EXPERIMENTAL PROOF OF THE OBSTRUCTIVE ORIGIN OF APPENDICITIS IN MAN*†

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IN a preliminary study,[10] reported two years ago, from observations made upon the exteriorized, unobstructed appendix, evidence was presented which suggested that the vermiform appendix of man secreted fluid. It was also shown, at that time, that obstruction of the cecal appendage of the rabbit was followed consistently by evidence of rapid fluid secretion. During the time that has intervened since then, these studies have been extended considerably. In the present communication evidence of the secretory capacity of the vermiform appendix of man will be cited.

The behavior of the appendix when obstructed temporarily will be described and factual proof of the reproduction of the pathologic picture of spontaneous appendicitis through the agency of obstruction will be presented.

Method.—From studies made upon the obstructed cecal appendage of the rabbit and the vermiform appendix of the chimpanzee,[11] it was apparent that in order to adduce convincing proof of the secretory capacity of the appendix of man it was necessary to incannulate the obstructed exteriorized appendix. Unobstructed appendicostomies permitting incannulation had been established incidentally when colostomy was performed for malignant disease of the colon. Exteriorization of the appendix in this manner had been accomplished readily through a button-hole incision and did not complicate the operative procedure.[10]

In a patient presenting a carcinoma of the ascending colon, it was possible to exteriorize, with the blood supply intact, after the Bloch-Mikulicz principle, the greater portion of the right half of the colon and the terminal ileum. A few days later, when the exteriorized bowel had become fairly well covered with fibrin and effectual sealing of the wound had occurred, the base of the appendix was ligated securely. The attachment of a closed water system connected to a recording manometer permitted determination of the ensuant increase in intraluminal pressure. The manometer used required addition of 0.58 cc. of fluid to raise the pressure reading 100 cm. of water.

It was obvious that this type of case, permitting determination of the secretory capacity of the vermiform appendix, would not be encountered frequently. After considerable deliberation the method depicted in Figure I was worked out. When preliminary colostomy was being performed for malignancy of the large bowel or rectum prior to excision of the lesion, the appendix

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was exteriorized and obstructed. Through a button-hole incision placed over the base of the cecum, the appendix was delivered and the cecum around the base of the appendix was anchored securely to the parietal peritoneum by a number of fine silk sutures, thus placing the appendix in an extraperitoneal position. The base of the appendix was ligated with plain catgut No. 00, a cannula was placed in the appendix and as soon as the patient was returned to his room attachment was made to a manometric recording system. After it was determined whether or not the obstructed exteriorized appendix developed an increase of intraluminal pressure, the closed system was broken and the cannula was attached to a small Wassermann tube (atmospheric pressure)

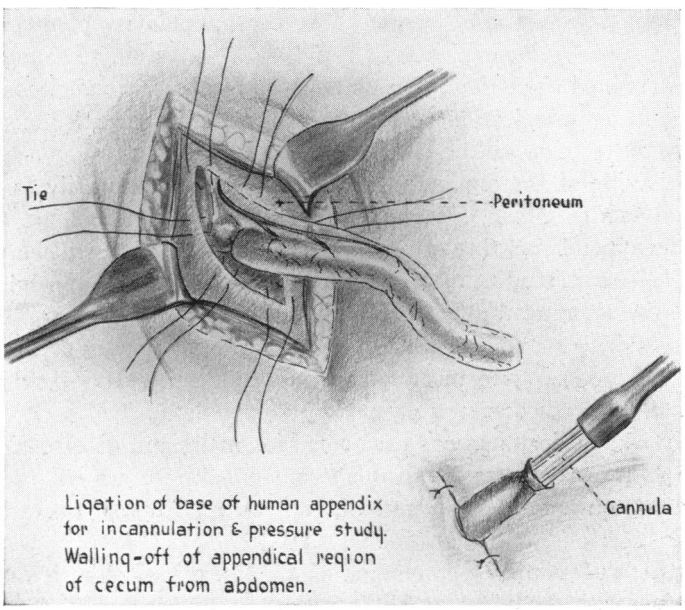


FIG. 1.—Technic of exteriorizing and obstructing an appendix as employed in this study for purposes of measuring the secretory pressure—a procedure performed coincidentally at the time of colostomy.

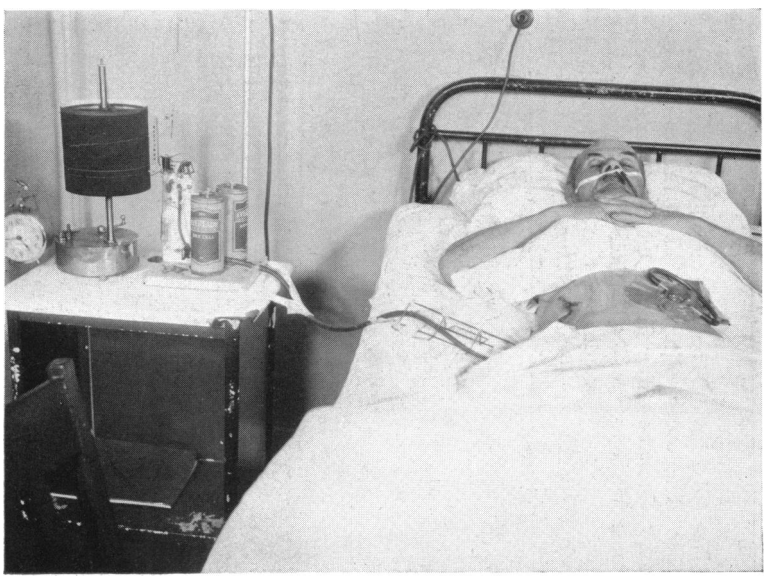
to note whether fluid could be collected. At this juncture a segment of the distal portion of the appendix was excised for purposes of histologic comparison with the segment removed as a control section at the time of operation. In a few instances leukocyte counts were made to determine whether increases of intraluminal pressure caused leukocytosis. No appendix was allowed to go on to perforation.

Before dismissal of the patient from the hospital, the appendix was snipped off at the level of the skin and granulations grew over its orifice and skin soon covered the site where the appendix had been eviscerated.

In a few instances in which the appendiceal stump continued to secrete fluid, extraperitoneal excision of the residual segment beneath skin level was made.*

* No patient in the series came to harm through any of these manipulative procedures incidental to exteriorization of the appendix.

