt, recognized this mucosal fold and it has come to be known as Gerlach's valve. Many, however, deny the existence of such a mucosal fold guarding the appendiceal orifice.

The presence or absence of folds about the appendiceal orifice was carefully noted in 526 specimens. If such folds are present, almost invariably they are to be found on the superior cecal wall. The primary fold overlying

TABLE III

COMPARATIVE SIZE AND SHAPE OF ORIFICES OF 477 ADULT APPENDICES

Size (Mm.)	Round Per Cent	Oval Per Cent	Irregular Per Cent	Crescent Per Cent	Slit Per Cent
15 plus	0.9	0.7	—	—	—
10–15	45.5	12.5	11.8	6.8	—
6–10	6.2	0.7	—	3.1	—
4– 6	16.1	36.8	41.2	44.3	24.6
2– 4	0.9	1.3	—	3.1	—
0.5–2	25.9	47.3	47.0	41.2	72.3
0.5	4.5	0.7	—	1.5	3.1
Total	100.0	100.0	100.0	100.0	100.0
Shape	23.5	31.8	3.6	27.5	13.6

the orifice has been described here as Gerlach's fold. A large number were subjected to microscopic examination to determine whether muscle fibers continued into the fold. With the exception of three fetal specimens, in which circular muscle definitely projected into the fold, muscle fibers were invariably

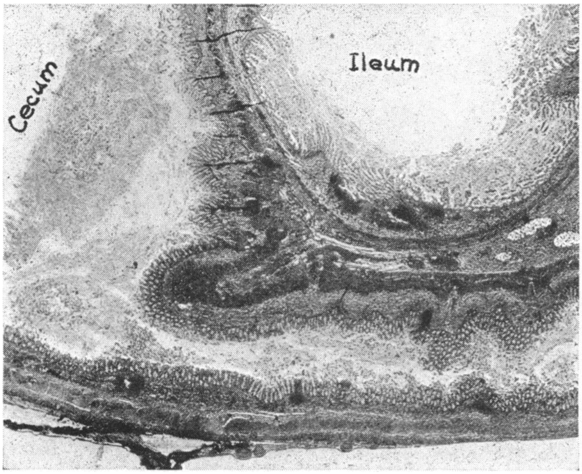

FIG. 2.—Gerlach's fold in a term fetus. There is definite evidence of muscle in the fold—an observation which apparently escaped notice heretofore. The presence of circular muscle in this fold has not been observed by us in the appendixes of adults. We would infer, therefore, that as the ileum and appendix increase in size that circular muscle disappears from Gerlach's mucosal fold.

absent (Fig. 2). In some instances, secondary mucosal folds were present on the superior cecal wall. These circular folds of mucous membrane form an inverted V over the orifice. They extend laterally for 1 to 2 cm. and fuse with the mucosa of the cecal wall. Folds lying at a distance greater than 2 cm. from the superior margin of the appendiceal orifice do not appear in Table IV. Gerlach's mucosal fold was noted in 81.5 per cent of 526 specimens.

TABLE IV

MUCOSAL FOLDS ABOUT THE APPENDICEAL ORIFICE *

Folds Present on Superior and Inferior Cecal Wall	Number of Specimens		Per Cent	
Gerlach's mucosal fold	183		34.8	
Gerlach's and one semilunar mucosal fold	147		27.9	
Gerlach's and two semilunar mucosal folds	82		15.6	
Gerlach's and three semilunar mucosal folds	1		.2	
Gerlach's and Nanninga's mucosal fold	16		3.0	
Total with Gerlach's mucosal folds		429		81.5
No folds about the orifice	89		16.9	
No Gerlach's fold; one secondary mucosal fold	1		.2	
Longitudinal mucosal folds	5		1.0	
Complete ring	2		.4	
Total without Gerlach's folds		97		18.5
Total orifices		526		100.0

* Mucosal folds about the appendiceal orifice of 526 adult and fetal cases, or 77.92 per cent of the total series of 675 specimens.

Table V indicates to what degree the appendiceal orifice was obscured by mucosal folds. It is to be noted that in the fifty-seven fetal specimens there was direct continuity between appendiceal lumen and cecal cavity.

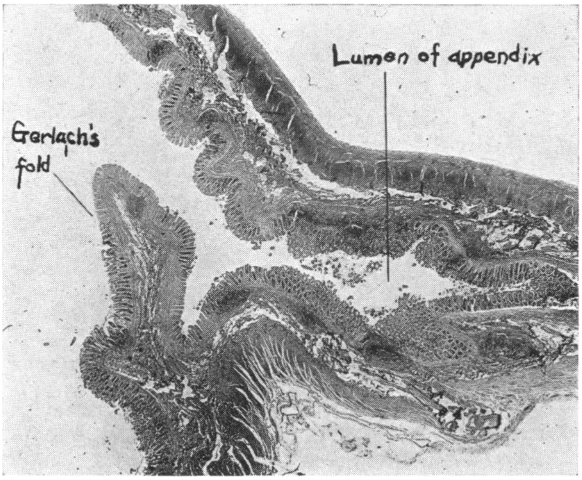

FIG. 3.—The more usual mucosal fold of Gerlach. Note the presence only of submucosa in it and the absence of muscle.

(4) *Disposition of Muscle Fibers at the Site of Appendicocecal Union.*—A study of the arrangement of muscle fibers where vermiform appendix and cecum merged was undertaken to determine whether a true sphincter of circu-

TABLE V

INCIDENCE OF OBSCURATION OF APPENDICEAL ORIFICES BY MUCOSAL FOLDS

	Hidden	Partially Hidden	Not Hidden	Total
Fetal	0	0	57 (100.0%)	57
Others	57 (12.3%)	77 (16.5%)	331 (71.2%)	465
Total	57 (10.9%)	77 (14.8%)	388 (74.3%)	522

lar muscle fibers was present. That such a circumstance might obtain was suggested in the occurrence of resistance to luminal outflow of fluid from the appendix. To this end, blocks about 1 cm. in length were cut including the tip of the cecum and the proximal portion of the appendix in 250 specimens. These blocks of the appendicocecal union were embedded in paraffin and cut—the larger number in the axis of the appendiceal lumen, a lesser number transversely. The former type of section was found to be more suitable for our purposes of studying the musculature. The majority of the sections were cut ten micra in thickness. Most of the sections were stained for microscopic study with hematoxylin and eosin and a lesser number with Mallory's azan-carmine stain. In many instances complete serial sections of the blocks were available for study.*

The results of this study will be reported in detail in a subsequent communication (Buirge and Wangensteen). It will suffice to say that no indication of a sphincter muscle at the site of union of appendix and cecum was observed. The more usual type of arrangement is indicated in Figs. 3 and 4. It was noted that thickening of the circular muscle in excess of that attending union of appendix and cecum occurred in 59 per cent of 250 specimens studied microscopically on the medial or ileal side of the appendicocecal union (Fig. 4). On the lateral side no such thickening was observed. The thickness of the combined muscle layer (both circular and longitudinal) was determined 1 Mm. beyond and proximal to the point of appendicocecal union in 74 of these specimens. A variable diminution of muscle fibers in the cecal wall was found to continue over into the appendix on both medial and lateral walls. Dipping and fusion of the longitudinal muscle fibers into the circular muscle bundles occur frequently and suggested the necessity for making dissections of the disposition of the longitudinal muscle bands of the cecum as they ramify over the appendix.

Dissection of the Taeniae Coli (Longitudinal Muscle Bands) at the Site of Appendicocecal Union.—How the longitudinal muscle bundles of the taenia coli dispersed themselves over the proximal portion of the appendix was studied in 18 cases. The specimens were prepared for dissection by digestion in 0.5 per cent hydrochloric acid solution. Employing a micro-dissector (mag-

* The authors desire to express their appreciation to Drs. E. A. Boyden and E. T. Bell for helpful suggestions and advice in the matter of procedure as well as interpretation. Also to Miss Nancy Harrison, technical assistant in the surgical laboratory, for the studied care with which she executed the difficult and arduous task of cutting thousands of sections.

nification about ten diameters) the serosa was separated readily in most instances from the muscle fibers. The longitudinal muscle bands, when teased apart, appeared to be constituted of three layers, superficial, middle and deep fibers.

The taeniae coli were cut 3 to 4 cm. from the cecal apex and with gentle teasing, the peripheral distribution of the muscle fibers could be readily ascertained. The superficial fibers of the three taenia continued over the appendix as the longitudinal muscle of the appendix. It should be stated here that continuance of the taeniae coli over the length of the appendix as such was not noted in any of the gross specimens available for examination. The deep layer of muscle fibers in the taeniae coli were noted to take various courses about the base of the appendix. In all specimens the deep fibers were found

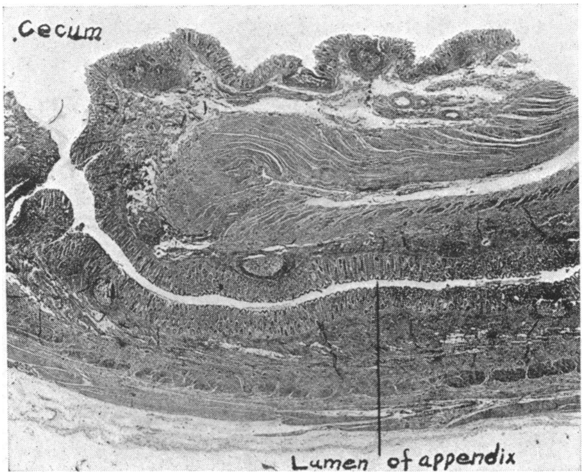

FIG. 4.—On the upper or medial wall of the appendicocecal union, the thickening of the muscle at the apex is apparent—a frequent occurrence.

to be intimately attached to the circular fibers at the cecal apex. In ten instances, all the taeniae sent muscle fibers to encircle the base of the appendix in an iris diaphragm-like manner. In six instances this decussation of the fibers of the taeniae about the appendix was missing. In two instances the anterior taenia divided into a Y-like arrangement sending middle fibers to both lateral and posterior taeniae. The anterior taenia sends the strongest band to the posterior taenia.

