MANAGEMENT OF OBSCURE ALIMENTARY BLEEDING*

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Obscure alimentary bleeding presents two major problems: firstly, iron-deficiency anaemia due to chronic blood loss, and, secondly, massive upper gastrointestinal haemorrhage of obscure origin.

CHRONIC BLOOD-LOSS ANAEMIA

Recent absorption studies have shown that a "primary" failure to absorb iron is exceedingly rare, and it can be said that most iron deficiency in men, and much of that in women, can be traced to chronic bleeding (Callender, 1958). The alimentary tract comes high in a list of probable sites of haemorrhage. How do we ascertain that bleeding is occurring from the alimentary tract? What means are available to us in a quest for the site of bleeding in unexplained gastrointestinal haemorrhage with resultant anaemia?

Determination of Alimentary Bleeding

When frank bleeding occurs from the gastro-intestinal tract, fresh or altered blood may be found in the vomit or in the faeces, and recognition of this type of bleeding rarely proves difficult. However, it has been estimated that about 100 ml. of blood is required to produce a melaena stool; minor degrees of bleeding usually fail to alter the appearance of the faeces and require other methods for their detection. The examination of the faeces for occult blood is a routine investigation in the diagnosis of haematological and gastro-intestinal disorders. Three techniques are available: the commonly employed chemical tests, spectroscopic examination of the faeces, and radioactive measurement of blood loss using ^{51}Cr -labelled red cells.

As a result of the recognized high incidence of cancer in individuals concerned with the preparation of benzidine, this substance is no longer available as a chemical test for occult blood in faeces. The orthotoluidine test, the "occultest" tablet, and the "haematest" tablet are recognized substitutes. In our experience the haematest tablet shows inadequate sensitivity, with a consequent risk of false-negative results. The other two tests would seem to be good substitutes for benzidine, but, like the original compound, err on the side of oversensitivity when applied to the faeces of patients on an unrestricted diet, and it must be admitted that it is extremely difficult to devise a standard chemical test which is neither too sensitive nor too insensitive.

Some of the difficulties which may be encountered in interpreting the results of chemical tests are illustrated by the following simple experiment in six healthy

medical students. In this study the presence of faecal occult blood was assessed in all instances by means of the orthotoluidine test. On ordinary hospital diet for three days prior to faecal collections two subjects gave a negative result, two a weakly positive result, and two a definitely positive result. During the second week, in which the subjects were on a strict meat-free diet and had been carefully instructed to avoid brushing teeth, the test became negative in five subjects and remained weakly positive in one. In a third week, when the strict dietary regime was continued and in addition the subjects took 30 gr. (2 g.) of aspirin daily, the test became strongly positive in five subjects and weakly positive in one (see Table). From this study, planned mainly for its instructive value to medical undergraduates, it is apparent that the results in the first week illustrate the excessive sensitivity of the orthotoluidine test, while

Orthotoluidine Test for Faecal Occult Blood in Six Normal Subjects

Week	Regime	Result of Test		
		Negative	Weakly Positive	Positive
1st	Ordinary diet	2	2	2
2nd	Strict (no meat: no teeth-brushing)	5	1	0
3rd	Strict + 30 gr. (2 g.) aspirin daily	0	1	5

those in the second week illustrate the importance of a meat-free diet and other restrictions if significance is to be given to the results of this test. The chemical pathologist reports that blood is present; it is the responsibility of the clinician to decide its significance. Finally, the results of the third week illustrate the effect of aspirin in producing gastro-intestinal blood loss.

The studies of Grossman *et al.* (1961) on the effects of aspirin and related compounds are of practical interest. Faecal blood loss as measured by the technique of ^{51}Cr -labelled red cells was found to be significantly elevated in patients given oral aspirin, enteric-coated aspirin, buffered aspirin, calcium aspirin, and sodium salicylate. We must not be deluded by the aspirin tablet no matter its guise. It would, however, be misleading if the impression was gained that aspirin is a dangerous drug for all patients. In the absence of gastro-intestinal disease, the administration of aspirin is likely to be of importance as a cause of anaemia only when other factors tending to produce an iron deficiency coexist; in such cases aspirin administration may tip the scales towards a frank deficiency with anaemia. Perhaps the most significant observation made by recent workers is that aspirin and related drugs may initiate major haemorrhage when taken by a subject who has a lesion which is already bleeding slightly, and there is

*Blackham Lecture delivered to the Royal Faculty of Physicians and Surgeons of Glasgow on December 14, 1961.

no type of aspirin and no route of administration of proved safety in such circumstances.