Results.—The secretory activity of the obstructed appendicostomies is summarized in Table I. The cases have been grouped in the table with reference to the heights of secretory pressure attained. It is to be noted that the highest recorded pressure was 126 cm. of water, a level reached 22 hours after exteriorization and obstruction of the appendix in a man age 68. The next highest pressure recorded was 125 cm. of water, reached after 14 hours and 15 minutes in a man age 47. In a man, age 70, pressure of 92 cm. of water was reached 14 hours and 30 minutes after incannulation. The oldest patient in the series was age 75 (Case 20). No evidence of fluid secretion was noted. The appendix had a lumen but microscopic examination showed no evidence of mucosa. One patient in the series, R. A., Case 7 in the table, was age 29;



A

FIG. 2.—A. The patient and the manometric recording system for determining secretory pressure (Case 1, Table I).

G. L., Case 3, was age 33; the next youngest patient in the entire group was age 41. The average age for the group was 56.

No secretory pressure developed in three of the 22 exteriorized, obstructed appendixes. One of these was M. F., Case 20, age 75, referred to immediately above. In another, Case 22, G. B., age 53, whose cecum was exteriorized for polyposis, the blood supply of the appendix had been damaged in the manipulative maneuvers necessary to exteriorize the cecum and appendix and the negative result is essentially without significance. In the instance of a third patient, Case 21, A. C., age 61, the cannula had not entered the lumen and no secretory pressure was recorded. When the appendix was removed, however, exudate was found in the lumen.

In six other instances, however, a secretory pressure of less than 20 cm.

TABLE I

STUDIES OF SECRETORY CAPACITY OF OBSTRUCTED, EXTERIORIZED APPENDIXES IN MAN

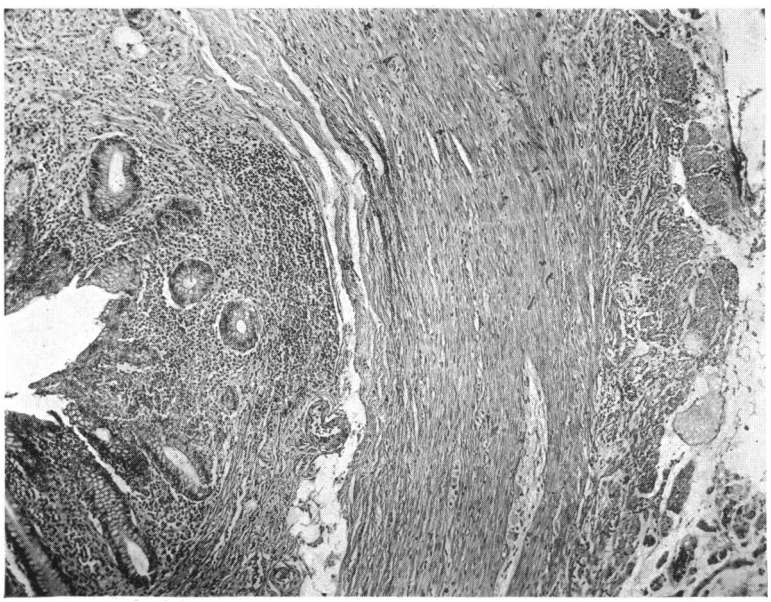
Case No.	Initials, Univ. Hosp. No. Sex and Age	Maximum Pressure (Cm. Water)	Time Required to Reach Maximum Pressure (Hrs.)	Duration of Time Maximal Pressure Was Sustained (Hrs.)	Total Fluid After End of Recording (Cc.)	Period of Fluid Collection (Days)	Lapse of Time Between Onset of Experiment and Removal of Appendix	Histologic Study	
								Control Section	After Pressure
(1)	T.W. No. 665959 M. 68	126	22	2¾	3.5	2	25 hrs.	Good mucosa	A.D.A.*
(2)	O.N. No. 662989 M. 47	125	14¼	½	12.5	6	3 days	Good mucosa	A.D.A. with necrosis
(3)	G.L. No. 660228 F. 33	114	35	14	3.25	5	50 hrs.	Good mucosa	A.D.A.
(4)	P.G. No. 661973 M. 70	92	14½	7½	1.5	2	48 hrs.	Good mucosa	A.D.A.
(5)	C.P. No. 663022 M. 56	90	16½	3	0.5	1	20 hrs.	Good mucosa	A.D.A. Loss of mucosa with fragmentation of muscle
(6)	U.T. No. 666978 M. 53	86	25½	0	?		Not removed	Good mucosa	No sections
(7)	R.A. No. 661380 M. 29	85	27	0	7.0	7	Not removed†	Good mucosa	
(8)	M.K. No. 667935 M. 54	60	3¼	5½	0.5	2	Not removed†	Good mucosa	No sections
(9)	W.P. No. 660521 M. 45	42	12	9	0	0	21 hrs.	No sections	Mild A.D.A. with exudate in lumen
(10)	F.H. No. 661415 F. 60	32	7	0	5.5	5	2 mos.	No sections	
(11)	P.S. No. 664561 M. 73	24	24	0	0	—	Not removed†	Atrophic mucosa at distal end	
(12)	W.H. No. 671573 M. 53	20	(See text—pressure not allowed to rise above 20 cm.)				Not removed	Good mucosa	
(13)	T.C. No. 666127 M. 66	20	24	0	0	2	Not removed	Much fat in submucosa	

(14) A.O. No. 665635 F. 53	17	20	0	7.2	8	Not removed	Fair mucosa with much lymphoid tissue	No sections
(15) E.B. No. 665350 M. 58	15	18	0	0	—	Not removed†	Atrophic mucosa with much fat	No sections
(16) W.B. No. 665646 M. 67	11	17	0	0	—	Not removed†	Atrophic mucosa with much fat	No sections
(17) A.B. No. 664251 F. 41	8	2	24	7.4	13	13 days	No mucosa in control	Serositis; few leukocytes in muscle layer
(18) J.S. No. 667657 M. 57	6	25	0	0	—	Not removed	No mucosa in control	No sections
(19) A.T. No. 662354 M. 62	5	1	18	1.1	4	Not removed†	No mucosa in control	No sections
(20) M.F. No. 663863 M. 75‡	0	—	—	0	—	26 hrs.	No mucosa in control	Mucus with leukocytes in lumen
(21) A.C. No. 653835 F. 61‡	0	—	6 days	0	—	6 days	No sections	No sections
(22) G.B. No. 661495 M. 53§	0			1.0	2	6 days	No sections	No sections

* A.D.A. abbreviation for acute diffuse appendicitis.
† Too short for removal.
‡ Short mesentery; appendix under tension when exteriorized.
§ Appendix devascularized during exteriorization.

of water was recorded. In one of these, Case 17, A. B., age 41, the appendix had no mucosa. In the five others (Cases 14, 15, 16, 18 and 19), the segment of obstructed, exteriorized appendix was so short that on removal of the cannula, no specimen could be removed for biopsy.