II. Resistance to Luminal Outflow from the Vermiform Appendix.—It was the observation of resistance to luminal perfusion of the intact appendix (previously briefly described) which suggested the necessity for an investigation of the anatomic features of the vermiform appendix related above. At the time of appendicectomy, in suitable cases, a No. 19 gauge needle was inserted into the tip of the intact appendix. When the appendix could not be readily delivered, it was found necessary to divide its mesentery first. The needle in the lumen of the appendix was attached to a water manometer in the manner indicated in Fig. 5. The pressure in the system was increased every two minutes by increments of 5 cm. of water, beginning initially with atmospheric pressure until the resistance to luminal perfusion was overcome and water ran freely into the cecum as indicated by a sudden drop in the column of water in the manometer. Later it was found that the resistance to outflow from the lumen could be determined more quickly by the following means, the results checking closely with the method just described: Fluid was added to the manometer-appendix system by means of an intravenous flask and Murphy drip bulb, the pressure being raised to 80 or 100 cm. of water at the start, forcing fluid on into the cecum, thus washing any possible fecal or foreign matter out of the lumen. Thereafter the flow through the Murphy drip was stopped, and the level to which the meniscus settled above the appendix was termed the absolute resistance to outflow. In the majority of instances the determination was repeated, raising the level very slowly and very close checks were the rule. In some instances, the degree of resistance was determined before cutting the mesentery as well as after, and finally, also immediately after removal of the appendix. In the main, fairly constant levels of pressure were observed in each specimen under these varying conditions. The measurements noted are indicated in Table VI. In the most severe types of acute appendicitis, no determinations of resistance to intraluminal pressure were undertaken until the appendix had been removed.

TABLE VI

RESISTANCE TO INTRALUMINAL PERFUSION *

	No. of Cases	Centimeters of Water Pressure Sustained			
		Average	Median	Maximum	Minimum
1. Normal	11	38.0	28	110	16
2. Interval	45	54.4	45	130	16
3. Acute	27	73.0	68	120	12 †
4. Normal from cadavers	13	2.9	3	7	0

* This table also contains pressure determinations made upon the excised appendix directly after removal.

† This appendix was infested with pinworms; the next lowest readings in this group were four cases with readings of 30 cm.

III. Appendicostomy Studies.—An appendicostomy with delayed opening of the appendiceal lumen was established in fifteen patients with cancer of the bowel.* In another, with ulcerative colitis, a double barreled terminal ileostomy was performed and, simultaneously, appendicostomy. In each instance the appendix was brought out through a stab wound, large enough to obviate compression of the appendix and mesentery. As much as possible of the appendix was exteriorized and fastened to the skin to prevent retraction. During convalescence from the initial operation, the projecting tip of the appendix was amputated, and a No. 8 French soft, urethral catheter (with its end cut squarely off) was inserted into the appendiceal lumen. A tie was placed about catheter and distal appendiceal wall sufficiently tight to preclude discharge around the catheter. As a preliminary measure, to insure the presence of a lumen free from fecal material, 20 cc. of saline solution were washed

* No patient has come to harm through the performance of these appendicostomies.

through the appendiceal lumen into the cecum. In a number of instances, the catheter tied into the lumen of the appendix was pushed into the cecum, to be certain that no strictures were present. In the main, it was found easier to push a catheter into the cecum through the appendiceal lumen than a probe, which was very likely to become engaged in the folds of the mucosa.

The resistance to luminal outflow from the appendicostomies was determined in two ways. In the cases done in the early months of 1936, the method described above with reference to the perfusion of the intact appendix at operation was employed (Fig. 5). During the past ten months, the pressure

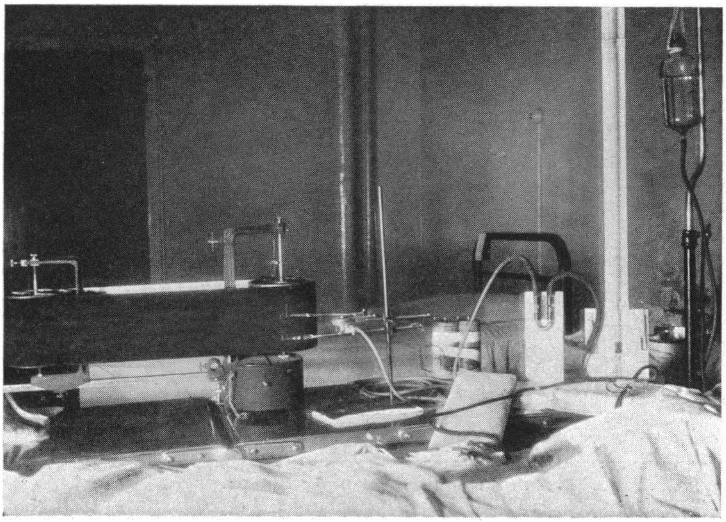

Fig. 5.—The apparatus used in determining the resistance to luminal outflow. In the determinations made in the operating room only the manometer was used. A kymographic record was regularly made in the instance of appendicostomies as shown here.

determinations have been registered directly on very slowly revolving smoked drums, employing a recording float connected directly to the catheter in the appendiceal lumen and a mercury manometer. This apparatus was carefully calibrated and it was observed that the change of volume of the fluid in this closed system, resulting from displacement of mercury and distention of the rubber tubing, necessary to raise the pressure from 0 (zero) to 100 cm. of water pressure was 0.62 cc. The resistance to luminal outflow from these appendicostomies was in general of the same order of magnitude as had been observed in the intact vermiform appendix at operation (Table VII).

TABLE VII

RESISTANCE OF THE APPENDIX IN PATIENTS WITH APPENDICOSTOMY TO INTRALUMINAL PERFUSION

	Centimeters of Water Pressure Sustained			
No. of Cases	Average	Median	Maximum	Minimum
12	47.7	42.0	100.0	8.75

Most of these determinations were made after an interval of five to seven days subsequent to the establishment of the appendicostomy—at which time, the appendix had become well healed in the wound. To exclude the possibility of pyramiding of the resistance to outflow by the contraction of the healing tissue immediately adjacent to the appendix, an observation was made in one instance two hours following the performance of appendicostomy. An intraluminal pressure of 40 cm. of water was sustained for two hours.

The plan pursued in most instances for the study of the contractile activity of the appendix over a long period of time was as follows: Water was permitted to run into the lumen under the influence of gravity pressure by the drip method at a constant rate, usually 20 drops per minute. The contractile activity of the appendix was recorded quantitatively on the revolving drum. Peaks of activity were observed to come in the fasting patient every seven to 15 minutes, each consisting of one or many momentary rises of

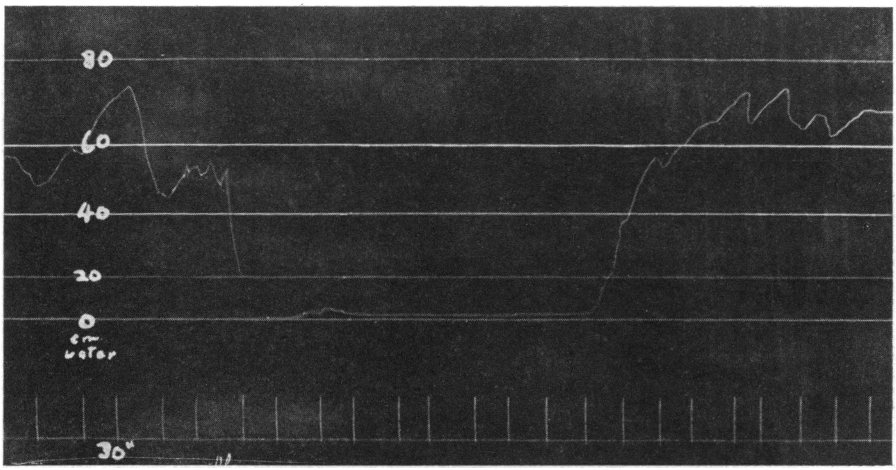

FIG. 6.—On the left margin of this tracing the intraluminal pressure of the vermiform appendix is recorded (appendicostomy); the catheter is then pushed into the cecum with a resultant fall in pressure, which returns again when the catheter is withdrawn once more into the lumen of the appendix, as indicated on the right extremity of the tracing.

pressure to 30 to 50 cm. of water. Between these active periods were intervals when the pressure hovered around 15 to 25 cm. of water pressure. During such intervals, the pressure tracings usually exhibited, every eight to ten seconds, small rises of 2 to 5 cm. increases in pressure.

