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PERITONEOSCOPY

ENDOSCOPIC REFINEMENT PAR EXCELLENCE

BY

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Endoscopic procedures are usually carried out by a specialist surgeon to diagnose the condition for which he will later carry out the indicated treatment. This is true of cystoscopy for the urologist, of bronchoscopy and oesophagoscopy for the thoracic surgeon, and of culdoscopy for the gynaecologist. When it comes to gastroscopy, the procedure may be carried out by a gastro-enterologist so as to save the patient from a needless surgical exploration: few gastroscopies are carried out by abdominal surgeons. Peritoneoscopy stands nevertheless by itself as the endoscopic procedure for which there is no decided assignment to surgeon or physician. As peritoneoscopy consists in examining the peritoneal cavity, it seems logical that the surgeon should be asked to do it; his constant meeting with gross intra-abdominal disease makes him more likely to diagnose correctly what he sees through the peritoneoscope; but although the physician, even if he specializes in gastro-enterology, is less likely to be so familiar with the inside of the abdomen, it is for him that peritoneoscopy is most useful, and his usual attitude of trying to keep patients away from surgery may enhance his enthusiasm for peritoneoscopy. The opposite occurs with the surgeon: he is usually impatient, and he may feel that a diagnosis is unsatisfactory when he cannot introduce his hands in the abdominal cavity to palpate the diseased organs.

These seem to be the reasons why peritoneoscopy has not been universally accepted. These are also the reasons why surgeons often criticize peritoneoscopy; but there is little doubt in my mind that the inconclusive findings, the complications, and the failures, which are frequently mentioned as criticisms of the procedure and as justification for the absence of a peritoneoscope in hospital, are in most cases explained on the basis of failure not of the method but of the one who carried out the procedure. When the technique is carefully and patiently followed, when the limitations, indications, and contraindications of the procedure are known, and when the endoscopist has acquired experience and enthusiasm, the results of peritoneoscopy will be most gratifying and will prove that the procedure has not only an academic but a truly practical interest.

Technique

The technique of the procedure is simple and varies little with the different instruments available to-day. The one with which we have experience is the peritoneoscope designed by Ruddock (1934). The patient is

prepared as for a coeliotomy and placed in the dorsal decubitus position on a table which allows changes in position in the lateral and horizontal planes. After infiltration with 1% procaine locally, a 1.5 cm. incision is made in the midline transversely 2 cm. below the umbilicus. The subcutaneous fat is pushed away, an additional dose of procaine is infiltrated in the fascia and peritoneum, and a pneumoperitoneum is created with a small blunt trocar. When the abdomen is well distended (to the point of slight discomfort but not of pain for the patient) the blunt trocar is removed and the large trocar, with its sheath through which the peritoneoscope will be passed, is put in its place. During the introduction of both trocars it is useful to have the patient blow up his stomach so as to offer better resistance. It is also important to direct the trocar away from any known masses or previous incisions.

The trocar is removed from its sheath and the wide-vision telescope is introduced slowly, while looking through the objective, until it reaches the free space created by the pneumoperitoneum. The latter may require intermittent refilling and the lens of the telescope will usually become fogged up by condensation, but will clear up spontaneously (it may be warmed in hot water before being introduced, but hot saline should not be used because this will deposit crystals that will harm the lens).

Examination of the abdominal cavity must be systematic so as not to leave any area unexplored. We start to the right of the falciform ligament and follow the right lobe of the liver until the dome of the gall-bladder comes into view. The surface of the liver as well as the parietal peritoneum over it can then be examined as high up as the right diaphragm. By withdrawing the telescope and turning it approximately 340 degrees anti-clockwise and close to the parietal peritoneum the edge of the left lobe of the liver is seen. This is examined as was the right lobe, and underneath it can be seen the anterior wall of the stomach. The left diaphragm transmits the cardiac beat. The spleen is usually not seen unless it is enlarged; but occasionally, if the patient is rotated towards the right, its tip may come into view. If the examiner moves from the right to the left side of the patient he may then point the telescope towards the omentum and examine it carefully. While the patient is being placed in the Trendelenburg position the lower parietal peritoneum is observed as far as the pelvis, and loops of bowel come into view and are seen migrating towards the chest.

The pelvic structures can be examined best when the patient has reached the extreme Trendelenburg position. The iliac vessels can be followed and peristaltic waves can often be seen in the ureters. The urinary bladder, uterus, tubes, and ovaries can usually be seen, even though incompletely; but if the pelvic floor is rather deep, or there are adhesions, it is helpful to ask the assistant to do a rectovaginal examination so as to push up the pelvic organs towards the examining instrument. The sigmoid and caecum can be identified before the patient is straightened out once again. If the head of the table is raised beyond the horizontal position, the bowel and omentum fall back into the lower abdomen and it may be possible to see the gall-bladder and gastrohepatic ligament, which were previously hidden by omentum. The pancreas cannot be identified even in thin patients, but inferences may be drawn from any large mass in it (if there should be a bulge which raises either the stomach or the gastrohepatic or gastrosolic ligaments). The presence of recent pancreatitis may be diagnosed with certainty if there are nodules of fat necrosis (Herrera-Llerandi, 1945).