In nine instances, the highest secretory pressure exceeded 40 cm. of water; in seven of these the pressure was sustained above 85 cm. In four instances, pressures intermediate between 20 and 40 cm. of water attended obstruction of the exteriorized appendix. In one of these, Case 12, W. H., age 53, the pressure was not allowed to mount over 20 cm. of water. As soon as that level of pressure was reached, the recording lever was lowered to zero by re-

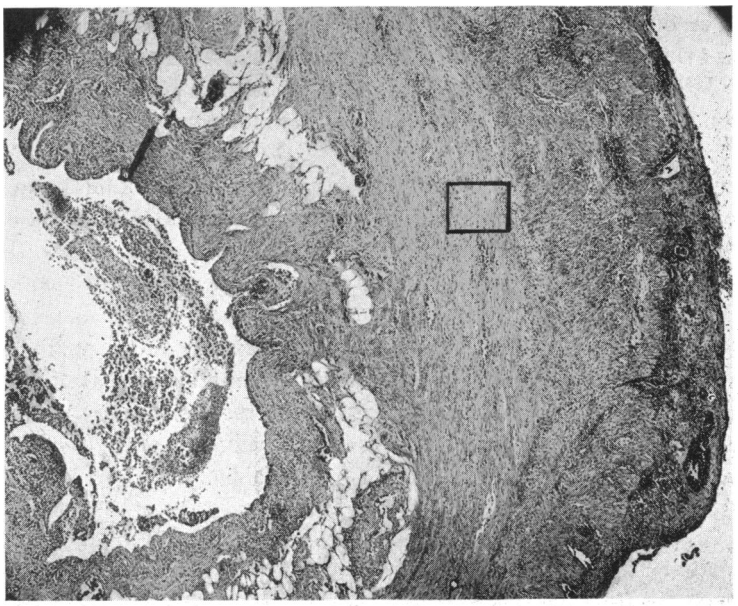


B

FIG. 2.—B. The control section—cut from the distal end of the appendix at the time the exteriorization was performed. (×60)

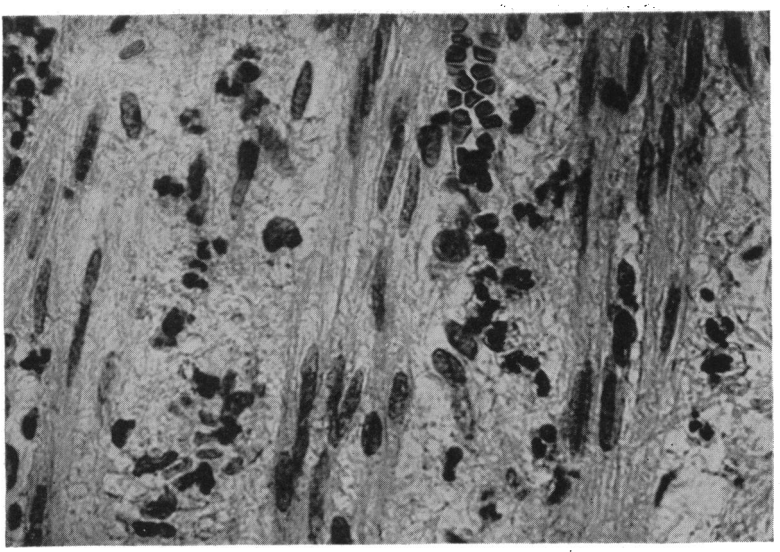
moval of fluid from the system by an aspirating syringe. On the first occasion, it took but 30 minutes for the level of 20 cm. of water pressure to be developed. After a wait of 20 minutes, it took 50 minutes to develop the same level of secretory pressure. After an interval of 24 hours, the level of 20 cm. pressure was reached in 18 minutes; on the third day it took 80 minutes and the same amount of time on the fourth day.

Discussion.—These data support the thesis that the vermiform appendix of man, when obstructed, will develop a secretory pressure in the majority of instances which will threaten the viability of the appendiceal wall. It is to be noted, however, that there are instances in which no evidence of secretory pressure attends luminal obstruction. Such appendixes undoubtedly would tolerate luminal obstruction without hazard to their owners. The instance of W. H., Case 12, suggests that luminal obstructions which are survived di-



C

FIG. 2.—C. After 25 hours of pressure. (×30) The square indicates the site from which D was taken. There is a diffuse cellular infiltrate with exudate in the lumen. The fat in the submucosa is also apparent.



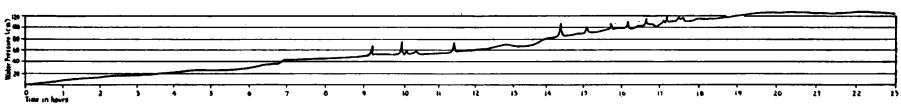
D

FIG. 2.—D. A free exudation of polymorphonuclear cells has occurred into the muscular layer. (×500) (The print has been turned to include visualization of a greater length of the muscle layer.)

minish the secretory capacity of the appendix. It is apparent, not alone from the small amount of fluid secreted by the normal appendix but by instances in which no evidence of fluid secretion was obtained, as well by the observations made on W. H., Case 12, cited above, that the balance between secretion and absorption, though weighted in the favor of the former, is poised on a somewhat narrow margin.

In the main, a fairly definite correlation was found to exist between normal microscopic appearance of the mucosa in the control section and the development of a high secretory pressure. This factor would appear to be the most significant item in determining whether an obstructed appendix will secrete fluid. Obliteration or connective tissue replacement of the luminal mucosa is certain to be correlated with a lack of secretory capacity in the vermiform appendix. The presence of fat in the submucosa, if the mucosa itself is normal, does not militate against the development of high secretory activity (Fig. 2C). An abundant lymphoid tissue, beneath an atrophic mucosal layer, does not assure rapid fluid production (A. O., Case 14, Table I).

