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THE EFFECT OF PERITONEAL IRRITATION ON THE ACTIVITY OF THE INTESTINE

BY

D. M. DOUGLAS, M.S., Ch.M., F.R.C.S.

Late Commonwealth Fellow in Surgery on assignment in the Mayo Foundation; First Assistant in Surgery, British Postgraduate Medical School

AND

F. C. MANN, M.D.

Director of the Institute of Experimental Medicine, the Mayo Foundation

The management of abdominal distension occurring in the course of diffuse peritonitis is still a major surgical problem. Two principal views are widely held concerning the pathogenesis of the condition, the one contending that the distension is the result of multiple adhesive obstructions in the intestine, and the other that the activity of the intestine is reflexly inhibited by reason of the peritoneal irritation. The views might reasonably be termed respectively "mechanical" and "neurogenic." These two concepts are of more than academic interest, since the mode of treatment, operative or conservative, is influenced by the view held by the individual surgeon. There are, of course, cases in which the obstructive element is quite obvious. The patient who is suffering from painful attacks of colic and in whom peristalsis is audible often even without the use of a stethoscope is evidently not suffering from inhibition of intestinal activity. But it must be confessed that such cases are less common than those in which little evidence of intestinal activity can be detected.

The purpose of this paper is to present some observations on the effect of peritoneal irritation on the activity of the intestine. It is apparent that, in order to study reflex phenomena adequately, it is necessary in some way to separate the receptor and the effector elements in the hypothetical reflex arc. In other words, if equivocal results are to be avoided the adequate stimulus must be delivered at a site remote from that in which the reflex effect is to be studied. It was by the application of this principle that Pavlov was enabled to study the various phases of gastric secretion. The pouch which bears his name was so devised that he could collect samples of gastric juice from a portion of the stomach which, while retaining its nerve supply, was completely cut off from the adequate stimulus, which was the entry of food into the remainder of the stomach.

We endeavoured to find a method whereby this principle could be applied to the study of paralytic ileus; in other words, we wished to devise a preparation which would permit of the production of diffuse peritoneal irritation without at the same time producing local peritonitis of the intestine in which the reflex effect of the peritoneal irritation was to be expected. We believed that any effect which might be observed could, if time relations were compatible, be reasonably regarded as reflex in

character, and would be a suitable phenomenon for the study of mediation of inhibition in the intestine in response to peritoneal irritation.

A complete review of the literature which has accumulated, particularly on the clinical side of this field, would be outside the scope of a communication of this type. Accordingly, it is proposed to refer only to the more important papers in the experimental field on which the neurogenic concept of paralytic ileus is based. Van Braam Houckgeest in 1872 made the observation that abdominal section and exposure of the intestines had an inhibitory effect on intestinal activity. It was not till 1899 that Bayliss and Starling found that this inhibition could be overcome after a short latent period by section of the splanchnic nerves. Cannon and Murphy (1907) showed that a similar type of intestinal inhibition could be caused in cats by local trauma to the intestines or reflexly by trauma to the testes, and, similarly, that this inhibition could be prevented by previous splanchnicotomy. In the rabbit, Melzer and Auer (1907) and Hotz (1909) demonstrated that certain inhibitory intestinal reflexes could be prevented by destruction of the cord to the third dorsal segment or by splanchnic section. Arai (1921) observed intestinal inhibition in cats after the intraperitoneal injection of irritant solutions, and King (1924) demonstrated similar inhibition in dogs from stimulation of bladder, rectum, peritoneum, and various skin areas. Olivecrona (1926-7) concluded that, in the cat, local reflexes mediated by way of the coeliac ganglia were capable of causing intestinal inhibition. Markowitz and Campbell (1927) and Ochsner, Gage, and Cutting (1928) showed that the inhibition of peritonitis in dogs could be prevented by spinal or splanchnic anaesthesia. Alvarez and Hosoi (1929) suggested that in the ileus of peritonitis a flattening of the normal gradient of forces occurred. Demel (1926) reported that atony of the bowel of the dog could be produced by retroperitoneal injection of blood. The recent work of Youmans, Herrin, and Meek (1938) suggests that distension of one part of the intestine causes inhibition of other parts.