Spectroscopic tests, including the examination for protoporphyrins and Snapper's test for pyridine-haemochromogen, offer greater reliability, but their relative complexity renders them unacceptable for the examination of a large number of specimens. When the faeces are examined for protoporphyrins, chlorophyll-containing foods should be avoided, since chlorophyll gives a similar band in the spectrum. Snapper's test, in which the chlorophyll band is readily differentiated from the pyridine-haemochromogen band, gives a satisfactory degree of sensitivity, and we have come to place greater reliance on it than on any of the chemical tests.

A Reliable Test

The most reliable method of testing for faecal occult blood, and certainly the only quantitative one, is that employing red cells labelled with ^{51}Cr . The detection of blood leak being dependent upon the escape of labelled cells into the lumen of the gastro-intestinal tract, diet need not be restricted, and the only point to ascertain is that the patient is not taking drugs which may of themselves cause alimentary bleeding. Again, however, the method does not have the simplicity of performance given by chemical tests. Furthermore, this isotopic method cannot be recommended for routine use, particularly in young patients, and its main value is as a research technique for quantitation and timing of blood loss.

There is clearly a need for a practical policy in determining blood loss from the alimentary tract, and the following plan is the one which we have adopted. In cases of suspected alimentary bleeding it is first essential to take a careful drug history (aspirin, salicylates, phenylbutazone, iron fumarate, etc.) and to exclude the presence of a potentially bleeding lesion in the mouth or anal canal. This done, a routine occult test is made. If strongly positive, the test is then repeated with careful instruction to the patient to avoid meat in the diet and to avoid teeth-brushing for three days prior to the collection of faeces. If the test remains positive, a spectroscopic test of the faeces is made before embarking on an extensive series of time-consuming investigations to locate the site of presumed haemorrhage. When such a plan is followed few patients with active bleeding will miss the screening procedure, the incidence of false-positive results will be low, and there will therefore be a considerable saving in radiological and other special investigations.

Quest for Site of Blood Loss

Lesions causing haemorrhage into the alimentary tract can usually be diagnosed by conventional x-ray techniques. Small lesions in the oesophagus, stomach, and distal colon which escape identification by barium studies rarely elude the direct scrutiny afforded by oesophagoscopy, gastroscopy, and sigmoidoscopy. There are instances, however, in which the source of bleeding cannot be determined even when all such methods have been employed. Faced with the request to operate on this type of case, the surgeon is well advised to do so at a time of active haemorrhage; even then, although this improves the chance of detecting the bleeding-point, some cases will remain obscure.

New techniques are available or are being developed which may be of assistance in resolving this not uncommon clinical dilemma.

The *small-bowel enema*, first described by Scott Harden (1960), is claimed by Pygott *et al.* (1960) to be the most effective technique for the study of the small bowel when bleeding from this situation is suspected. Our own experience with this method has not been encouraging, and it must be admitted that all lesions cannot be detected by the most refined radiological methods at present available.

The *fluorescein string test* merits wider application as a means of locating the site of gastro-intestinal bleeding, particularly in the upper reaches of the alimentary tract. Initially described by Einhorn (1909), the test has been modified by Traphagen and Karlan (1958). It consists in the patient swallowing a weighted string which contains a radio-opaque filament knotted at intervals of 1 in. (2.5 cm.). A straight x-ray film of the abdomen is taken, and, with the patient lying on the x-ray table, 20 ml. of 5% fluorescein is injected into an arm vein and the dye allowed to circulate for four minutes before removal of the string. The string is now examined under ultra-violet light. Dye on the tape is due to bleeding, and the monofilament marker nearest the dye is noted by counting back the number of inches from the weight at the end of the string. The comparable marker is found on the exposed x-ray plate by counting back the same number of inches from the radio-opaque weight (Fig. 1). This marker represents the site of bleeding within an error of not more than one or two inches in the experience of Haynes *et al.* (1960), who claim to have located accurately the site of bleeding in 51 out of a total of 83 subjects examined. It is helpful to remember that if the appearance of the dye on the string seems equivocal the fluorescence can be made strikingly apparent by immersing the string in a basin of water prior to examination under ultra-violet light.

