TABLE II.
Plasma Concentrations of D-Tubocurarine Found at Time of Rabbit Head-drop After Administration of D-Tubocurarine Chloride or Intocostrin.

	D-Tubocurarine chloride		Intocostrin	
Animal No.	Amt. inj. mg/kg	Plasma level at time of head drop mg/liter	Amt. inj. mg/kg	Plasma level at time of head drop mg/liter
5	.385	2.1	—	—
10	.264	2.2	—	—
6	.252	1.8	—	—
4	—	—	.408	1.6
3	—	—	.221	1.6
5	—	—	.333	1.5

methyl orange. The plasma level for paralysis in rabbits is about 1.5 to 2.2 mg per liter.

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Experimental Production of Sterile Closed Intestinal Loops. (17910)

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The purpose of this paper is (1) to report a method for the production of sterile closed intestinal loops, and (2) to report some subsequent observations upon these loops.

Methods. Several combinations of phthalylsulfathiazole and dihydrostreptomycin were used. However, the simplest and most reliable method consisted of the following. Healthy adult dogs were given, prior to surgery, 6.0 g of phthalylsulfathiazole each 12 hours for 3 days and 0.5 g of dihydrostreptomycin each 12 hours for 2 days before surgery. The animal was fasted for 24 hours and anaesthesized with pentobarbital and ether. All operative procedures were performed with strict aseptic technic. The ligatures and sutures were 000 silk. The abdomen was entered through a midline incision beginning at the xyphoid process and extending inferiorly for 4 inches. Both jejunal and ileal closed loops were made. The segment of either jejunum or ileum was chosen with a good blood supply that would not be embarrassed when brought through the abdominal wall and transplanted subcutaneously. Therefore the length of the loop and its distance from either the ligament of Treitz or the ileocecal valve varied in different dogs; the details are listed in Table I. Having determined the level of the loop and its length, the gut was transected in two places between hemostats. The loop was brought up through the abdominal incision, the continuity of the bowel reestablished by the aseptic anastomosis technic, and the linea alba was closed in a manner which would not interfere with the mesenteric pedicle supplying blood to the loop. The clamps were removed from the ends of the loop, and the loop irrigated five times with 200 cc of 1:1000 aqueous zephiran chloride followed by similar irrigations with sterile water. The ends of the loop were next closed by inverting with a purse string suture followed by interrupted inverting sutures. The closed loop was transplanted subcutaneously by undermining the adjacent skin edges. The skin was then closed by a running suture. Seven

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TABLE I.
Level of the Closed Loop, Its Length, and Time of Culture.

Dog No.	Distance from ligament of Treitz, inches	Length of loop, inches	Culture days post operative
	A. Jejunal closed loops		
81	13	9	7th day negative
84	25	14	10th " "
87	21	12	2nd day positive-*B. coli* 80 colonies per cc
90	26	7	13th day negative 27th " "
91	20	9	13th " "
135	15	13	21st " "
136	15	10	21st " "
	B. Ileal closed loops		
Dog No.	Distance from ileo-cecal valve, inches	Length of loop, inches	Culture days post operative
94	16	9	8th day negative 14th " " 53rd " "
157	18	11	19th " " 24th " "
114	19	20	8th day positive for *Clostridium welchi* and *B. proteus*

dogs with closed jejunal and 3 dogs with closed ileal loops were prepared. The loops were aspirated almost every day with a sterile needle and syringe. The secretions of the closed loops were cultured for both aerobic and anaerobic organisms by Dr. Ernest Witebsky of the Department of Bacteriology. The anaerobic cultures were observed for 5 days before giving a negative report.

Eight additional dogs with either a jejunal or ileal loop were prepared in a similar manner except that the ends of the loop were not closed but were introduced from their subcutaneous pocket into the peritoneal cavity through a rectus stab wound. The serosa around the periphery of the opening into the lumen was sutured to the peritoneum. A Crosby-Cooney button was inserted into the lumen of the loop and anchored with sutures to the peritoneum. This kept the peritoneum from closing over the lumen of the loop. Such a loop had free drainage into the peritoneal cavity. The animals were sacrificed from 2 weeks to 6 months later. The loop was examined histologically by fixing the tissue in 10% formaldehyde and staining with hematoxylin-eosin.

Results and observations. There were two failures to produce a sterile closed loop in the 10 dogs. The level of the loop, its length, and time of culture are listed in Table I.

The secretions aspirated from the closed loops were at first blood tinged but between the fourth and seventh day, clearing had usually taken place. The quantity of fluid aspirated daily usually varied from 50 to 75 cc for the first week. By the time the animal was taking a normal diet, the secretions increased to from 150 to 200 cc per day. However, with time secretions became less. This was particularly striking in dog No. 94 who in approximately 6 weeks was secreting only a few cubic centimeters of almost pure mucus. Two months after the closed loop had been made, 100 cc of 5% glucose in 0.9% NaCl was injected into the lumen. On the following morning fluid could not be reaspirated. A similar amount of 5% amigen was also absorbed. If 1% methylene blue was injected into the lumen it would appear in the urine. Peristalsis was always easily visible beneath the skin.

If the loop was not aspirated and allowed to distend, loss of appetite usually occurred. Appetite was rapidly regained if either the loop was aspirated or it ruptured.