Experimental Methods

Three main problems confronted us at the outset of this study. The first has already been referred to—namely, the devising of a suitable preparation. The second was the difficulty of finding a standard by which

inhibition of intestinal activity could be judged; the third was the choice of a method for the production of peritoneal irritation.

The first problem was solved by means of the preparation described by Biebl (1930) for the collection of samples of intestinal contents and used later by Castleton (1934) and Wangenstein (1937). It consists of an exteriorized loop of intestine, in continuity, with extrinsic nerve and blood supply intact, enclosed in a bipediced tube of skin exactly similar to that used in plastic surgery (Fig. 1). The parietal and visceral peritoneum at the

FIG. 1.—Types of exteriorized loops of intestine enclosed in bipediced skin tubes. A: In continuity as used in the present study. B: Short-circuited. C: Isolated—analogue to the Thiry-Vella loop.

exit and entrance of the loop from the peritoneal cavity become firmly adherent to each other and so effectively seal off the whole loop from the peritoneal cavity, while the lumen of the bowel, exactly comparable to a colostomy loop before opening, remains patent. By virtue of the exteriorized position of the loop and of the effective sealing off of its visceral peritoneal surface from the general peritoneal cavity it is possible to set up an inflammatory process within the latter without in any way directly affecting the former. The operative procedure involved in the preparation of these loops is simple, the operative mortality is low, and the animals can be observed in good health for many months. The advantages and disadvantages of the preparation have been discussed in a previous communication (Douglas and Mann, 1939). For the present purpose the advantages appeared to outweigh the disadvantages.

As to the second problem, it requires only a cursory glance at the literature to realize that no accurate con-

cept exists as to what constitutes inhibition of intestinal activity. One of the main causes of this confusion appears to lie in the fact that a great diversity of methods have been used to study intestinal activity. Thus workers with an intraluminal technique naturally tend to regard inhibition in terms of tonus; workers using enterographic methods lay stress on diminution of amplitude and rate of contraction; and those using radiographic technique speak in terms of the progress of food residues. Since coincident with a fall in tonus there may be an increase in the amplitude and rate of contraction, and vice versa, it is easy to see how conflicting results may arise. In order to avoid confusion of this type the term "inhibition of intestinal activity" in the present study has been taken to mean absolute quiescence of the intestine—that is, where neither by the recording technique nor visually could any movement whatever be observed. Inhibition was considered to have come to an end when the first contraction, however small, reappeared. Thus it was possible with some degree of accuracy to measure quantitatively the duration of inhibition.

In the production of peritoneal irritation the intraperitoneal injection of irritant solutions was adopted for the following reasons: (1) the technique of intraperitoneal injection is a well-standardized procedure, simple of execution, requiring no anaesthesia, and without detrimental effect on the animal; (2) the method has been used extensively in studies of this nature, and the injection of a known quantity of irritant solution is in some respects quantitative and is easily controlled by the injection of bland non-irritant solutions; (3) the injection is in the nature of a sudden peritoneal insult analogous to the perforation of a hollow viscus, and is therefore well suited to the present study; (4) finally, recovery from the small quantities of irritant solution used was rapid and uneventful.

In view of the species differences which are said to exist with respect to intestinal activity it was thought wise to study two types of animals. The rabbit and the dog were therefore used, and, in order to have data on the small and large intestine, loops were prepared from the caecum of the rabbit and the ileum of the dog. Records of intestinal activity were taken in the rabbit by an enterographic method and in the dog by a double-tambour air-displacement system (Fig. 2).