Appendicostomy—with base tied
Closed System
Case of T. W.
(Case I, Table I)



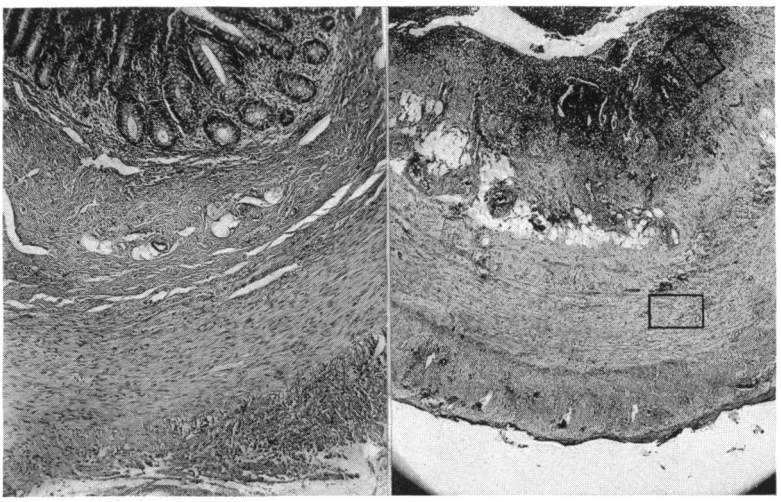
E

FIG. 2.—E. Retraced pressure record—the slope of the rising pressure is indicated. A pressure of 126 cm. water was reached 22 hours after obstruction.

It would appear, therefore, that the more normal the appendix, the more likely it is when obstructed to secrete fluid rapidly, pyramiding the intraluminal pressure with resultant anoxic effects upon the appendiceal wall. The disintegration of the wall of the appendix eventuating in perforation or gangrene is owing in part to the fluid transudation occasioned by the resistance of the high intraluminal tension and in part by cellular migrations into the wall as well as through bacterial invasion. A normal appendix which will withstand an intraluminal tension of approximately three atmospheres of pressure without rupturing, immediately after excision will perforate at very low values (20 to 70 cm. of water pressure) if it had been subjected to prolonged maintenance of sustained intraluminal pressures within the range of secretory pressures recorded in Table I. It is to be recalled that the luminal capacity of the normal appendix at atmospheric pressure is essentially zero, and that at 60 cm. of water pressure the usual luminal volume of the normal appendix is about 0.5 cc.[10]

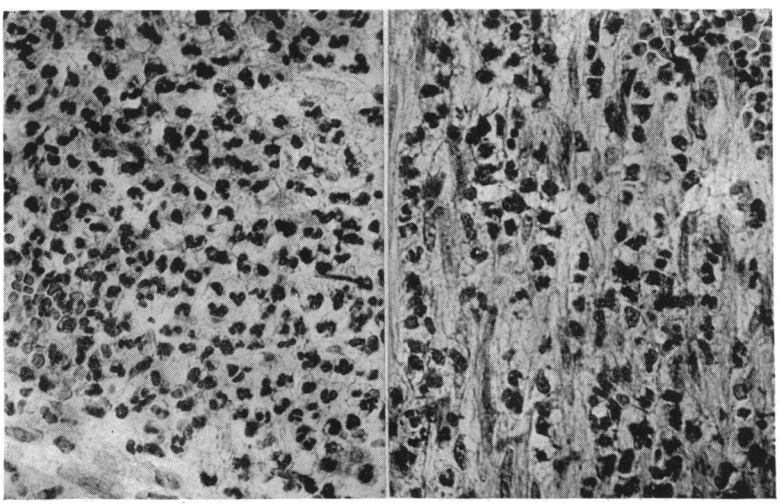
Whereas, in an earlier study,[10] the impression was lent on the basis of a study of the secretory behavior of the cecal appendage of the rabbit that catharsis accelerated fluid secretion, a more adequately detailed controlled study of this item suggests that neither fluid secretion nor perforation is hurried by purgation.[4] In the rabbit, obstruction of the cecal appendage will be followed

by perforation in 75 per cent of instances within 10 hours after ligature of the base. The administration of cathartics induces movements of the appendix



A B

FIG. 3.—Photomicrographs of Case 3, Table I. A pressure of 114 cm. of water was reached after 35 hours. (A) The control section removed at the time of obstruction and exteriorization of the appendix. (×65) (B) After 50 hours of sustained pressure. There is a diffuse cellular reaction throughout the wall—some exudate is present in the lumen (×65).



C D

FIG. 3.—(C) Higher magnification of the submucosa as shown in B. (×550) The exudation of polymorphonuclear cells into the submucosa is apparent. A few muscle cells may be seen in the lower portion of the section. (D) Higher magnification from lower square as shown in D. (×550) The section is turned on the side to permit inclusion of a greater portion of the muscle layer. Many polymorphonuclear cells may be seen scattered among the spindle-shaped muscle nuclei.

which preclude effectual sealing-off at the site of perforation by adjacent coils of intestine or other peritoneal surface.[4]

Histologic Study of Obstructed Appendixes.—It is to be conceded freely, that the vermiform appendix exteriorized upon the abdominal wall is not a properly controlled experiment for histologic observations. Every appendix exteriorized in this manner, whether or not it develops a high secretory pressure, exhibits evidence of thickening of the peritoneal tunic of the appendix (serositis). In two unobstructed, exteriorized appendixes, employed for purposes of control in which a catheter was left in the lumen, in one instance (case of C. S., age 65, U. H. No. 670933) for six weeks before excision of the specimen and in the other 12 days (case of B. N., age 33, U. H. No.

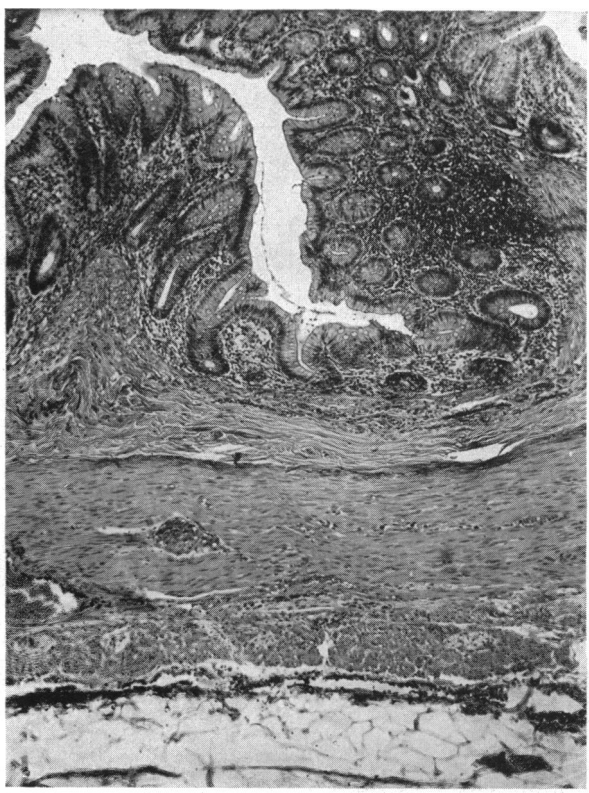


FIG. 4.—Section of a gibbon's obstructed appendix after 22 hours of incannulation. The highest pressure reached was 19 cm. of water—a pressure sustained for less than one hour. There is evidence of serositis. Otherwise the section is normal.