The patient with ileostomy and appendicostomy afforded an opportunity to record simultaneously cecal and appendiceal pressures, one catheter being in the appendix; the other led into the cecum through the ileum. Whereas the basal pressure in the cecum was 3 to 4 cm. of water, in the appendix it was 15 to 25 cm. In the quiet intervals of the appendix, the cecum was inactive and when the appendix exhibited periods of increased activity, the cecum simultaneously became more active.

In a number of instances, somewhat similar information was obtained by recording the intraluminal pressure of the appendix, then advancing the catheter into the cecum and later withdrawing it again into the lumen of the appendix. The greater contractile activity of the appendix is easily discernible in Fig. 6. The intraluminal pressure sustained by the ileocecal sphincter, the catheter being tied into the ileum, was found to be 18 to 20 cm. of water.

(2) *Secretion of Fluid by the Appendix.*—The calibrated preparation described above in which entry of 0.62 cc. of fluid into the closed system indicated a pressure rise of 100 cm. of water, supplied a means of investigating fluid secretion by the appendix. The slope of the tracing on the kymographic record indicated the rate of fluid accumulation and from the pressure attained the increases in fluid volume were readily calculated (Fig. 7). In other instances the fluid secreted by the appendix was collected simply by permitting the catheter securely fastened in the appendiceal lumen to drain into a small glass tube properly stoppered and fixed to the dressing.

By both these methods 1 to 2 cc. of a slightly turbid fluid was collected

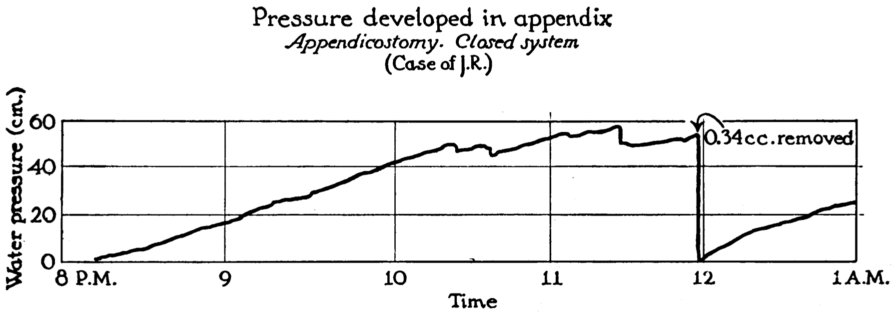

FIG. 7.—Pressure tracing made with a catheter in an appendicostomy. The spontaneous rise of pressure from atmospheric to almost 60 centimeters in four hours is shown. When 0.34 cc. of fluid was aspirated from this closed system, the pressure fell to zero and mounted again. The lumen of the appendix was patent. Secretion of fluid by the appendix only can explain this occurrence. Faradic stimulation will produce temporary elevations which are not sustained. Fluid was also later collected from the appendicostomy in a test tube fastened to the dressing.

every 24 hours. In one instance it was quite clear. It is at once apparent that in either instance, such fluid accumulations do not represent all the fluid secreted, for the opportunity for escape of fluid into the cecum was ever present. Though one cannot wholly exclude the possibility that the fluid came in part from the cecum, it is not believed that such was the case, not alone because of the pressure differences in cecum and appendix, but moreover because of the want of admixtures of cecal content with the fluid collected. The nature of this secreted fluid still remains to be determined.*

(3) *Effect of Drugs upon the Contractile Activity of the Appendix.*—In the main, the effect of drugs was essentially that noted below upon the excised appendix suspended in oxygenated Locke's solution. These findings will be elaborated in a subsequent communication (Dennis). Adrenalin administered subcutaneously or intravenously lowered the base pressure and abolished the contractile waves of activity—spinal anesthesia did essentially the same thing. Amyl nitrite (the fumes of two broken pearls inhaled) was

* Since this paper was written, three cases presented themselves in which a part or all of the appendix could be exteriorized. In these the organ was ligated near the base, following which fluid secretion was evident, pressures being permitted to develop as high as 40 centimeters of water. These experiments definitely exclude the possibility of the fluid having come from the cecum.

without constant effect, as were also benzedrine and atropin. Papaverine was followed by no consistent phenomenon. Morphine sulphate 0.010 Gm. (gr. 1/6) raised the basal pressure and increased the frequency of the smaller waves but decreased their size. Seven cubic centimeters of 3 per cent procaine solution placed in the lumen evoked no effect. Five cubic centimeters of 1 per cent cocaine solution, allowed to drip into the lumen over a five minute interval, caused a smoothing out of the finer waves and raised the height to which the pressure rose at the subsequent peak of activity. Betamethylacetylcholine, 10 mg. given hypodermically, increased the size and frequency of the small waves sufficiently to hold the base line up 10 cm. for several minutes. These observations were made after a period of fasting. The ingestion of food appeared to raise the basal level of pressure and increased the amplitude and frequency of the waves of contraction.

(4) *Placement of Bacteria Obtained from Instances of Acute Suppurative Appendicitis into the Lumina of Appendicostomies.*—Organisms cultured from the appendiceal lumen of two suppurative appendixes were without effect when 2 cc. of such a suspension were slowly injected into the lumina of two patients with appendicostomies. In neither instance was there fever or other reaction attending such injection during the succeeding 48 hours. At the time that the nature of the organism present in the initially inflamed appendixes was determined, *Bacillus coli* in each instance had overgrown the cultures.

(5) *Fate of Birdshot Placed in the Appendicostomy Stoma.*—A No. 9 birdshot (2.79 Mm. in diameter) was placed in the lumen of the appendicostomy in several patients and its position noted roentgenographically. In a few instances, it was extruded on to the dressing. In one instance the shot persisted in the appendix for more than two months. The introduction of bacteria from an instance of acute suppurative appendicitis into the lumen of the appendicostomy with the shot in place was also tolerated without reaction. In one instance the birdshot entered the colon in 24 hours; in another in 36 hours; in yet another in less than two hours. This latter patient suffered cramps as the shot progressed toward the cecum, which ceased after the shot had negotiated this passage.

(6) *Microscopic Study of Segments of Exteriorized Vermiform Appendices Subjected to Increase of Intraluminal Pressure.*—In a number of the patients with a good length of the appendix exteriorized, segments became available for purposes of microscopic study both before cannulation and after long intervals of sustained intraluminal pressure. Because of the serosal reaction attending exposure to the atmosphere, the histologic changes were difficult to evaluate. It was always felt desirable for purposes of safety to allow the exteriorized appendix to become firmly adherent (five to seven days) before prolonged distention was undertaken. This portion of the study will have to await suitable instances in which the whole appendix can be safely exteriorized and subjected early to increases of intraluminal pressure to avoid the complication of serosal irritation.

It may be properly related here, however, that abdominal pain and nausea, occasionally, and vomiting less commonly, attended long sustained increases of intraluminal pressure. Some of these exhibited slight febrile and leukocytic responses as well.

In this connection, the appendix of one patient is particularly interesting. The exteriorized segment when opened at the tip, five days after the establishment of appendicostomy, appeared unusually distended. Several cubic centimeters of a yellowish-gray pus exuded when its lumen was entered. The mouth temperature was 99.2° F. and the leukocytic count made directly after opening was 13,000. The amputated distal end of the appendix showed evidence of suppuration in the wall. Unfortunately a culture of the extruded pus was not obtained immediately and a culture from the lumen made after a few hours became overgrown with *Bacillus proteus*. The appendicostomy was cannulated and the absolute resistance to outflow determined. At first no fluid could be forced; after eight hours the resistance to outflow was found to be 85 centimeters of water. A catheter was left in the lumen for many days but no evidence of fluid secretion was obtained. Water could be injected into the cecum through the appendiceal lumen with a syringe but a catheter could not be introduced into the cecum. A lipiodol injection revealed two strictures on roentgenologic examination.

IV. Studies upon the Excised Appendix.—(1) *Resistance to Outflow:* It was found necessary to determine the resistance to outflow upon the excised specimen *immediately* after excision, for it was observed when the appendix lay exposed at atmospheric temperature for periods exceeding ten minutes that a gradual decrease in resistance resulted, which became minimal in 30 to 40 minutes. The absence of definite resistance to outflow from the appendix of the cadaver is noted in Table VI, item 4. The determination of the resistance to outflow was therefore made in the operating room directly following appendicectomy. Not uncommonly an increase in resistance over that observed prior to appendicectomy was noted in the excised specimen, due, in some measure probably, to the stimulation of the trauma accompanying excision; for it was noted contraction in length attending excision was not an uncommon circumstance. Control measurements of the length of the appendix before severance of its mesentery and after, as well as following removal, showed that shortening frequently attended these procedures and occasionally by as much as one-third of the total length of the appendix. Great shrinkage in length was accompanied by similar increases in resistance to outflow. In the main, however, these pressures sustained by the excised specimen corresponded fairly well with those observed before removal of the appendix.

It was further noted that when successive segments of 1 cm. in length or less were amputated from the base toward the tip that the resistance to outflow still persisted, and, as a matter of fact, often exhibited increments of gain owing to the greater contraction of the residual portion occasioned by the consecutive cuttings. It was found that this hyperirritability of the excised appendix could be circumvented by placing the specimen in an ice box at a temperature maintained between 2° and 7° C. Then, when the appendix was suspended in a temperature controlled water bath (37° C.) containing Locke's solution (with glucose eliminated, as suggested by Magnus and Alvarez), kept thoroughly oxygenated, good rhythmic muscular contraction occurred spontaneously. By inserting a cannula into the distal end of the appendix and attaching a thread to the proximal, which in turn ran around a pulley and was fastened to a recording lever, both the changes in length and variations in pressure required to force fluid into the system at a given rate could be graphically recorded. In this fashion it was shown that the rhythmic contractions of the two sheets of muscle are usually synchronous, but that either layer (circular or longitudinal) may contract spontaneously independently of the other. The pressures sustained with such preparations were usually about one-third of those observed just before or immediately after the removal of the appendix.