FIG. 1.—Radiograph showing application of the fluorescein string test.

The *fiberscope*, a completely flexible optical instrument embodying the principle of fiberoptics, has been developed by Hirschowitz *et al.* (1958). The essential light conduction takes place through a bundle, 5/16 in. (8 mm.) in diameter and 1 metre long, composed of glass fibres of hair thickness. Image transmission is accomplished by having the spatial arrangement of the fibres exactly the same at each end of the bundle, each fibre separately transmitting through its length a tiny portion of the image. The extreme ends of the fibre bundle are cemented in resin, while the rest is unbound, thus allowing extreme flexibility in the instrument.

The fibroscope is claimed to be more efficient than the gastroscope for examination of the stomach, may occasionally permit direct visualization of a duodenal ulcer, allows ready inspection of the jejunum through a gastro-jejunal stoma, and offers promise in the future of permitting direct observation of the hidden reaches of the small intestine.

Mesenteric arteriography has been used by us in experimental studies similar to those described by Schobinger (1959). In dogs the mucosa of a loop of small intestine was scarified by a scalpel inserted through a small incision in the anaesthetized dog's bowel prior to the injection of 10 ml. of 37.5% "hypaque" into a related mesenteric artery. Some of the contrast medium immediately enters the lumen of the bowel through the mucosal defect. This technique could, however, be applied only *during* the course of an operation for unexplained alimentary bleeding. A technique for percutaneous selective angiography of the superior mesenteric artery has been described by Odman (1959). It is based on the use of a pre-modelled radio-opaque "polythene" catheter introduced via the femoral artery. Odman found the superior mesenteric artery to be the most easily catheterized branch of the lumbar aorta and reported an absence of untoward side-effects in 27 pre-operative examinations.

An *intestinal capsule* has been developed by Crosby *et al.* (1960) by means of which it is possible to sample serially the contents of the small intestine. Specimens less than 0.5 ml. in volume can be delivered rapidly through tubes as long as 5 metres. The sampling may be continuous or intermittent, at one level or at many levels between the duodenum and the ileo-caecal valve. In cases of intestinal bleeding it is suggested that it may be possible to establish the level at which blood is lost by testing each sample as it is received. The method has the merits of simplicity and safety but requires further evaluation.

The intraluminal detection of labelled red cells by means of a minute Geiger counter, the Mullard MX150, has been studied in dogs by McKibbin (1962) in this department. This counter detects energetic beta particles, and ^{32}P was chosen as the most suitable isotope for labelling the cells by the technique of Mollison *et al.* (1958). In a first series of experiments the possibility was excluded that radioactivity in gastro-intestinal secretions might pose a major problem. In a second series of experiments, contrary to the findings of Healey *et al.* (1961), a high background activity was found in the gut wall which could be expected to reduce the chance of detecting minor leakage of red cells into the lumen of the gut. This problem was overcome in a third series of experiments by surrounding the counter with a 1-mm. copper shield having an annular space between the shield and the Geiger counter (Fig. 2). Using this device, it has been possible to detect with

accuracy the site of less than 1 ml. of free blood in the lumen of the intestine as the shielded counter is advanced. We consider that this technique can now be applied to patients during the course of operation when laparotomy has been otherwise completely negative.

FIG. 2.—Device for detecting the site of free blood in the lumen of the intestine.

To be applicable as a method for pre-operative determination of the site of bleeding a smaller Geiger counter would be required, and steps have been taken to construct one of 3-mm. external diameter. The recent development of semiconducting devices from which minute detectors can be made offers still greater promise. These would seem to hold out the possibility of incorporation within an ingestible radio-pill; this would dispense with the need for electrical leads, which with the present counter must carry 400 volts.