660885), the lumen and mucosa in each instance were normal. Both exhibited marked serosal thickening and cellular infiltration was apparent in the muscle layer.

Our best controlled observations were upon the obstructed appendixes[11] of apes. Here, it was possible to leave the obstructed appendix within the peritoneal cavity or at least well beneath the skin. In the chimpanzee, which develops with luminal obstruction a secretory pressure not unlike man or the rabbit, a diffuse cellular infiltration of all the walls attends obstruction. In

the gibbon, on the contrary, in which the highest pressure attained was 20 cm., and not long sustained, luminal obstruction was not attended by leukocytic invasion of the walls (Fig. 4). A mild serositis only attended the exteriorization.

As has already been related in the statement concerning the results of luminal obstruction of the vermiform appendix of man, the best determinant of whether an appendix will secrete fluid and develop the histologic picture of acute diffuse appendicitis consequent upon obstruction, is the presence of a normal mucosa. All instances in which high secretory pressures followed obstruction were attended by the histologic pictures of acute diffuse appendicitis. The histologic study of two of these (Cases 1 and 3, Table I) is shown in Figures 2 and 3. The details of the histologic findings are listed in Table I.

Dr. R. E. Buirge,[3] of this Clinic, has made cell counts of the exudate found within the lumen of appendixes exhibiting no demonstrable evidence of inflammation within its wall as well as upon the exudate within the lumina of appendixes exhibiting definite evidence of acute diffuse appendicitis. Similarly, he has made cell counts upon the exudate appearing in the lumina in a number of the patients in this series whose appendixes were obstructed and exteriorized. It is well known that cells are extruded constantly into the intestinal canal and the exfoliation of epithelial cells from the appendiceal mucosa as well as extrusion of white blood cells through the intact appendiceal mucosa is generally accepted as a constantly occurring phenomenon.[6, 7, 9]

Buirge observed that this exudate, which may be observed not uncommonly within the lumen of an appendix, the wall of which fails to exhibit evidence of inflammation, possesses regularly a predominantly lymphocytic character.[3] In a group of seven such cases in the appendixes of man, out of 100 cells within the lumen the average lymphocytic count was 90. In instances of spontaneously occurring appendicitis, on the contrary, a count of the luminal exudate showed invariably a definitely predominant polymorphonuclear leukocytosis. In a group of 13 such instances, the average polymorphonuclear count on the luminal exudate was 86 cells out of every 100 counted. Similarly in a group of six obstructed, exteriorized appendixes in which fluid secretion was active, the cell counts on the luminal exudate showed the average polymorphonuclear count to be 82 cells out of every 100 cells counted. It is apparent, therefore, that the same type of cellular response attends obstruction of the exteriorized appendix as is observed in instances of spontaneous appendicitis. The exudation of polymorphonuclear cells into the muscle layer in obstructed exteriorized appendixes is apparent in Figures 2 and 3.

Effect of Appendiceal Obstruction Upon Production of Pain, Fever and Leukocytosis.—In a number of instances, careful notations were made with reference to pain or discomfort attending obstruction of the exteriorized appendix. The presence or absence of pain in these cases was difficult to determine in most cases or was rendered actually inconsequential by the administration of opiates to relieve postoperative pain. In the main, it would appear that a colicky pain not unlike that observed in spontaneously occurring appen-

dicitis could be reproduced by luminal obstruction in those patients whose appendixes secreted fluid actively and developed a high secretion pressure. In Case 5, Table I, the details of which are listed below, it is apparent that the pain could be reproduced almost at will by elevating or lowering the intraluminal tension within the appendix. It is obvious, however, after a fairly high intraluminal pressure has been sustained for some time, that the occurrence of pain may be modified in proportion to the degree with which the circular muscle of the appendix resists distention.

Both fever and a polymorphonuclear leukocytosis were fairly constant accompaniments of the intraluminal pressure which attended obstruction of the exteriorized appendix. It is difficult, of course, to evaluate with exactness the temperature and leukocyte response to the performance of the colostomy.

Determination of how the factors of pain production, fever* and leukocytosis were influenced by obstruction of the appendix was made in a large number of the group. Observations noted at the time of the recording of the secretory pressures with reference to the occurrence of pain, fever and leukocytosis is indicated in a few of the actively secreting appendixes as listed below:

Case 1, Table I.—T. W., age 68. Obstruction and exteriorization of a rather long and free appendix. Insertion of cannula for recording pressure.

1 day prior to operation—W.B.C., 7,700; P.M.N., 62%.

At start of record—Temperature, 99.2° F.

After 4 hrs.—Temperature, 99.6° F.; pressure, 22 cm. water.

After 12 hrs.—Temperature, 99.8° F.; pressure, over 60 cm. water.
Waves occur with peaks every five to ten minutes (peaks up to 80 cm. water pressure).

After 14 hrs.—Pressue, 78 cm. water. Waves becoming smaller; W.B.C., 15,600; P.M.N., 82%.

16 hrs. after exteriorization—Pressure, 100 cm. water; temperature, 99.4° F. Appendix pale and distended, no serosal discharge; circulation present; no pain.

At 18 hrs.—Pressure, 115 cm. water. Waves smaller and peaks less high (up to 125 cm. water).

At 20 hrs.—Pressure, 125 cm. water; temperature, 100° F. Waves even smaller (see Fig. 2E).

At 22 hrs.—Pressure, 126 cm. water; W.B.C., 15,000; P.M.N., 89%.
Pressure recording stopped and pressure removed. The patient had denied pain earlier, but on removal of the pressure he stated that he was suddenly relieved of a dull aching pain in the right lower quadrant. This dull ache was not reproduced, however, by raising the pressure again.

38 hrs.—W.B.C., 13,000; P.M.N., 77%. There was a slight elevation of temperature for two days after release of pressure.