At the end of the examination a biopsy specimen can be taken either with the special biopsy forceps or with a needle. The former is introduced through the peritoneoscope sheath, together with its smaller-field telescope, and is used for obtaining specimens of omentum, peritoneal implants, or other nodules, and the instrument carries a cauterization connexion. The biopsy needle is used either in large tumours with carcinomatosis (where there is little danger of spreading the disease) or in the liver. We prefer needle to forceps for obtaining liver specimens not only because it gives a deeper sample but also because it is difficult to bite into the organ with the biopsy forceps without creating a rather large bleeding area. Before taking a specimen of the peritoneum, it is useful to infiltrate the area with procaine. The same thing is done before the introduction of the biopsy needle through the skin and abdominal wall. We usually prefer not to take a specimen of the spleen, although it has been done occasionally with impunity by others and by us, at the time of transperitoneal splenopography (Herrera-Llerandi *et al.*, 1955). A Franseen needle has been used with satisfaction, although other modifications of the Iversen needle may be as good or better (Abrams, 1958; Menghini, 1958; *British Medical Journal*, 1959).

At the end of the procedure inspection is made of the biopsy site to make certain that it does not bleed and the instrument is removed. The pneumoperitoneum is allowed to escape as completely as possible and the skin is closed with one or two deep mattress sutures. The patient is then returned to the ward and allowed a full diet and bathroom amenities unless there are contra-indications to these.

It is occasionally useful, particularly in tuberculous peritonitis or carcinomatosis, to allow the omentum to herniate through the peritoneoscopy incision as the instrument is withdrawn, so as to obtain a large satisfactory biopsy specimen under direct vision and ligation. We have occasionally used a second trocar (from a thoracoscope) to obtain a specimen under guidance of the wide-angle peritoneoscope.

Coeliotomy affords a more complete method of exploration than peritoneoscopy: one can palpate instead of only seeing, and one can lift up and explore hidden or retroperitoneal structures. Peritoneoscopy, on the other hand, allows only a superficial visual

exploration. But peritoneoscopy is almost entirely painless, it does not produce shock, it is short in duration, it is done under local anaesthesia, it requires minimal personnel and operating-room accessories, the stay in hospital need not be more than 36 hours, and mortality and morbidity are almost nil. Coeliotomy, on the other hand, is accompanied by post-operative pain and potential shock; and usually general anaesthesia and complete operating-room personnel and accessories are indispensable. The cost of abdominal exploration is ten times greater (Narancio *et al.*, 1945) than that of peritoneoscopy, and convalescence lasts several weeks after a stay in hospital for about one week. Mortality and morbidity are far from negligible—for example, an exploratory operation for inoperable cancer of the stomach is accompanied by a mortality that varies between 8 and 22%.

Indications

The following are the main indications for peritoneoscopy.

1. To establish a diagnosis of medical intra-abdominal disease which will not require surgical treatment—for example, portal cirrhosis.
2. To establish the aetiology in cases of hepatomegaly, splenomegaly, ascites, or jaundice which cannot be diagnosed satisfactorily using only clinical, radiological, and laboratory data—for example, portal hypertension.
3. To establish the presence or absence of an intra-abdominal tumour when this is not certain on the basis of physical and radiological examinations—for example, to distinguish between a follicular ovarian cyst and a small fibroid of the uterus.
4. To help in deciding the best approach to an intra-abdominal mass, and to decide whether this exploration is necessary; the presence of metastases is easy to establish usually, but the technical resectability of a tumour cannot be judged satisfactorily (Benedict, 1944a).
5. To establish the prognosis in a patient who refuses coeliotomy and to follow the progress of a patient under treatment for intra-abdominal disease. An example of this would be a patient with ascites from an inoperable ovarian carcinoma which has been treated with radioactive gold.

Other indications have been suggested by some authors who have tried to change peritoneoscopy from a diagnostic to a therapeutic procedure. Such is the case of feminine sterilization by electrocoagulation of the tubes (Anderson, 1937), of implantation of radium in an inoperable intra-abdominal tumour (Hope, 1937), or of aspiration of a large ovarian cyst (Benedict, 1944a). It has also been used in combination with hysterosalpingography (unpublished data) and with transvesicular cholangiography (Royer *et al.*, 1942). It is our feeling that on rare occasions one of these *tours de force* might prove useful and wise, but asking too much of peritoneoscopy will only lead to errors, disappointments, and a bad name for the classical procedure.