Appendixes which exhibited evidence of mild inflammation developed strong rhythmic contractions, occasionally greater than those noted in the normal specimens. When the effects of suppuration and damage to the appendiceal wall were plain, however, the contractile activity was feeble; in specimens in which only a portion of its length was involved in the inflammatory process, the healthy part exhibited satisfactory contractile activity, while the former showed no or poor movement. No suggestion of a gradient of activity was observed in these excised appendixes, but this matter will require further study.

A better opportunity, on the whole, was afforded in these preparations for the study of the effect of drugs upon the muscular contractions of the appendix than in the appendicostomies by the simple addition of the chemically pure drug in a certain dilution to the medium of the water bath. This portion of the study will later be reported in detail (Dennis). Briefly it may here be said, the addition of 0.5 cc. of adrenalin hydrochloride (1 : 1000) to the 180 cc. of Locke's fluid in the water bath almost invariably caused a decrease in rhythmic contractions or stopped them entirely, affecting the tone of both muscle layers; the addition of papaverine 0.016 Gm. (gr. 1/4) usually, but not always, caused diminution or cessation of movements; benzedrine sulphate in a concentration of 1 : 1000 uniformly increased the tone of both sheets of muscle and tended to accelerate the rhythmic contractions; atropine had a variable effect, in concentrations of 0.013 per cent the tone of the muscle was increased, whereas, in concentrations over 0.025 per cent, paresis occurred. The effect of barium chloride was most marked, a 30 mg. crystal suspended in the bath often provoking rhythmic contractions after futile waiting of two hours or more for them to appear spontaneously. The effect of the application of cocaine hydrochloride (1 per cent) was most interesting when applied to the serosa. All muscular activity stopped immediately; when injected into the lumen, it had a similar but less marked effect, and only after a latent period of about five minutes.

V. Retention of Foreign Material by the Vermiform Appendix.—The retention of birdshot in appendicostomies has already been described. To investigate the matter further, it was proposed to examine the intraluminal content of the excised vermiform appendix for barium in patients who had previously had a suspension of barium sulphate injected by enema for roentgenographic examination of the colon. At first the flame test was employed to examine for the presence of barium, but it was found to be subject to so many discrepancies that it was abandoned in favor of the spectrophotometric method. With the kind assistance of Dr. Irwin Vigness of the Department of Physiology, the absence or presence of barium in excised appendixes could be readily determined. The entire content of the washed appendix and half of the bisected appendix were ashed over a hot flame in a platinum crucible. The residue was then dissolved in strong acetic acid and the solution was submitted to spectrophotometric examination. The barium lines in the spectrum occur at 45.54 and 23.32 Angström units.

Thirteen appendixes removed from six to 790 days following the administration of barium, in which the appendix was not visualized by roentgenologic examination, failed to show spectrophotometric evidence of barium. In four other instances in which the appendix was visualized by roentgenologic examination and removed after intervals of ten, 13, 93 and 257 days following the barium enema, no spectrographic evidence of barium was found. In six other specimens, however, in which the appendix had been visualized on roentgenologic examination from eight hours to six days prior to appendicectomy, barium was detected by the spectrophotometric method in all. The approximate concentrations of barium in these specimens varied from .05 to 10 per cent. In patients who were known not to have had barium for roentgenologic examination at any time, the removed appendixes and their content showed no trace of barium by this method of examination.

Retention of barium for some time within the appendix has now and then been observed roentgenographically. In the instance of a recent patient with cardiospasm, barium entered the appendix after oral ingestion and when a scout film of the abdomen was made 31 days later, the barium was still present in the appendix. Barium was then again given by mouth without altering the opaque shadow in the appendix. Every ten to 14 days, a film was taken of the cecal region. The barium shadow in the appendix continued to be visualized for 64 days more. If no more barium entered the appendix at the time of the second examination—a plausible inference from the roentgenologic study—barium was retained in the vermiform appendix of this patient for 95 days.

VI. Is Fluid Secreted or Absorbed by the Obstructed Cecal Appendage of Animals?—Many studies have been made on the comparative anatomy of the cecum and its appendage. The studies of Huntington, Kelly and Hurdon and Reider are particularly well known. No study has previously been made with reference to a secretory or absorptive function of this segment of the gut. The evidence related above (Group III, item 2) concerning fluid secretion from the vermiform appendix of man suggested the necessity for making a similar investigation on animals which are readily available. Only the chimpanzee and the gibbon, according to comparative anatomists, have a true vermiform appendix. Other animals have a cecal appendage which communicates more directly with the cecum. There are, to be certain, many well recognized anatomic variations in form, size and shape of such appendages.

Because of the absorption of water from the intestinal content in the right half of the colon, it might reasonably have been believed that water would be absorbed by an appendage of the cecum. As has been indicated, however, the unobstructed vermiform appendix of man afforded no evidence of water absorption—on the contrary, definite evidence of fluid secretion was obtained. Other animals exhibiting a wide mouthed communication between cecum and its appendage and a larger lumen failed in consequence to exhibit any resistance to outflow from the appendage. In such experiments, therefore, it was necessary to ligate securely the base of the appendage to determine

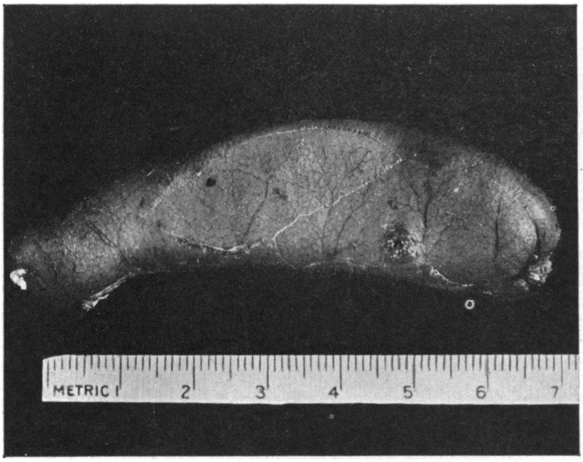

FIG. 8—Obsructed cecal appendage of rabbit which perforated 5 hours and 18 minutes after the administration of croton oil (Table IX, Rabbit No. 77). The site of perforation near the mesenteric border in the distal third is quite obvious.

whether fluid was absorbed or secreted. The distal tip of the appendage was then cannulated in the same manner that had been employed in the appendicostomies of man. Aseptic technic and intraperitoneal or intravenous pentobarbital sodium anesthesia were employed throughout.

The results of these experiments are extremely interesting and would appear to shed light upon the problem of appendiceal obstruction in man. Only in the cecal appendage of the rabbit was evidence of fluid secretion observed—in all other animals, so far investigated, obstruction of the cecal appendage is not attended by fluid production.

(a) *Obstruction of the Cecal Appendage in the Rabbit.*—Briefly it may be said that almost invariably unmistakable evidence of rapid fluid secretion accompanied obstruction of the cecal appendage. In ten to 14 hours, the intraluminal pressure had increased because of fluid production to the extent that rupture occurred. When croton oil (three minims) was administered