Ultimate Outcome.—Dismissed from hospital and returned later for posterior excision.

Case 2, Table I.—O. N., age 47. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

At 7 hrs. after start of record—Pressure, 80 cm. water with 4 cm. waves; temperature, 99.2° F.; W.B.C., 24,000; P.M.N., 86% (waves synchronous with pulse).

At 9 hrs.—Appendix looks tense. The larger vessels on the surface were engorged, but the areas between were blanched. Patient denied pain even to leading questions.

* All temperature determinations are rectal.

At 14 hrs.—Pressure, 125 cm. water with 2 cm. waves synchronous with pulse; W.B.C., 16,000; P.M.N., 86%. Appendix more blanched and there were fewer vessels holding blood. The volume of the appendix at this time was 1.25 cc. The temperature rose to a maximum of 101° F. at 21 hrs., then returned to normal in a few hours (Fig. 5).

Ultimate Outcome.—Carcinoma inoperable. Radon insertion.
Dismissed from hospital.

Case 3, Table I.—G. L., age 33. Obstruction and exteriorization of appendix followed by incannulation for recording pressure. Preliminary volume-elasticity determination showed a leak occurring between 80 and 120 cm. of water pressure (base not tied tight).

At 3 hrs.—Pressure, 22 cm. water; temperature, 99.6° F.

At 12 hrs.—Pressure rise ceased and pressure leveled off abruptly, presumably due to leakage into cecum or seepage; pressure 97 cm. water. Slight peristalsic waves every few minutes and also pulse waves.

At 15 hrs.—Pressure, 96 cm. water waves disappearing; temperature, 100° F.

At 18 hrs.—Pressure, 98 cm. water; W.B.C., 11,800. Patient has no complaints—occasionally questioning elicits confession of vague lower abdominal soreness "like a stomach ache."

At 19 hrs.—Pressure, 99 cm. water; temperature, 99.6° F. Pulse waves rise 1 to 1½ cm.

At 20 hrs.—Pressure, 101 cm. water. There are occasional peaks to about 120 cm. due to movements of the patient and followed by a gradual fall to a lower level as if some fluid had been lost.

At 23 hrs.—Pressure, 95 cm. water; temperature, 100.2° F.

At 26 hrs.—Pressure, 102 cm. water; W.B.C., 9,800; P.M.N., 89%.

At 27 hrs.—Pressure, 104 cm. water; temperature, 100.4° F.

At 28 hrs.—Pressure, 110 cm. water.

At 29 hrs.—Pressure, 106 cm. water. Lower abdominal discomfort.

At 30 hrs.—Pressure, 105 cm. water; W.B.C., 10,200; P.M.N., 86%.
Waves bigger. Appendix more blanched than earlier.
No necrosis evident.

At 42 hrs.—Pressure, 108 cm. water. Almost no waves now.
W.B.C., 8,300. There was a pressure peak lasting ten minutes after taking blood for W.B.C.

At 44 hrs.—Pressure, 96 cm. water; temperature, 100.8° F.

At 47 hrs.—Pressure, 100 cm. water; temperature, 101.2° F. Still vague abdominal aches.

At 49 hrs.—Pressure, 105 cm. water; W.B.C., 13,000; P.M.N., 94%.

At 49½ hrs.—Pressure released. No change in abdominal pain. Volume elasticity determination showed no demonstrable stretching of the lumen.
Still 0.17 cc. at 100 cm.

At 50¼ hrs.—Temperature, 98.6° F.

At 62 hrs.—Temperature, 100° F.; W.B.C., 7,200; P.M.N., 92%.

Ultimate Outcome.—Colostomy was performed for obstruction due to spread of cancer of cervix uteri.

Case 5, Table I.—C. P., age 56. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

After 16 hrs.—The pressure had risen to 90 cm. water with waves up to 95 to 130 cm. coming every 10 to 15 minutes, the high points being climaxed by a spike. Careful questioning of the patient showed that he had sharp severe pains coming just as the pressure commenced to rise for each of these peaks, reaching its climax about two-thirds of the way up to the peak and ceasing just as the pressure commenced to drop. This was right lower quadrant pain. Just as it

ceased each time (after lasting 20 to 30 seconds) the patient had a pain in the left side in the region of the Mikulicz exteriorization of the carcinoma. Slightly more severe and evidently of the same nature (Fig. 6).

Ultimate Outcome.—Bloch Mikulicz resection of carcinoma of sigmoid. Recovery.

Case 6, Table I.—U. T., age 53. Obstruction and exteriorization of appendix followed by incannulation for recording pressure. The mesentery was too short to allow stretching the organ out straight and it was, therefore, kinked on itself in and just above the muscle layers of the abdominal wall.

At start—volume-elasticity determination D.4 cc. at 120 cm. water pressure.

After 16½ to 18½ hrs.—Pressure rose from 19 to 72 cm. water in a few small and one large jump suggesting that at this point fluid passed the kink.

At 19½ hrs.—Pressure, 73 cm. water; temperature, 100.2° F.
Pulse waves visible from this point onward.

At 20½ hrs.—Pressure, 74 cm. water; W.B.C., 13,000; P.M.N., 82%.

At 23½ hrs.—Pressure, 85 cm. water; temperature, 102° F. No pain at any time.

At 25½ hrs.—Pressure, 86 cm. water; temperature, 101.6° F.; W.B.C., 15,000. Pressure released; no change in sensations resulted.

Volume-elasticity determination at end of pressure recording—0.13 cc. at 120 cm. of water pressure.

At 29 hrs.—W.B.C., 11,000; P.M.N., 76%.

At 32 hrs.—Temperature, 101.6° F.

At 36 hrs.—Temperature, 100.8° F.

At 40 hrs.—Temperature, 100° F.

Ultimate Outcome.—Failed to return for posterior excision of rectum.

Case 8, Table I.—M. K., age 54. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

Barium in lumen from 24 hrs. before start—W.B.C., 10,000.

After 6½ hrs.—W.B.C., 13,200.

At 8¾ hrs.—Pressure, 51 cm. water.

At 24 hrs.—Pressure, 45 cm. water.

At 25 hrs.—W.B.C., 12,800.

At 26 hrs.—Waves begin to appear. Peaks come every 20 mins. and there are sharper waves between. The basal level rose gradually to 56 by 30 hrs.

At 30 hrs.—Sudden drop in pressure to 26 cm. with loss of waves suggesting rupture. Temperature, 101° F. No leak, however.