MASSIVE UPPER GASTRO-INTESTINAL BLEEDING OF OBSCURE ORIGIN

The majority of patients in this category present with bleeding of sufficient degree to cause oligaemic hypotension followed by a rapidly diminishing haemoglobin level. One of the more common emergencies which may threaten a patient's life—massive upper gastrointestinal bleeding—has shown a rising incidence in the past 30 years (Fraenkel and Truelove, 1956; Avery Jones, 1956; Large, 1960), and with advancing years haematemesis becomes a progressively more dangerous condition.

The indications for surgical treatment of bleeding peptic ulcer have now been clarified. Early operation is advocated for the known chronic gastric ulcer, where pain continues after the initial bleed, where early exsanguination indicates erosion of a large blood-vessel, and where haemorrhage is complicated by perforation or by pyloric obstruction. In general, there is a bias towards surgery in patients over the age of 50; in younger patients a fatal outcome is relatively uncommon under conservative management, and, in keeping with the general tendency to select the operation for the individual patient with duodenal ulcer and to avoid gastrectomy whenever possible, elective surgery is preferred.

One of the difficulties, but indeed one of the greatest fascinations, of the management of massive upper gastrointestinal haemorrhage is the diagnosis of the obscure case of bleeding. This constitutes approximately one-third of the total problem. Constant vigilance is needed if any of the less common causes of bleeding are not to be missed—acute peptic ulcers, oesophageal ulceration, primary capillary haemorrhagic disorders, the Mallory-Weiss syndrome, etc. When patients in this group continue to bleed and surgery becomes imperative there is uncertainty in planning the surgical approach; the diagnosis may not be established even at operation; unnecessary gastrectomy may be performed, and this

may be followed by continued bleeding from an unidentified site.

In the past, efforts to achieve early diagnosis of the cause of massive haemorrhage have been inhibited by the fear of encouraging further bleeding. It is now clear that the risk of pre-operative investigation is small in comparison with the risk of ill-planned surgery, and the need for an intensification of effort towards early accurate diagnosis is mandatory. We have gained increasing confidence in the following plan of action.

General Investigations

The clinical history, which may require to be obtained from a relative, should always include the taking of a careful drug history, having in mind aspirin, salicylates, and steroids. Particular attention is paid to preceding dyspepsia, previous hospital investigations undertaken for such relevant disorders as jaundice, hepatic cirrhosis, or blood dyscrasia, and symptoms indicating impaired cardio-respiratory reserve. Clinical examination at this stage should be brief and be directed mainly towards an estimate of the degree of oligæmic hypotension. Laboratory investigations may usually be limited to obtaining the patient's blood group and immediate haemoglobin value, appreciating that this level may be unreliable within the first 12 hours of a severe bleed.

There is nothing to be lost and perhaps much to be gained by doing a bromsulphthalein-retention test at this time: 5 mg. of dye per kg. of body weight is injected intravenously and the retention in the blood determined at the end of 45 minutes. When the degree of retention is less than 5% at the end of this period the likelihood of oesophageal varices is remote; when greater than 15% the diagnosis of varices must be seriously entertained and efforts to identify them should be made. The test has several limitations. Firstly, the development of varices is directly dependent on a state of portal hypertension rather than on hepatic dysfunction; consequently, the retention of bromsulphthalein would be in the normal range in most patients having bleeding varices due to extrahepatic portal obstruction. Secondly, it is well known that patients with liver disease may bleed from a source other than varices—in particular from a peptic ulcer. Thirdly, the presence of severe hypotension and anoxia may itself lead to an elevation of the amount of bromsulphthalein retained in the plasma. Despite these limitations, the bromsulphthalein-retention test is a helpful adjunct in the diagnosis of obscure upper alimentary bleeding.

These simple investigations can all be initiated within a few moments and blood loss corrected without delay.