Procedure of the Experiments.—The same technique was used throughout. The animal was fed before the experiment to ensure maximum activity of the intestine. It was then placed on an observation table, upon which it had been previously trained to lie. A 20-gauge needle was inserted into the peritoneal cavity and a length of rubber tubing attached to it, secured to the abdominal wall by adhesive tape. A control tracing of intestinal activity was then taken for a period of fifteen minutes. A measured quantity of Ringer-Locke's solution at 39° C. was now injected into the peritoneal cavity and the tracing was continued for thirty minutes. A similar quantity of irritant solution at 39° C. was then injected and the tracing was continued for a period of two to three hours. Since the tracing was taken continuously throughout the whole of the experiment it was possible to record the reaction of the exteriorized loop of intestine to the intraperitoneal irritative process. In no instance did the injection of Ringer-Locke solution have any effect on the intestinal activity.

Preparations.—Experiments were carried out in the following preparations: (1) the normal animal; (2) the animal with bilateral splanchnic section; (3) the animal with bilateral vagal section; (4) the animal with unilateral splanchnic section; (5) the animal with bilateral adrenal-

ectomy. The splanchnic nerves were severed through a lumbar approach, the vagi through a thoracic approach immediately above the oesophageal hiatus in the diaphragm. No experiments were carried out after the nerve sections until a period of at least three weeks had elapsed. This was to allow of degenerative processes in the synaptic connexions which these nerves make in the myenteric plexus. The adrenalectomized animal was given a daily maintenance dose of adrenal cortical extract and a diet

FIG. 2.—Simple air-displacement system. The receiving tambour is attached to the intestinal loop by an inelastic aluminium clip.

low in potassium. Both the animals with nerve sections and the adrenalectomized animal maintained good health and, so far as could be judged by bowel habits and tracings of intestinal activity, showed no deviation from the normal in respect of the alimentary canal. This is in accordance with the findings of other observers.

Results

THE RABBIT

The Normal Rabbit.—Eleven experiments were carried out in the normal rabbit. In all of them immediate and prolonged inhibition of the movements of the loop was observed in response to the intraperitoneal injection of a small amount of irritant solution (Table I). The nature of the irritant solution did not appear to be of importance, since sodium ricinoleate solution, turpentine emulsion, and Lugol's iodine solution produced a similar result.

TABLE I.—Effect of Intraperitoneal Injection of Irritant Solution on the Activity of the Intestine of the Rabbit

Animal	Irritant	Quantity in c.cm.	Dilution	Inhibition	Duration in Mins.
Normal Rabbit :					
1	Sodium ricinoleate	5	1 : 50	+	120
2	Lugol's solution	3	1 : 10	+	35
3	Turpentine	2	1 : 20	+	108
4	Lugol's solution	2	1 : 10	+	30
5	"	2	1 : 10	+	48
6	"	3	1 : 10	+	47
7	"	3	1 : 10	+	62
8	"	2	1 : 10	+	40
9	"	2	1 : 10	+	32
10	"	3	1 : 10	+	45
11	"	2	1 : 10	+	33
Splanchnicotomized Rabbit :					
12	Lugol's solution	3	1 : 10	Nil	
13	"	3	1 : 10	"	
14	"	3	1 : 10	"	
15	"	3	1 : 10	"	
16	"	3	1 : 10	"	

The Splanchnicotomized Rabbit.—Five experiments were performed in the rabbits which had had both splanchnic nerves previously sectioned. Although these animals showed a similar systemic response to the injection of the irritant, in no case was inhibition of movements of the extraperitoneal loop observed (Table I).

THE DOG

The Normal Dog.—Five experiments were carried out in the normal dog. As in the normal rabbit, immediate and prolonged inhibition of activity in the extraperitoneal loop was observed (Table II and Fig. 3).

TABLE II.—Effect of Intraperitoneal Injection of Irritant Solution (Lugol's Iodine) on the Activity of the Intestine of the Dog

Animal	Quantity in c.cm.	Dilution	Inhibition	Duration in Mins.
Normal Dog :				
1	4	1 : 2	+	75
2	3	Undiluted	+	240
3	4	1 : 3	+	54
4	4	1 : 3	+	53
5	4	1 : 3	+	94
Splanchnicotomized Dog :				
6	4	1 : 2	+	1
7	4	1 : 2	Nil	0.25
8	4	1 : 2	+	(15 sec.)
Vagotomized Dog :				
9	2	1 : 3	+	75
9	3	1 : 2	+	64
Unilaterally Splanchnicotomized Dog :				
10	4	1 : 4	+	81
10	3	1 : 4	+	72
Adrenalectomized Dog :				
11	4	1 : 2	+	32
11	4	1 : 2	+	32
11	4	1 : 2	+	24