The total protein content of the secretions of loop varied from 0.2 to 1.7 g %, and the

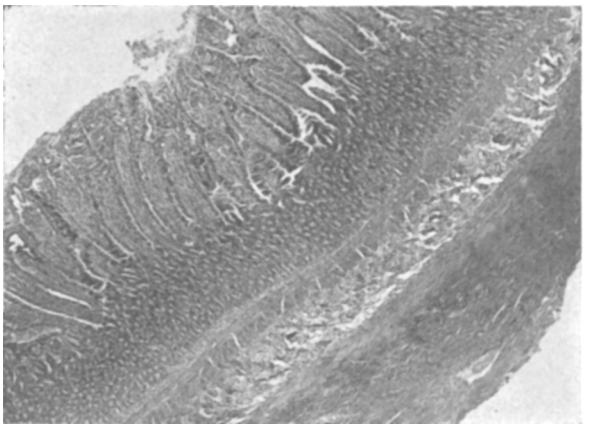

FIG. 1.
Dog No. 90. Cross section of intestine 88 days after closure. There is a normal mucosa and lack of inflammatory changes. 30 ×.

chloride content varied from 492 to 561 mg %.

In the 8 dogs in which the loop had free drainage into the peritoneal cavity there were no deaths, and no evidence of peritonitis when sacrificed up to 6 months after operation.

Discussion. As far as we know primary closed sterile loops have not been produced before, Dragstedt(1) however did sterilize loops by prolonged drainage into the abdominal cavity; such loops could be secondarily converted into closed sterile loops without untoward symptoms. Dragstedt(2) was unable to produce sterile loops by mechanical washing with the usual antiseptics and caustics. This was confirmed by studies of Wangensteen and Waldron(3). The fact that no deaths occurred in the series of animals in which one end drained into the peritoneal cavity we believe is significant. In Dragstedt's series of animals there was a 50% mortality when the gut was mechanically washed with the usual antiseptics followed by ether. The drainage of intestinal secretions into the peritoneal cavity for as long as 6 months had no untoward effect on the animal. It is not surprising that as time went on absorption from the loop exceeded secretions. It is well known that Thirry-Vella loops and gastric pouches secrete less after prolonged drainage. Clinically, we know that in iliostomies and colostomies, absorption gradually exceeds secretions. The reason for this is not well explained in the literature. Even though secretion became minimal in these loops it was significant to find absorption preserved several months after the loops had been made.

The animal with a closed sterile loop, at no time, showed signs of "toxemia" as has been described many times. Even when the intra-luminal pressure was allowed to increase sufficiently to cause rupture the "toxemia" syndrome was not observed.

Histological examination of each loop did not reveal abnormal findings. The mucosa and villi were intact and well preserved. There was no evidence of inflammation within the wall of the loop.

We believe from the evidence presented that closed sterile intestinal loops lend themselves to various physiologic or pharmacologic investigation. The length of time a loop will remain sterile is dependent upon aseptic aspiration.

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Summary. 1. A method is presented for the preparation of sterile closed intestinal loops. 2. The animal does not show signs of toxemia. 3. Evidence is offered that absorption continues in the sterile loop.

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Utilization of the Labile Factor During Normal and Abnormal Coagulation of Blood.* (17911)

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The study of the extent of utilization of the different factors known to be necessary for the formation of thrombin is a fruitful technic of investigation of the clotting process. Thus, in the hands of Quick and associates, the quantitative determination of the consumption of prothrombin has given conclusive evidence of the existence of a preliminary phase in the coagulation of blood, namely the formation of thromboplastin from an inactive plasmatic precursor through the action of a platelet factor(1). It has also helped to identify the mechanism of the coagulation defect in hemophilia and thrombocytopenic purpura(1,2). The factors taking part in the formation of thrombin are not totally utilized during coagulation. Examination of the serum by one-stage technics, after the thrombin formed has been neutralized by the natural antithrombin, reveals the presence of at least 3 proteins active in promoting the coagulation of blood: (a) unconverted prothrombin; (b) unconverted labile factor (factor V, plasma Ac globulin); and (c) a new agent, capable of accelerating the conversion of prothrombin to thrombin (serum Ac globulin, factor VI, spca, etc.). The concentration of these 3 factors varies according to the normality or abnormality of the coagulation process.

The present paper introduces data on the utilization of the labile factor during coagulation in healthy subjects and in patients with different disorders of the clotting mechanism. The relationship of the utilization of the labile factor to the consumption of prothrombin and to the development of the accelerator in serum has also been investigated, since previous findings have suggested that the accelerator may derive from the labile factor through the action of thrombin(3).

Materials and methods. A 20-gauge needle on a glass syringe was neatly inserted into a vein and a few ml of blood were drawn. The glass syringe was then exchanged for a second one coated with Silicone and chilled in ice prior to use. Four ml of blood, apparently uncontaminated with tissue thromboplastin, were collected and divided into 2 samples of 2 ml each. The first was decalcified by the addition of 1/10 volume of sodium oxalate 0.1 M and the second allowed to clot in a glass test tube in a water bath at 37°C. Plasma was obtained from the first sample by centrifugation at 1,500 r.p.m. for 5 minutes and its labile factor activity determined by the method of Quick and Stefanini(4) as described by Stefanini(5). This consists essentially in determining the ability of the plasma under observation to reduce towards normal values the

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