The advantages to be gained by the passage of a stomach-tube have now almost dispelled fears that it might dislodge clot from an eroded vessel. Removal of blood clot from the stomach and relief of gastric distension reduce the vascularity of the stomach and encourage cessation of haemorrhage. Furthermore, repeated gentle aspiration provides information on progress of bleeding.

These various measures having been performed, it will usually be safe to embark on the second phase of the plan—special investigations designed to locate the site of haemorrhage.

Special Investigations

Early x-ray examination of the stomach, formerly considered to be fraught with danger in patients suffering

from haematemesis, is now gaining support from many quarters. Examination during the initial bleeding phase has proved safe and much more informative than the conventional investigation of such cases three weeks or more after bleeding has ceased (Samuel, 1960). Movement of the patient on the x-ray couch is limited to a minimum and the abdomen is not compressed, although simple palpation is not thought to be harmful. The entire examination is undertaken with the patient lying on the table, and, by using gravity and posture to keep the bolus of medium from diffusing, satisfactory mucosal relief can usually be obtained. The fundus of the stomach and lower end of the oesophagus are well seen with the patient in the supine position. The body of the stomach is demonstrated when the patient makes a slight turn on to his right side. Finally, the right lateral position gives opportunity to demonstrate the pyloric antrum of the stomach and the duodenal cap.

The *fluorescein string test* may be performed while the patient is in the x-ray department or when the portable machine is in the ward. The test is of particular value in distinguishing the site of bleeding where two or more suspicious areas have been demonstrated radiologically.

Early gastroscopy no longer requires an advocate. It is rarely helpful within the first six hours after a bleed, but thereafter may be invaluable in diagnosing such conditions as acute gastric ulceration, multiple haemorrhagic areas, or the Mallory-Weiss syndrome.

Oesophagoscopy in an ill and restless patient may prove difficult, but the examination is performed after induction of anaesthesia in cases when the diagnosis remains obscure or a bromsulphthalein-retention test has indicated the possibility of oesophageal varices. The identification of a lesion at oesophageal level clarifies the surgical approach and thoracotomy replaces abdominal exploration. It is implicit that the surgeon dealing with many cases of massive upper gastro-intestinal haemorrhage should be thoroughly trained in the technique of oesophagoscopy.

Diagnostic Operation

Despite the most assiduous attempts to establish a diagnosis, some cases of massive bleeding will remain obscure. For these each surgeon will have his own plan of action.

Adequate exposure is essential; in the thin subject a vertical midline incision gives ready and adequate access; in the obese patient a transverse abdominal incision running from the tip of one eleventh rib to its fellow on the other side provides an approach which facilitates mobilization of the duodenum and is usually adequate for exploration of the cardiac end of the stomach. If the oesophago-gastric junction cannot be examined satisfactorily, the incision can readily be converted into an inverted T by means of a vertical incision running upwards towards the xiphisternum.

The presence of distended portal collateral vessels and the gross appearances of the liver and spleen are noted. The gastro-colic ligament is opened to permit bimanual examination of the stomach. Mobilization of the duodenum by Kocher's manoeuvre is a requisite for its thorough inspection and palpation. The presence of enlarged and fleshy glands along the left gastric vessels may indicate an impalpable acute gastric ulcer on the lesser curvature of the stomach.

If a lesion has not been demonstrated at this stage, the oesophageal hiatus is now carefully examined to exclude the possibility of a hiatus hernia; a gastric ulcer may occur within the thoracic pouch of stomach and may escape discovery unless the hernia is reduced.

When the source of bleeding still remains unidentified a plea is made for *pyloroduodenotomy*. An incision is made across the pylorus and the axis of the gut extending for 1½ in. (3.8 cm.) into both the antrum and the duodenum. The exposed mucosae of duodenum and antrum are inspected and the interior of the duodenum is palpated as far down as the ampulla of Vater. If a duodenal ulcer is found the bleeding-point is underrun, the incision closed as a pyloroplasty, and a vagotomy added. In this way haemorrhage is controlled and resection of the stomach avoided. If the bleeding-point still remains elusive it is useful, before closing the pyloro-duodenal incision, to aspirate both the stomach and the duodenum and observe the nature of the fluid which wells up from the duodenum and downwards from the stomach; if clear bile comes from the duodenum it can be assumed that the bleeding-point is above the level of the pylorus. This information gained, the incision is closed as a pyloroplasty.