The Splanchnicotomized Dog.—Three experiments were carried out in the animals with bilateral splanchnic section (Table II). In one experiment no inhibition was noted in response to the intraperitoneal injection of the irritant solution; in the two others transitory delayed inhibition was noted (Fig. 3). The same experimental manœuvre produced in the normal dog immediate and prolonged inhibition.

The Vagotomized Dog.—Two experiments were carried out in the vagotomized dog. Prolonged inhibition of intestinal activity was observed in both (Table II). The reaction was similar to that seen in the normal dog (Fig. 3).

The Unilaterally Splanchnicotomized Dog.—Two experiments were carried out in the unilaterally splanchnicotomized dog. As in the normal dog and the vagotomized dog, prolonged inhibition of activity in the extraperitoneal loop occurred (Table II and Fig. 4).

The Adrenalectomized Dog.—Three experiments were carried out in the dog which had had both adrenal glands removed three weeks before. In all three experiments

nature of the irritant solution, and no arrest was observed when a non-irritating solution such as Ringer-Locke was used. A direct effect on the bowel could be excluded because of the extraperitoneal situation of the bowel under study.

The experiments after bilateral vagal section indicate that the vagus nerves play little part in mediating the inhibition either as afferents or efferents, since the inhibi-

FIG. 3.—Effect of intraperitoneal injection of irritant solution on the activity of the intestine. At arrow, standard quantity of solution injected into peritoneal cavity. Large numbers indicate minutes. Time in 5-second intervals. A: Normal dog. B: Dog with bilateral splanchnic section. C: Dog with bilateral vagal section.

FIG. 4.—Effect of intraperitoneal injection of irritant solution on the activity of the intestine. At arrow, standard quantity of solution injected into the peritoneal cavity. Large numbers indicate minutes. Time in 5-second intervals. A: Dog with unilateral splanchnic section. B: Dog with bilateral adrenalectomy. C: Effect of intravenous injection of 0.25 c.cm. of adrenaline on the activity of the intestine.

a result similar to that seen in the normal dog was noted—namely, immediate and prolonged inhibition of intestinal activity (Table II and Fig. 4).

Comment

The arrest of intestinal activity consequent on the injection of irritant solutions into the peritoneal cavity noted in this study is in all likelihood true reflex inhibition, since no drugs were used, there was no handling of the bowel, and no foreign bodies were introduced into the bowel. Moreover, the arrest occurred irrespective of the

tion is similar to that seen in the normal animal. Similarly, the observations after unilateral splanchnic section indicate that the absence of the splanchnic nerves on one side alone does not prevent the mediation of the inhibition. The experiments after bilateral splanchnicotomy, on the other hand, indicate that the inhibitory process is mediated through the splanchnic nerves, since either no inhibition occurred or, as in two experiments, it was momentary.

It is well known that adrenaline causes inhibition of intestinal activity (Fig. 4). It was with this consideration

in mind that experiments were carried out in the adrenalectomized animal. The inhibition seen in the adrenalectomized animal was similar to that in the normal animal, though of shorter duration. It may be that part of the inhibition observed in the normal animal is mediated by the adrenal medullary principle and that the transient inhibition seen in two experiments in the splanchnicotomized animal was similarly effected.

Olivecrona (1926-7) attempted to draw a distinction between rhythmic and peristaltic activity in respect to their response to peritoneal irritation, indicating that the latter type is very readily inhibited whilst the former persists. An analysis of this type is extremely difficult under reasonably normal experimental conditions, and it was therefore purposely avoided in this study. Since, however, we took absolute quiescence as the criterion of intestinal inhibition the problem did not arise.