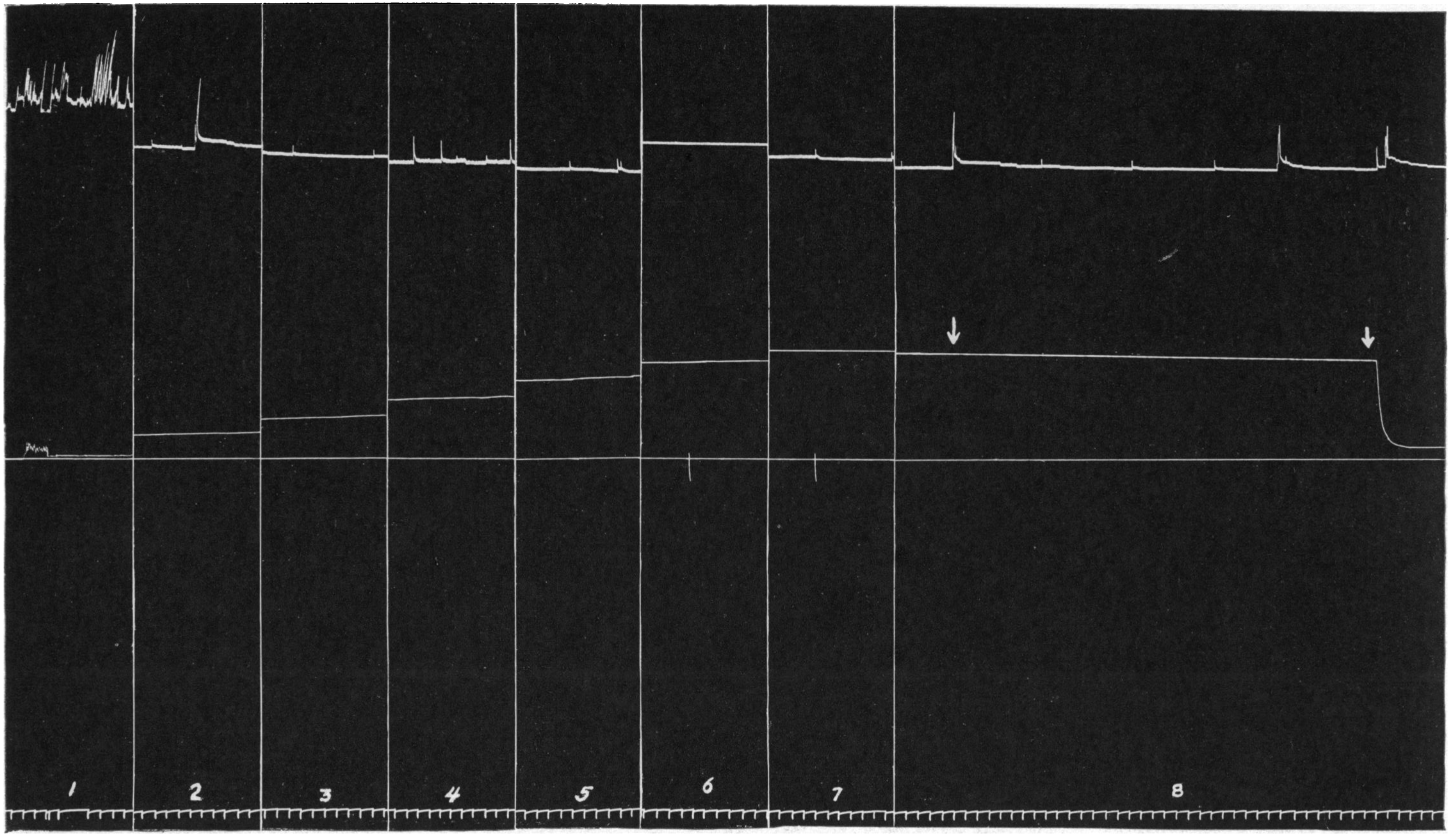

FIG. 9.—Kymographic tracing of hydrostatic changes in obstructed cecal appendage of Rabbit No. 46 (Table VIII). (1) Irrigation of cecal appendage with 25 cc. of Ringer's solution, followed by ligation of the base. (2) Three hours after ligation. Pressure 16.3 centimeters water. (3) Four hours after ligation, hydrostatic pressure 24.4 centimeters of water. (4) Five hours after ligation, pressure 38.0 centimeters of water. (5) Six hours, pressure 50.0 centimeters of water. (6) Seven hours, pressure 59.4 centimeters of water. (7) Eight hours, pressure 68 centimeters of water. (8) Nine hours after ligation, pressure 66.0 centimeters of water. Tear occurred in the serosa as indicated by the arrow. Note the respiratory change at the time of the serosal tear and rupture of the wall. Rupture 9 hours and 35 minutes after ligation. The respirations are indicated above; the arrow at the left indicates the second tear, the one at the right, the fall of the pressure to the base line. The marks of the signal magnet are spaced one minute apart.

by gavage, rupture occurred in considerably shorter time (Fig. 8 and Table IX, Rabbit No. 77); earlier perforation was particularly striking after the injection of hypertonic saline solution intravenously (0.3 Gm. of sodium chloride per kilo—a 15 per cent solution being employed). The effect of other drugs has also been investigated but will not be reported upon here. When the artery to the cecal appendage or the artery and vein were ligated, rupture did not attend simple obstruction of the cecal appendage nor even after croton oil (orally) or hypertonic intravenous saline solution was given. The results of these various procedures are indicated in Tables VIII and XI. The gradual rise of intraluminal pressure attending obstruction and the effect of perforation are illustrated in Figs. 9 and 10A.

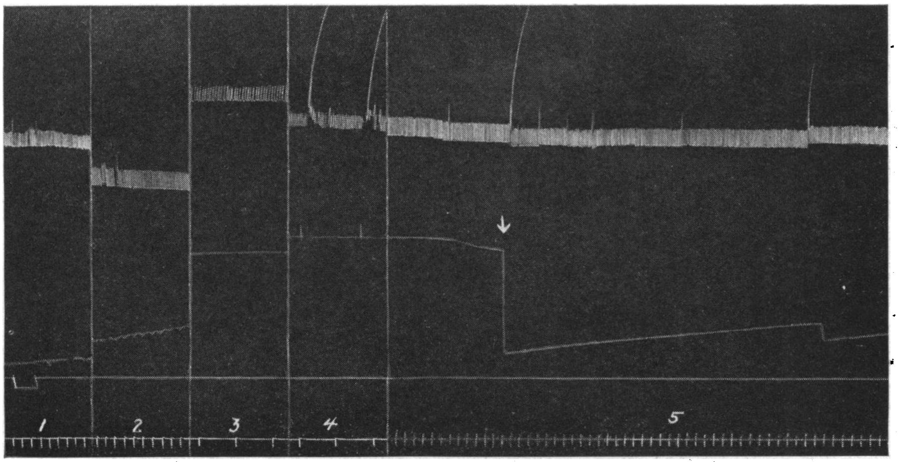

FIG. 10A.—The effect of the intravenous injection of hypertonic saline solution upon the intraluminal pressure of the obstructed cecal appendage of the rabbit (Table X, No. 91). (1) Intravenous injection of 2.2 cc. 15 per cent solution of sodium chloride 20 minutes after ligation; pressure 13.0 centimeters of water. (2) Thirty minutes after hypertonic saline; pressure 34.3 centimeters of water. (3) Pressure 90 centimeters of water one hour after hypertonic saline solution. (4) Two hours after saline solution; pressure 136 centimeters of water. (5) Rupture of the wall of the cecal appendage 3 hours and 30 minutes after obstruction by ligation. Removal of the specimen 2 hours and 30 minutes after rupture.

In a number of other instances the cecal appendage of the rabbit has merely been tied off, and at intervals of from two to 48 hours, the abdomen has been reopened and the appendage has been inspected or excised for purposes of study (Fig. 11). Perforation and sealing off by the adjacent mesentery or mesentery to close the perforation in the wall of the cecal appendage during coils of bowel are common occurrences.* The ineffectual effort of the adjacent mesentery to close the perforation in the wall of the cecal appendage during the course of a pressure experiment is well illustrated in Fig. 10A.

* Since this paper was written, a paper by Mr. A. Q. Wells of St. Bartholomew Hospital in London has appeared in the British Journal of Surgery, April, 1937, in which it is suggested that obstruction of the cecal appendage of the rabbit is without effect—that it is injury to the mucosa that is the important determinant in bringing perforation about. We have as yet not investigated how fluid production is influenced by mucosal injury, but it is difficult to follow Mr. Wells' deductions made from his own experiments in which he relates the appearance of abdominal masses accompanying obstruction of the cecal appendage of the rabbit.

TABLE VIII

INTRALUMINAL PRESSURE RISES AND EFFECTS ATTENDING OBSTRUCTION OF CECAL APPENDAGE OF THE RABBIT

No. of Rabbit	Procedure	Variation	Duration in Hours	Pressure in Cm.	Volume in Cc.	Cc. Output* per Minute	Rupture	Microscopic Study
R-48	Washed. Incannulated. Obstructed		8.17	71.9	14.64	.0298	Yes	Acute
R-39	Washed. Incannulated. Obstructed	Ileal vein injured	10.00	68.0	13.6	.0226	Yes	Gangrenous
R-46	Washed. Incannulated. Obstructed		10.00	60.4	12.08	.0201	Yes	Acute
R-49	Washed. Incannulated. Obstructed		11.00	55.7	11.44	.0188	Yes†	Gangrenous
R-43	Washed. Incannulated. Obstructed		17.17	42.7	8.54	.0082	Yes	Acute
R-50	Washed. Incannulated. Obstructed	Spontaneous production of fluid	2.25	20.0	4.0	.0296	No	Reactive appendix. Serositis
R-42	Washed. Incannulated. Obstructed	Spontaneous production of fluid	3.16	18.5	3.7	.0194	No	Reactive appendix. Serositis
R-40	Washed. Incannulated. Obstructed	Fluid removed at 23 cm.	7.3	22.8	9.76	.0208	No	Serositis
R-35	Washed. Incannulated. Obstructed	Spontaneous production of fluid (fluid twice removed)	10.0	39.0	12.62	.0191	No	Acute
Average of ruptured cases.............			13.26	60.0	12.06	.0195		
R-63	Washed. Incannulated. Not obstructed	Control experiment	10.0	0	0	0	No	Normal appendix. Serositis

* Rate of fluid production is prorated over the entire time period, even though the rate of rises in pressure varied somewhat.

† Microscopic rupture.

The histologic reaction in the cecal appendage of the rabbit attending spontaneous perforation in consequence of obstruction of the cecal appendage is not very much different from that observed in the spontaneous occurrence of suppurative appendicitis in man. A microscopic section near the site of perforation in rabbit No. 91 (Table X) is shown in Fig. 10C. A drawing of the same specimen is illustrated in Fig. 10B. This interesting portion of the study will be elaborated upon later.

TABLE IX

OBSTRUCTION OF CECAL APPENDAGE OF RABBIT AND ORAL ADMINISTRATION OF CROTON OIL (THREE MINIMS)

No. of Rabbit	Procedure	Variation	Duration in Hours	Pressure in Cm.	Volume in Cc.	Cc. Output per Minute	Rupture	Microscopic Study
R-77	Washed. Incannulated. Obstructed	Croton oil, 3 minims, orally	5.3	69.3	13.86	.0446	Yes	Acute
R-76	Washed. Incannulated. Obstructed	Croton oil, 3 minims, orally	6.0	54.4	10.9	.0363	Yes*	Acute

* Microscopic rupture.