At 32½ hrs.—Pressure, about 20 cm.; W.B.C., 8,600. Pressure released. The temperature returned to normal in a few hours thereafter.

Ultimate Outcome.—Resection of carcinoma of sigmoid colon. Recovery.

The Secretory Activity of the Obstructed Cecal Appendage in Animals.—*Rabbit.*—Two years ago, it was reported[10] that rupture of the rabbit's cecal appendage attended luminal obstruction quite regularly. In about 75 per cent of instances perforation occurs within 10 hours after ligature of the base. The highest secretory pressure that has been observed to date (136 cm. of water) followed luminal obstruction of the cecal appendage in the rabbit. A large number of observations have been made upon rabbits, and failure to secrete has not yet attended obstruction.[4] The character of the secretions may be modified, however, by regulating the pressure at which secretion occurs.[8]

Other Animals.—The secretory behavior of the cecal appendage of a large number of other animals has been investigated, including most of the domestic animals as well as fowl, carnivorous mammals, rodents and monkeys. No

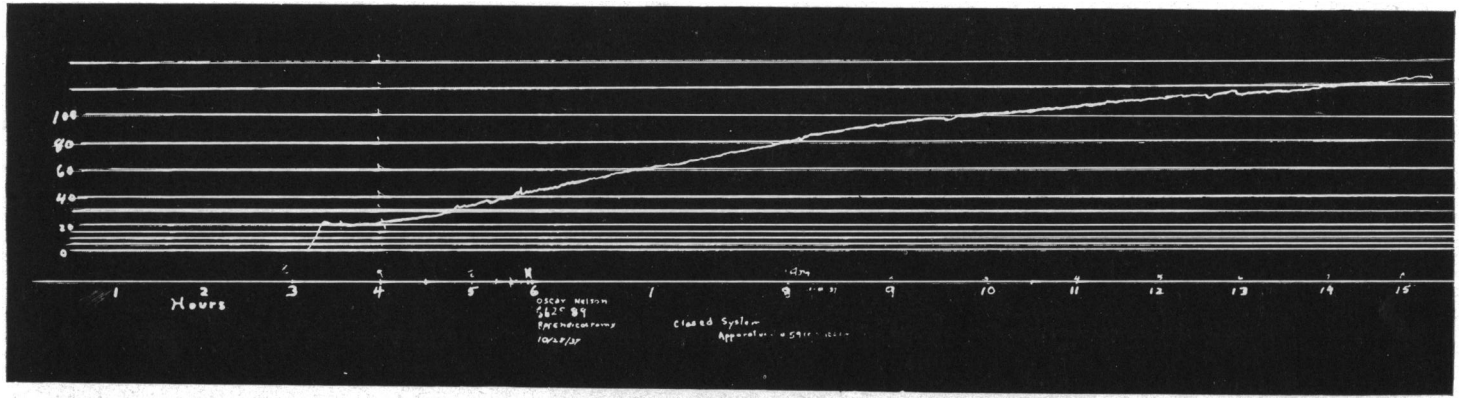
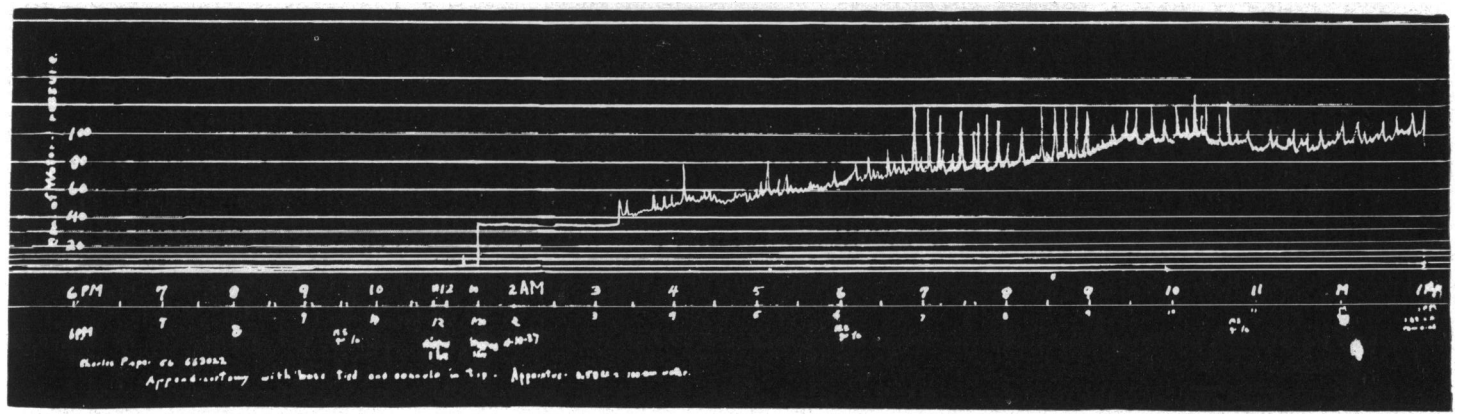


FIG. 5.—Pressure tracing of O.N., Case 2, Table I. A pressure of 125 cm. water was reached 14 hours and 15 minutes after obstruction.

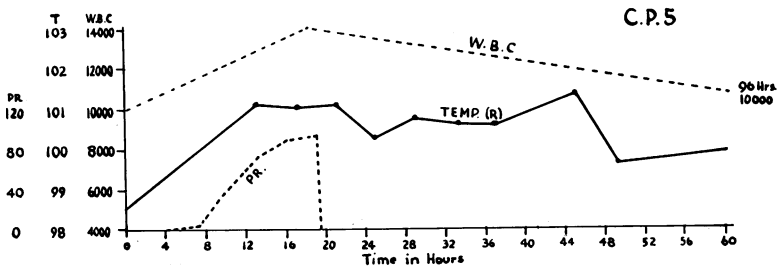


A

FIG. 6.—A. Pressure tracing of C. P., Case 5, Table I. A pressure of 90 cm. water was reached 16 hours and 30 minutes after obstruction.