We are well aware of the danger of applying experimental observations to clinical problems. Nevertheless it seems of considerable interest that an irritative process within the peritoneal cavity is capable of bringing about a prolonged arrest of activity in intestine which is entirely remote from the peritonitis. We take this as reasonable evidence that the neurogenic or reflex concept of distension in diffuse peritonitis is not the chimera which many authors suggest, particularly when so many cases recover without operative intervention. To enter into a discussion on the virtues of the various lines of treatment would be outside the scope of a paper of this kind, but it is permissible to suggest that enterostomy or entero-anastomosis is not likely to meet with success in cases in which the activity of the intestine is inhibited. We would therefore plead that, in the absence of obvious intestinal activity, there are good grounds for the adoption of conservative measures in the treatment of the distension of peritonitis. Measures calculated to overcome splanchnic inhibition such as splanchnic block or the use of acetylcholine protectives such as prostigmin would appear to be rational therapy.

Summary

1. Extraperitoneal loops of bowel in continuity were prepared in the rabbit and dog. A loop of the caecum was chosen in the former, of the small bowel in the latter.
2. Peritoneal irritation produced by intraperitoneal injections of a standard irritant solution was constantly associated with prolonged arrest of movements in the extraperitoneal loop in the trained animal.
3. The arrest of intestinal movements occurred after degenerative section of both vagus nerves, of one splanchnic nerve, and after bilateral adrenalectomy.
4. After degenerative section of both splanchnic nerves the arrest did not occur or was only temporary.
5. The arrest is in the nature of reflex inhibition, because by reason of the extraperitoneal situation of the loop of bowel the stimulus is delivered to afferents other than those in the loop.
6. The anatomical pathway of the reflex arc is not fully determined.

(a) The receptor endings are in the peritoneal cavity, but whether in parietal or visceral peritoneum or both is unknown. Cannon and Alvarez have each found evidence for visceral receptors; Hotz and King have found evidence for parietal receptors.

(b) The afferent limb of the arc is similarly unknown. Cerebrospinal afferents from the parietal peritoneum are almost certainly involved.

(c) The connector element is made up of the preganglionic neurones of the thoracic outflow which constitute the splanchnic nerves.

(d) The efferent limb of the arc is made up of the post-ganglionic sympathetic neurones issuing from the coeliac plexus.

(e) The effector endings are in the extraperitoneal loop of the bowel.

7. In the normal animal it is possible that part of the duration of the inhibition may be mediated by adrenaline, and that in the animal with bilateral degenerative section of the major splanchnic nerves the transitory inhibition noted was similarly mediated.

The findings are taken to indicate that prolonged intestinal inhibition may result reflexly from irritation of the peritoneum, that the inhibition is mediated by the splanchnic nerves, and that there is a sound physiological basis for the neurogenic concept of paralytic ileus.

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TREATMENT OF OPEN WOUNDS BY THE SULPHANILAMIDE PACK

BY

A. C. KING, F.R.C.S.

Major, R.A.M.C.

This is an account of a method of treatment for open wounds employed by the surgical specialist to a casualty clearing station during the fighting in France and Belgium which ended with the evacuation of Dunkirk. If the reader finds the article lacking in specific detail he is asked to remember that all the writer's records, together with the rest of his personal belongings, were lost at Dunkirk, and that the paper is not meant to be an exhaustive survey from which conclusions may be drawn, but rather one surgeon's experience in a limited number of cases.

The method used in this treatment of open wounds was to pack them with powdered sulphanilamide. Sulphapyridine (M & B 693) was never used. At no time during the treatment was sulphanilamide given by mouth, nor was it given to controls treated with a flavine pack. Any effect was exerted by the presence of sulphanilamide locally in the wounds. The anaesthetic employed was sodium pentothal, combined with gas-and-oxygen.

Technique

Pre-operative treatment was as in ordinary surgical procedure. The skin edges of the wound were then excised and the depths of the wound examined. After the extent of the wound had been ascertained the skin opening was enlarged and the whole area laid open to allow for drainage. As a general rule the area of damaged muscle was very much greater than the aperture which led to it through the skin. This was particularly the case in wounds from trench-mortar fragments.