TABLE X

OBSTRUCTION OF CECAL APPENDAGE OF RABBIT ACCOMPANIED BY INTRAVENOUS INJECTION OF HYPERTONIC SALINE SOLUTION

No. of Rabbit	Procedure	Variation	Duration in Hours	Pressure in Cm.	Volume in Cc.	Cc. Output per Minute	Rupture	Microscopic Study
R-91	Washed. Incannulated. Obstructed	⅓ Gm. NaCl per kilo in 15% solution injected intravenously	3.0	136.0	27.2	.1510	Yes	Acute, gangrenous (See Fig. 10A)
R-83	Washed. Incannulated. Obstructed	The same as above	6.0	40.8	8.16	.0340	Yes*	Acute
R-89	Washed. Incannulated. Obstructed	The same as above	7.2	30.0	6.0	.0139	No	Acute (anesthetic death)

* Microscopic rupture.

(b) *Obstruction of the Cecal Appendage in the Dog.*—That obstruction of the washed cecal appendage of the dog is well tolerated has previously been noted (Wangensteen and Bowers). It was proposed to determine here

TABLE XI

OBSTRUCTION OF CECAL APPENDAGE OF RABBIT AND LIGATURE OF ARTERY AND VEIN OF APPENDAGE

No. of Rabbit	Procedure	Variation	Duration in Hours	Pressure in Cm.	Volume in Cc.	Cc. Output per Minute	Rupture	Microscopic Study
R-78	Washed. Incannulated. Obstructed	Croton oil orally. Ligation of artery and vein	5.5	0	0	0	No	Normal appendix
R-79	Washed. Incannulated. Obstructed	Castor oil orally. Ligation artery and vein	18.5	0 (Pressure maintained 9 to 12 cm.)	0	0	No	Acute appendix
R-36	Washed. Incannulated. Obstructed	Ligation appendiceal artery and vein	21.0	0 (Pressure raised to 16.0 cm. when no fluid was produced)	0	0	No	Acute appendix
R-75	Not washed. Obstructed. Not incannulated	Ligation vein and artery and ⅓ of mesentery	Expired 24 hrs.	0	0	0	No	Normal appendix. Traumatic serositis

whether fluid production accompanied this procedure in the dog. As will be observed in Table XII, neither perforation nor evidence of fluid production attended obstruction of the cecal appendage of the dog.

TABLE XII

OBSTRUCTION OF CECAL APPENDAGE OF THE DOG

No. of Dog	Procedure	Variation	Duration in Hours	Pressure in Cm.	Volume in Cc.	Cc. Output per Minute	Rupture	Microscopic Study
D-51	Washed. Incannulated. Obstructed		16.0	8 to 24	0	0	No	Acute
D-54	Washed. Incannulated. Obstructed		50.0	16 to 24	0	0	No	Acute

(c) *Obstruction of the Cecal Appendage and Determination of Secretory Pressure in Other Animals.*—The cecal appendage has been obstructed in three monkeys and the cecal pouch in three pigs and the occlusion was tolerated without perforation or evidence of fluid secretion. In two of the monkeys and two of the pigs, secretory pressures were determined over quite long intervals.

In one monkey an intraluminal pressure of 12 cm. of water developed. In the pigs, water appeared to have been absorbed. The cecal appendage was obstructed in two rats, one cat, and two guinea-pigs—all of which tolerated the procedure well. The cecal pouches of three chickens and two pigeons were obstructed. There was no evidence of inflammation and the procedure was well tolerated.*

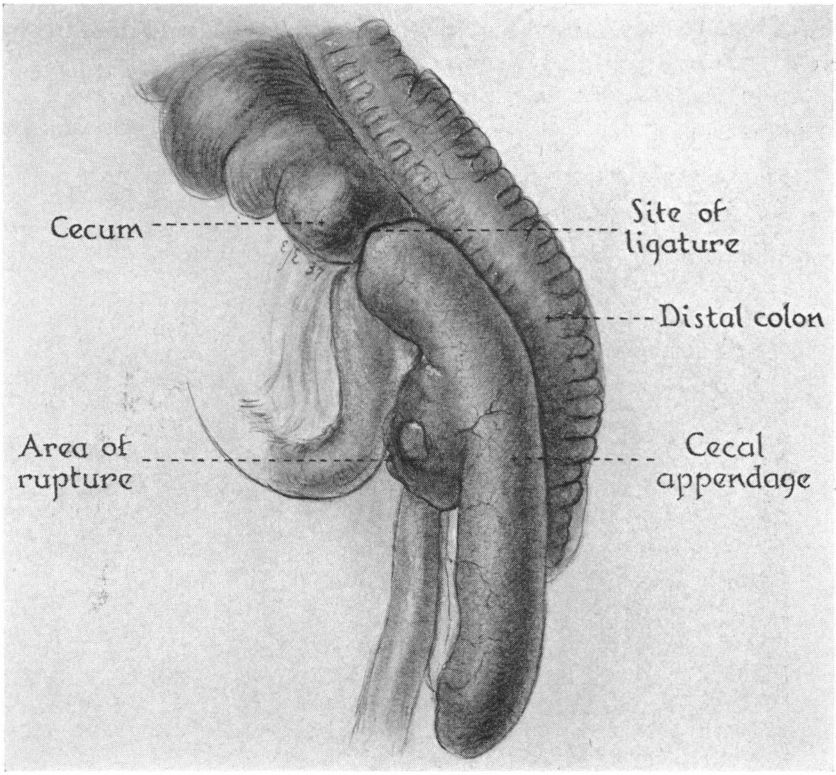

FIG. 10B.—The sealing over the site of rupture temporarily stems the fall in pressure as indicated in 10A, but that the walling-off is ineffectual is also apparent in the fall in pressure at the extreme right of the tracing (10A).

VII.—The Luminal Volume of the Appendix.—Whereas the length and thickness of the appendix have been determined in scores of studies, no observations on the volumetric capacity of the vermiform appendix have come to our attention. When the secretory behavior of the appendix is appreciated, it is immediately apparent that the capacity of the appendix in the presence of obstruction becomes a matter of great importance.

The volume of the cylindrical vermiform appendix has been determined in three ways:

(1) In three freshly excised appendixes, two per cent liquefied gelatin

* Recently we have found that the appendage of the calf, the duck, the striped gopher, the goose, the porcupine, the sheep, and the grey squirrel absorb Ringer's solution, while the appendage of the rat secretes at pressures below seven centimeters of water. In the red fox neither secretion nor absorption could be demonstrated.

(specific gravity 1.028) was gently injected from beneath into the suspended viscus through a needle inserted through the tip. When gelatin came out through the proximal end, the entire specimen was chilled in the refrigerator, the point of needle puncture being sealed by freezing with ethyl chloride. Later, the wall of the appendix was slit open and the appendix itself was dissected free from the gelatin, which weight was then carefully determined. The weight of the gelatin divided by its specific gravity determined the volume. The values determined for the volume of the cylinder in these instances were 0.357, 0.226, and 1.020 cc. respectively.

(2) In ten other formalin-fixed specimens, obtained at necropsy from patients varying in age from six months to 71 years, the volume was deter-

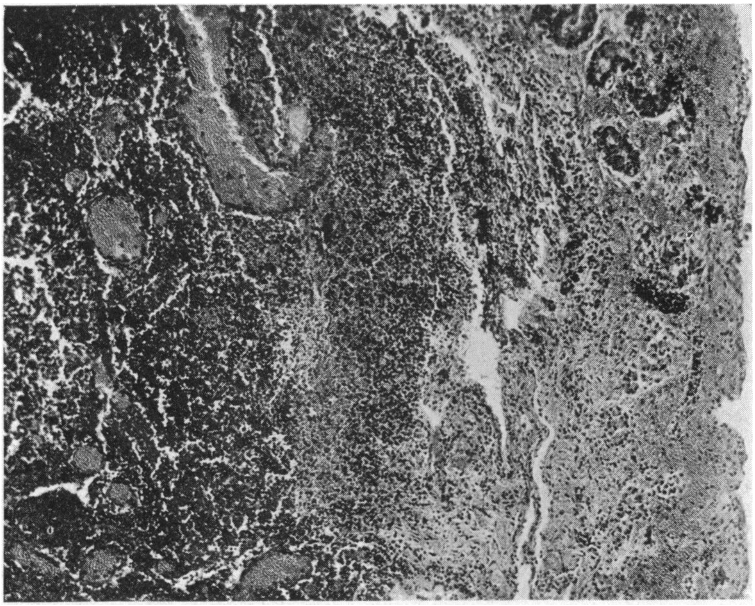

FIG. 10C.—The histologic reaction attending spontaneous rupture which occurred 3 hours and 30 minutes after obstruction of the cecal appendage. The specimen was removed and fixed for microscopic study six hours after the establishment of obstruction. The cytologic response is largely polymorphonuclear and extends through all the walls. A good portion of the mucosa is lost through ulceration. The section is taken in juxtaposition to the site of rupture.

mined in the following manner: The appendix was dried by rolling it in gauze and then milking it out gently. The appendix was then suspended in the manner of the group just described above and water was injected slowly through the tip with a No. 20 gauge needle and a tuberculin syringe. The volume of the appendix was indicated by the fluid injected when water appeared at the top. The average value for the volume of the vermiform appendix in this group was 0.10 cc.; the maximum was 0.24 cc., and the lowest reading, 0.00 (zero). The median value was 0.08 cc. The pressures employed were not measured.