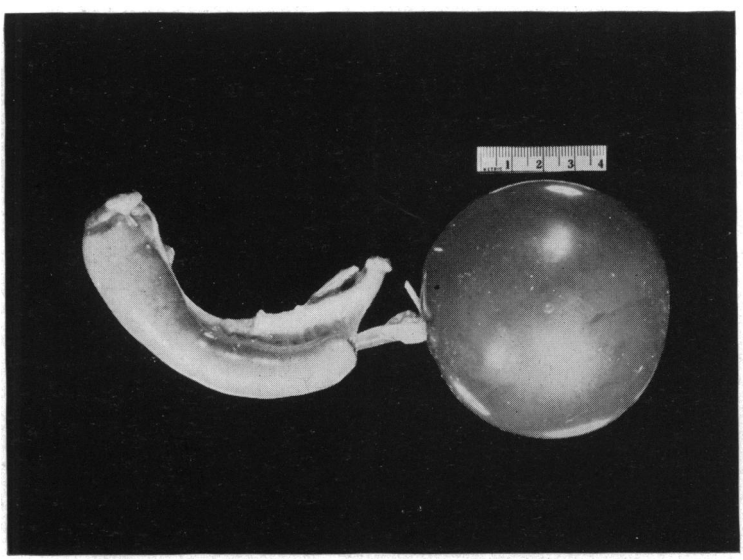
evidence of secretory activity in the obstructed cecal appendage was noted in any of these.[3]

Anthropoid Apes.—The secretory activity of the vermiform appendix has been studied in two species of anthropoid apes, the gibbon and chimpanzee.[11] The highest secretory pressure observed in two gibbons was 19 cm. of water and in neither instance was this maximal pressure sustained for long.



B

FIG. 6.—B. Chart indicating the leukocyte and temperature response incident to obstruction. (See details of case record No. 5.)



A

FIG. 7.—A. The obstructed cecal appendage of a rabbit from which fluid has been collected in a balloon. Two hundred cubic centimeters was collected in five days. The appendage is normal grossly and microscopically.

The vermiform appendix of the chimpanzee, on the contrary, exhibits a secretory pressure not unlike that of man and the rabbit. The highest pressure recorded in the obstructed appendixes of three chimpanzees was 106 cm. of water.

The Nature of the Fluid Secreted by the Obstructed Appendix.—Because of the small amount of fluid collectable from the obstructed vermiform

appendix of man, extensive observations on its nature have not been possible. The determinations made have been upon rather small quantities of fluid as is apparent from inspection of Table I. These would suggest that mineral salts such as calcium and phosphates may be present, as well as digestive enzymes. It is necessary, however, to rule out bacterial activity before concluding that digestive enzymes are present in the fluid.

Extensive observations have been made on the fluid secreted by the obstructed cecal appendage of the rabbit, however. About 20 cm. of fluid may be collected every six hours. Digestive enzymes are usually present in the fluid as it is collected in a small balloon within the rabbit's abdomen. After Berkefeld filtration to remove bacteria, however, no trace of proteolytic or other digestive enzymatic activity persists.[8]

B

FIG. 7.—B. Obstructed cecal appendage of a rabbit. Perforation occurred 5 hours and 18 minutes after recording was commenced, a pressure of 69 cm. water having been reached. Other areas of necrosis are apparent. This appendage showed evidence of diffuse cellular infiltration with areas of necrosis microscopically. (Reproduced from ANNALS OF SURGERY, 106, 927, 1937).

Is the Fluid a True Secretion or a Filtrate?—Whereas, no substance has been identified in the fluid which would stamp it definitely as a secretion of the mucosa of the appendix, there is every reason to believe that this fluid is secreted by the mucosa. First, fluid may be collected from the obstructed appendix at atmospheric pressure in both man and the rabbit (Fig. 7). Obstruction of the base of the cecal appendage in animals in which no secretory pressure develops is unattended by fluid secretion. Secondly, pressures attending obstruction of the appendix in man (126 cm. water or 92.6 Mm. mercury), chimpanzee (106 cm. water or 77.8 Mm. mercury) and the rabbit (136 cm. water or 100 Mm. mercury) have been observed to approach the systolic level of blood pressure. It has been remarked already that appendixes possessing an atrophic mucosa failed to exhibit evidence of fluid secretion (Table I). Observations made by Dr. C. J. Bellis,[1] in this clinic,

on the intraluminal pressures in spontaneously occurring appendicitis (obstructive) and the interstitial tissue pressures indicate that the intraluminal pressure distal to the obstruction, is higher in instances of acute appendicitis than is the interstitial pressure.

Clinical Significance of the Secretory Capacity of the Appendix.—The observations related above serve to emphasize the great importance of obstruction in the genesis of spontaneous appendicitis in man. The histologic picture of spontaneous diffuse appendicitis has been reproduced through the agency of obstruction alone. In the cecal appendage of the rabbit, all the varieties of appendicitis recognized by the pathologist from mere subserosal leukocytic invasion to gangrene or perforation may be produced by luminal obstruction.

That the rich lymphoid tissue of the vermiform appendix of man may play a rôle in initiating luminal obstruction in infections or other conditions which augment swelling in lymphoid tissue, is understandable. It would appear likely that this is the probable mechanism by which the lymphoid tissue of the appendix mediates its influence in causing appendicitis.

The usual causative agent in demonstrable obstruction of the appendiceal lumen is the fecalith.[2] How in turn it originates, still demands explanation.

It would appear necessary that the pathologist consider anew the obstructive concept of the origin of appendicitis. It is even more important that the clinician resurvey his concept of the early symptoms and findings of appendicitis. The dicta of Murphy; namely, pain, nausea and vomiting, abdominal tenderness, fever and leukocytosis, have been accepted almost universally as clinical desiderata of the disease. Appendicitis, however, is essentially a closed-loop obstruction in which the only early findings may be intermittent crampy pain and local tenderness. Elevation of temperature, quickening of the pulse and leukocytosis may not be in evidence until the anoxic effects of increased intraluminal pressure have set the infective characters of the disease in motion.[9] Finally, in order that the unwarranted mortality of the disease may be reduced more effectually, it would appear necessary to liberalize the indications for excision of the vermiform appendix. Appendicitis is probably still the most important of all surgical diseases. It ranks high as a cause of death and should be looked upon as a problem of the public health.[9]

CONCLUSIONS

The secretory activity of the vermiform appendix of man, possessing a normal mucosa, has been established. Such an appendix when obstructed and exteriorized may develop a secretory pressure approaching systolic blood pressure. The histologic picture of acute diffuse appendicitis has been produced in man by obstructing the exteriorized appendix. Appendixes having an atrophic mucosa fail to exhibit evidence of fluid secretion when obstructed. It appears likely that the chief inciting agency in bringing about appendicitis

in man is obstruction of an appendix in which the mucosa possesses the normal secretory capacity.

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