If the bleeding-point still remains unidentified a *wide gastrotomy* is advocated. The general surgical principles of adequate exposure and good illumination should be followed in examining the interior of the stomach as elsewhere. A longitudinal incision is made on the anterior surface of the stomach midway between the greater and lesser curvatures, beginning just proximal to the pyloroplasty closure and extending upwards for a distance of about 7 in. (17.5 cm.). The gastric mucosa, from the oesophago-gastric junction to the pylorus, must be inspected methodically. A small erosion may lurk in the depths of a mucosal fold, and it is important to apply tension to successive portions of the gastric wall so that the intervening folds of mucosa are stretched into a smooth surface. A superficial ulcer or erosion can be treated safely by local excision and suture, needless gastrectomy thereby being avoided. When gastrectomy is necessary, as with haemorrhagic telangiectasia, the resection may be expedited by rapid closure of the gastrotomy with a continuous suture.

In conclusion, obscure alimentary bleeding is intriguing, is full of subtlety, and offers a challenge which can best be met, not by blind ablative surgery, but by strategy and by devising even more subtle methods for the investigation and detection of the site of haemorrhage.

Summary

Alimentary bleeding, frequently obscure in its origin, may cause chronic anaemia or present as exsanguinating haemorrhage.

In patients with chronic iron-deficiency anaemia the proof that bleeding is occurring from the alimentary tract is not always easy. An attempt has been made to assess the relative merits of tests available for detecting the presence of occult blood in the faeces, and, on this basis, to outline a clinical policy. The identification of the precise site of blood loss in these patients presents an even greater problem. Generally accepted methods are reviewed and progress is reported on the development of newer techniques which, though largely experimental at present, offer hope of locating bleeding lesions in the hidden reaches of the small intestine.

Massive upper gastro-intestinal bleeding is amongst the most exacting conditions which the surgeon is called upon to treat. The difficulties are increased when the source of bleeding has not been identified before operation, and the view is expressed that greater effort should be made to achieve an early and accurate pre-operative diagnosis. A plan is described for the investigation and surgical management of patients admitted with exsanguinating upper gastro-intestinal bleeding of obscure origin.

In all cases of alimentary bleeding it is essential to obtain an accurate drug history. Aspirin, which regularly induces occult alimentary blood loss, is apt to initiate major haemorrhage when taken by subjects who have a lesion of the gastro-intestinal mucosa.

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The Ministry of Health is now offering two further posters on smoking and health to local authorities throughout England and Wales. Both are in colour. In one, on a red background, a series of figures shows the increase in lung cancer deaths from 1945 to 1961, set in grey on the "lids" of five black "coffins." The size of the "coffins" increases as the figures mount—starting with 5,303 deaths in 1940 and reaching 25,288 in 1961. Underneath the "coffins" it is stated in white and black lettering: "The more CIGARETTES you smoke the greater the risk"—"YOU HAVE BEEN WARNED." The other poster contains graphs showing the rise in the consumption of tobacco smoked as cigarettes and the corresponding rise in lung cancer deaths. For colour the poster has a "shocking-pink" background. A brown line gives the consumption of cigarette tobacco from 1920 to 1961, showing that it has risen during that period from 80.3 million lb. to 243.1 million lb. The rise in lung cancer deaths during the same period is shown by a red line, starting from 592 deaths in 1920 and rising to 25,288 in 1961. At the foot of the poster in large black type are the words: "YOU HAVE BEEN WARNED." These posters follow the three textual posters which were issued early in April. Orders from local authorities for the latter now total over 220,000. In co-operation with the Ministry of Education, the Ministry of Health is next producing two pictorial posters featuring respectively a teenage boy and girl. They are expected to be available shortly, and are intended primarily for display in secondary schools and youth clubs and will first be offered to local education authorities. Later on they will be available to other local authorities who may wish to use them.