In a group of eight vermiform appendixes obtained at autopsy and then placed in saline solution in an electric refrigerator for a few hours, an attempt was made to rupture the appendix and determine the volume at the time of rupture. The proximal end of the appendix was closed with a hemostat and water was injected through a No. 20 gauge needle in the tip by means of a 20 cc. Luer syringe. In one instance the appendix could not be ruptured by this means; in two others, the serosa tore and fluid oozed through. The average volume at rupture was 5.87 cc.; the median volume was 5.50 cc.; the maximum at rupture was 9.50 cc., and the minimum was 3.0 cc. The pressures employed were not measured, but were, of course, enormous.*

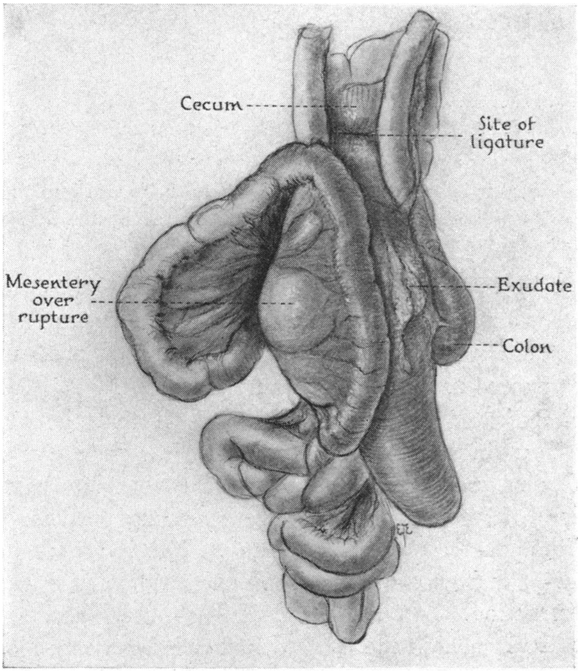

FIG. 11.—Perforation of obstructed cecal appendage of the rabbit. The site of rupture had become sealed over by the mesentery of the ileum. There is exudate on the free serosal surface of the appendage. Finding at reoperation 48 hours after the establishment of obstruction.

(3) The methods described above took no note of the pressure employed at the time of filling of the appendix, so its volume was determined, in eight appendixes (either at operation or immediately after excision, and in one postmortem specimen), in the following manner: The resistance to luminal outflow from the appendix was first determined and the lumen was then irrigated until the fluid returned fairly clear. Any residual content was then gently milked out. A hemostat was applied across the proximal end at the site of amputation and the needle in the distal tip was connected by means of a Y tube to both a water manometer and a syringe (Luer). The volume change in the entire system with changes in pressure could then be readily observed (Table XIII).

* The authors wish to acknowledge the helpful assistance of Mr. P. Beckjord and Mr. H. Svien, both senior medical students, in this and other phases of the work.

TABLE XIII

LUMINAL VOLUME OF THE APPENDIX AS RELATED TO PRESSURE*

Volume at Varying Degrees of Water Pressure.

	Atmospheric (zero)	20 cm.	60 cm.	100 cm.
Normal (four):				
Average	0	0.07 cc.	0.52 cc.	1.4 cc.
Maximum	0	0.18	0.7	2.0
Minimum	0	0	0.35	0.9
Acute, mild (three):				
Average	0	0.07 cc.	0.2 cc.	0.6 cc.
Maximum	0	0.23	0.6	0.9
Minimum	0	0	0	0
Interval (one)	0	0.05 cc.	0.05 cc.	0.3 cc.
Postmortem (one)	0	0.55 cc.	1.15 cc.	1.7 cc.

* From these readings it is apparent that no fluid can be forced into the appendix until the resistance to luminal outflow has been overcome. At atmospheric pressure therefore, the luminal capacity of the appendix is zero.

The findings by these three methods are essentially in agreement. It is evident that the volume of the appendix at physiologic pressures (60 cm. of water or below) did not exceed 0.7 cc. and at 20 cm. pressure the luminal capacity did not exceed 0.23 cc. in the intact appendix.

It has been indicated in Tables VIII and XI that the obstructed cecal appendage of the rabbit may burst at relatively low pressures (40 to 70 cm. of water). The normal cecal appendage of the rabbit (not subjected to spontaneous rises of intraluminal pressure attending obstruction) will burst at pressures from 120 to 150 cm. of water. The increases in intraluminal capacity attending the slow process of spontaneous distention varies under the influence of obstruction.

It has been observed that the excised, unruptured, gangrenous vermiform appendix of man may also rupture at relatively low pressures—in one instance at 20 cm. of water and in another at 70 cm. The excised normal appendix of man, however, when subjected to sudden increases of intraluminal pressure could not in a single instance be ruptured by pressures as high as 2400 cm. of water (approximately 2.3 atmospheres). In this process, a stretch to a luminal capacity of about 5 cc. occurs.

The implications in part are plain, *viz.*, that the luminal capacity of the vermiform appendix of man is much smaller than that of the cecal appendage of the rabbit, and that the bursting strength of the latter is considerably less than that of the appendix of man. It would appear therefore that interference with blood flow which results from maintained intraluminal pressure exceeding the capillary pressure brings about necrosis of the wall, which in turn accounts for perforation or gangrene of the obstructed vermiform appendix of man.

In 13 rabbits the thickness of the musculature was determined, also the thickness of the entire wall as well as the diameter of the lumen and the diameter of the cecal appendage, from formalin-fixed sections cut at the points of juncture of middle and distal thirds (Table XIV).

TABLE XIV

MEASUREMENTS OF THE NORMAL CECAL APPENDAGE OF THE RABBIT, IN MILLIMETERS

	Thickness of Musculature	Thickness of Wall	Diameter of Lumen	Diameter of Appendage
Average of 13 specimens....	0.0213 Mm.	1.53 Mm.	4.86 Mm.	8.15 Mm.

In a group of cases from the postmortem series, similar measurements were made upon the vermiform appendix of man (Table XV).

TABLE XV

THE MEASUREMENTS OF THE VERMIFORM APPENDIX OF MAN IN MILLIMETERS (KELLY AND HURDON)

Thickness of musculature......	0.4 to 0.8 Mm.
Thickness of wall.............	1.0 to 2.5 Mm.
Diameter of lumen............	1.0 to 3.0 Mm.

Kelly and Hurdon quote the diameter of the vermiform appendix as determined by seven other authors. Among these measurements there is a variation in diameter from 3 to 8 Mm. The average is 5.2 Mm. and the median value is 6 Mm. It is readily apparent, therefore, that the wall of the rabbit's cecal appendage is thinner than that of man, whereas the total diameter is greater—accounted for largely by the presence of the greater lumen.

SUMMARY

The nature of the appendicocecal union has been described (Table I). In about 80 per cent of instances a mucosal cecal fold (Gerlach's) overlies the superior aspect of the appendiceal orifice. Only rarely does this fold contain muscle fibers. None were observed in adult specimens and in 63 fetal and infant specimens studied, this occurrence was noted three times. The appendiceal orifice varies considerably in size and persists after appendicectomy, as do also the cecal folds. At the apex of the union between cecum and appendix there is a thickening of the muscle on the medial aspect of the superoir wall (Fig. 4). No true evidence of a distinct circular sphincter muscle has been found. It is to be stated, however, that the circular fibers, considering the size of the appendiceal lumen, constitute a generous sheet of muscle whose action is sphincter like.

The vermiform appendix exhibits a definite resistance to luminal outflow —the extent of which is apparently a resolution of the amount of circular muscle in its wall and the diameter of the lumen. It is by no means a property confined to the appendix but is also possessed by the ureter, vas deferens and other viscera with a small lumen and muscular walls. This resistance to luminal outflow, as studies continued over a long period of time in appendicostomies have shown, varies from hour to hour and in turn can be modified by the employment of drugs. In freshly excised appendixes it was shown that the application of a dilute solution of cocaine to the exterior largely abolishes this resistance. Application of cocaine to the interior is less effective. This

observation would suggest that the circular muscle and Auerbach's plexus are largely accountable for this property. Meissner's submucous nerve plexus apparently has less to do with it and there is no suggestion that the argentaffine cells in the crypts of Lieberkühn play any rôle in this behavior of the appendix. The extent to which the appendix may retain foreign bodies has been briefly reviewed.

Evidence of fluid secretion by the vermiform appendix was also obtained. The nature of this secretion still remains obscure. Its amount in the unobstructed appendix would appear to be from 1 to 2 cc. a day. Of a large number of animals, the function of whose cecal appendages were investigated, only in the rabbit has evidence been found of marked fluid secretion. It has been pointed out that rupture of the rabbit's appendage when obstructed will occur in ten to 14 hours and that this occurrence can be hurried considerably by the intravenous infusion of hypertonic saline solution or by the oral administration of croton oil. It is believed that this result is largely an effect of fluid secretion—muscle contraction is less responsible than the dilating force of secreted fluid. The luminal capacity of the vermiform appendix was found to be astonishingly small and relates itself intimately to the problem of fluid secretion under conditions of luminal obstruction.

Discussion.—In the light of the knowledge that the vermiform appendix of man secretes fluid, its behavior under conditions of obstruction becomes understandable. Whereas, it may have been more readily believed that this segment of the intestinal canal, so intimately related to the colon, should be identified with absorption,* the demonstration of its secretory function, even though it be slight, lends trustworthy credibility to an obstructive origin of appendicitis. It is not without interest that only the vermiform appendix of man and the obstructed cecal appendage of the rabbit of species thus far investigated exhibit this property. Both possess a generous deposit of lymphoid tissue in the mucous and submucous coats of the bowel.

That the vermiform appendix of man may become easily obstructed is obvious. How this obstruction may come about is not so readily discernible. That appendicoliths (whose exact origin yet remains to be explained) and foreign bodies may obstruct the lumen of the appendix is a matter of common experience. How the appendix may become totally obstructed in other manners still demands explanation. That swelling of the mucous and submucous lymphoid tissue may bring about obstruction of the lumen appears reasonable; that augmentation of the normal physiologic obstruction to emptying by reflex nervous causes may initiate circulatory damage to the appendiceal mucosa and set in motion the effects of continued luminal obstruction would seem to be not unlikely.

Why the lumen of the vermiform appendix of the older child, adolescent, or adult becomes more easily obstructed than that of the newborn or child

* It is likely that at every level of the intestinal canal, fluid is secreted and absorbed. Secretion is preponderately the function of the upper intestinal segments—absorption of the lower. In the appendix, this balance is in favor of secretion in that viscus.

under one year of age is understandable after considering the findings in Table I, in which the larger communication between appendix and cecum is indicated. Nagoya observed, with advance in years, a decline not only of the mucous and submucous lymphoid tissue of the appendix, but also a decrease in number of the intestinal glands—findings which would suggest that the mechanism for production of fluid by the appendix became less efficient with increase in age, when appendicitis is also less commonly observed.

A closed loop in which secretion occurs would appear to be particularly hazardous when the luminal capacity is small, as it is in the vermiform appendix. Burget and Dragstedt and their associates have indicated how temporary aspiration of a closed loop, or preliminary washing of it, may permit of its being tolerated with the avoidance of rupture. Undoubtedly the same holds true of the vermiform appendix. With gradual development of obstruction or obliteration, undoubtedly complete luminal obstruction may be withstood without rupture. The alteration of the normal secretory function of the vermiform appendix which comes about through such circumstances accounts for this paradox—an occurrence well known to all who have experimented with closed intestinal loops.

CONCLUSIONS

The vermiform appendix of man serves no known useful function. It apparently does have a function, however, *viz.*, the secretion of fluid. In this function lies the explanation of why the appendix is a treacherous organ when obstructed. What the nature of the fluid secreted by the appendix is, has, as yet, not been determined. How the lumen of the appendix may become obstructed in the absence of an evident cause yet remains to be demonstrated.

The minute anatomy of the vermiform appendix as it bears on the problem of acute appendicitis has been broadly studied. The resistance to luminal outflow which the appendix exhibits is in all likelihood a resolution of its small luminal capacity and strong sphincter-like circular muscle. No evidence of a true cecoappendiceal sphincter has been found.

The effects of obstruction of the cecal appendage have been studied in many animals; only that of the rabbit has so far been found to possess a secretory function similar to that evidenced in the vermiform appendix of man.

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Discussion.—Dr. Hubert A. Royster (Raleigh, N. C.): In my opinion, this is a very important paper. These studies are leading to what has been long admitted to be certainly a predisposing, if not a determining, cause of most cases of appendicitis, that is, obstruction. We cannot get anywhere in bringing about a reduction of a supposed high mortality in acute appendicitis unless we go behind the returns. For many years I have been interested in the anatomy, physiology and pathology of appendicitis, rather than in the study of technic, which should never get to the point of having a "brilliant surgeon" save somebody's life.

Anatomy, of course, goes back to embryology for its foundation. Doctor Wangensteen's studies, it would seem to me, upon the anatomic basis, are very sound. Embryologic study of the appendix causes us to admit one fact, that it is a so called vestigial organ. As far back as we can ascertain, the appendix was as large as, if not larger than, the cecum, and when the intestinal canal elsewhere underwent highly specialized growth to take care of what was probably the function of the appendix itself, nature began to lop it off, as in all rudimentary and retrogressive organs.

I still believe that the appendix has a function. The first research, undertaken many years ago, was to prove, I think, what Doctor Wangensteen has demonstrated so satisfactorily, that it has a secretory function. Some felt there was a secretion poured into the cecum for the purpose of helping the admixture of feces; others, that probably a fluid was abstracted from the cecum. It remained for Adami and McCrae, in 1914, to show that the appendix is the hydrostatic agent which initiates peristalsis in the colon. This explains constipation in the bedridden; it explains a desire for normal evacuation upon arising, or after taking the first meal; it explains constipation following some interval removals of the appendix; and it also explains some cures of constipation after the removal of a pathologic appendix.

The interesting thing to me about this, and Doctor Wangensteen stressed it, is the secretion of fluid by the appendix. I am absolutely convinced myself that whatever distends the appendix, either from the inside or the outside, is frequently the actual cause of appendiceal attacks.

It was shown by previous investigators, in 1921, in experiments on rabbits, that a fixed or abnormal position of the appendix with adhesions was a factor. A disturbed blood supply, to which Doctor Wangensteen referred, with kinking and obstruction of the vessels, is sometimes necessary to produce a gangrenous appendix. Even with all the obstruction that you might get, you would probably not get gangrene unless the artery of the appendix was occluded by thrombosis, and we have actually demonstrated in many cases the appearance of a thrombus in the meso-appendix, with gangrene below the point of obstruction throughout its whole extent.

It is quite often noted in perforated appendices that we will find fecal concretions either in or outside the appendix, which may go to prove the obstructive theory. The question of fecal concretions as an exciting cause of obstruction or distention is very interesting. It seems to me that upon this question hinges the whole pathology of appendicitis. We cannot understand any disease without a knowledge of its pathology. Upon pathology depends physiology, and behind both is anatomy.

This makes me feel sure that this study is very important; because it compels us to recognize that appendicitis is a going concern, a continuing process, and that all of these factors which Doctor Wangensteen has demonstrated are forerunners of what you and I call the acute attack. I maintain that the acute attack is *not* the disease, only a knock at the door saying, "Let me out," and that in every case that comes to operation, the disease has existed a matter of two or three years, with clinical signs which might be obscure or certain.

I further believe that once appendicitis, always appendicitis, until the little assassin is executed. I believe also that the study of these factors is going to do more to reduce our death rate, because it will prove absolutely that the conditions that we see at the operating table in the acute attack mean that the disease has existed previous to what we call the fulminating attack; otherwise, we know that certain things couldn't have happened. An appendix which is perforated early, following the first pain, in many cases is called the "first" attack, but in most cases it is the "worst" attack.

Dr. Owen H. Wangensteen (Minneapolis) closing: I believe it can truthfully be said that the appendix has a function; it does not, however, appear to be a useful one. This humble but treacherous occupant of the peritoneal cavity, to employ a characterization of Charles Dickens, may well be called the "Uriah Heep of the Abdomen." The suggestion of Doctor Royster that the vermiform appendix *must* have been previously diseased to give rise to acute suppurative appendicitis does not agree with my conception of the origin of the disease. As a matter of fact, one would anticipate more devastating effects of luminal obstruction upon the normal than upon a previously diseased appendix. Knowledge of the behavior of closed intestinal loops will serve to clarify this point. Several members of this organization, particularly Doctors Dragstedt and Morton, have worked with such loops and have been able to show that the physiology of a loop at certain levels may be modified by aspiration, lavage, and previous drainage of the loop. Every section of the gut probably *absorbs* and *secretes* fluid. In the duodenum, the function is preponderantly secretory. In the vermiform appendix it is more evenly balanced, but yet secretion would appear to be the predominant characteristic. That obstruction of the vermiform appendix may exist without giving rise to acute suppurative appendicitis is readily understandable in the light of how the function of a closed loop may be modified by various factors. Obstruction of the lumen in a previously healthy appendix, however, is undoubtedly always serious.

There is an experimental study of appendicitis by Mr. A. Q. Wells, reported in the April, 1937, issue of the British Journal of Surgery. Many of you will see this article. Our conclusions appear to be in direct conflict with those of Mr. Wells, who concludes that luminal obstruction of the cecal appendage of the rabbit is without significance—that it is the injury to the mucosa which is the important and determining factor. I would conclude from his own experiments, however, that luminal obstruction to the cecal appendage of the rabbit is hazardous. It would appear likely that when Mr. Wells perforated the cecal appendage of the rabbit beyond the ligature with a needle and scratched the mucosal interior that as fluid accumulated in the appendage incident to obstruction, escape occurred along the needle track before the adjacent tissues had an opportunity to wall off the site of leakage, as they can do quite effectively in the perforation attending ligature of the base of the cecal appendage. Whether mucosal injury slows or hastens the secretion of fluid within the obstructed lumen must, of course, be determined by actual experiment.

We have not had an opportunity to determine whether the function of the vermiform appendix in the higher apes such as the chimpanzee or the gibbon, like that of man, and the cecal appendage of the rabbit is more secretory than absorptive. I am inclined to believe that a study of the comparative physiology of this segment of gut in many animals may throw considerable light on the origins of appendicitis in man.