Dangers of Peritoneoscopy

No matter how enthusiastic one may become regarding peritoneoscopy, its limitations must be kept in mind, since it is not a complete abdominal exploration. The greatest danger is to forget this, and to deny the benefits of coeliotomy to someone who would profit from it. The other dangers are associated with its complications.

1. Subcutaneous emphysema will sometimes appear as a result of the patient's straining. It may also be caused by an incorrect position of the pneumoperi-

toneum needle. If this needle has not pierced the peritoneum it will give rise to a localized distension, which is easily recognized on the abdominal wall; this contrasts with the uniform tympanitic abdominal appearance after correct pneumoperitoneum.

2. Although I have described pain as minimal during peritoneoscopy, it must be remembered that the parietal peritoneum is very sensitive and the mere touching of it with the tip of the instrument will cause pain. The worse source of pain encountered was associated with the incomplete "rinsing out" of the instrument after it had been sterilized in the formaldehyde cabinet. It is most important to wash out the air bulb, and I usually blow some air from it gently towards my eyes before using it for the creation of the pneumoperitoneum.

3. Ascitic fluid may continue to escape through the peritoneoscopy incision after the procedure. This is, in cases of carcinomatosis, one of the causes of local malignant implants. These leaks are usually self-limited.

4. The peritoneoscopy wound may on rare occasions become infected. This is all the more likely in a teaching institution where the endoscopist allows observers to look through the instrument.

The above four complications are of little importance to the patient, but the next three must be regarded as serious.

5. Haemorrhage can present itself either as an immediate or as a late complication. It may be due to a biopsy, to hypoprothrombinaemia, or to trauma by the instrument. With regard to the biopsy, care must be taken, before removing the telescope, that no active bleeding is left behind. If there should be any, the use of electrocoagulation or of local pressure will be helpful: the latter, for example, can be used after needle biopsy of the liver if one presses the abdominal wall against the biopsy site after allowing the pneumoperitoneum to empty. Regarding improper prothrombin levels, it is paramount to have a near-normal prothrombin time before carrying out a peritoneoscopy. The possibility of trauma as a cause of haemorrhage can be due to "blind" use of the instrument without constant adequate observation through the telescope and represents a faulty technique; but it can also be due to the introduction of the instrument through a vascular channel in the abdominal wall: this presented itself in a patient with cirrhosis when the instrument was put through the midline above the umbilicus. Because of an enormous collateral venous channel which started bleeding profusely around the instrument, the incision had to be enlarged, and the bleeding was thus controlled without any ill effects. Since then we have always used the infra-umbilical incision for cases of portal hypertension.

6. Shock can present itself without haemorrhage. It may be a reaction to the premedication or to the local anaesthetic, or it may be the result of sudden intra-abdominal decompression in cases of massive ascites. We encountered this complication after the rapid evacuation of 12 litres of ascitic fluid in a patient with portal hypertension. Since then we have taken the precaution of emptying any large ascitic accumulations gradually in the course of the three or four days preceding peritoneoscopy; and if large volumes of fluid have been aspirated during peritoneoscopy, we apply local pressure to the abdomen for 24 hours after endoscopy without complete emptying of the pneumoperitoneum.

7. Perforation of a hollow viscus is probably the most severe complication of peritoneoscopy. According to Ruddock (1937), this happens in 1.6% of the cases. It usually occurs in patients with plastic peritonitis where intra-abdominal adhesions are responsible for the fixation of the viscus (Benedict, 1951). The most frequent site of perforation is the small bowel. This complication occurred once in our series of nearly 400 cases, and the perforation consisted of "tapping the gall-bladder" after introduction of the biopsy needle through the liver (see Case 2 below). Since that time we make it a point to take liver biopsies away from the level of the gall-bladder, the needle being directed diagonally upwards instead of vertically. The most important point about the complication of perforation is to realize what has occurred, and to carry out immediate coeliotomy without removing the endoscopic instrument. In another patient, because of the appearance of shock, the diagnosis of perforation with haemorrhage was made by a member of the resident staff, and a useless coeliotomy was carried out in the afternoon after peritoneoscopy. The shock in this patient was, as mentioned above, caused by the removal of ascitic fluid and would have been corrected by abdominal compression and vasopressors. Nevertheless, it seems better to carry out a needless exploration than to fail to explore the case that requires it.

8. One last complication of peritoneoscopy, even though not a true result of the endoscopic procedure, must be mentioned. It is associated with premedication: because routines are easily fallen into, one must guard against "the usual premedication" being given to a patient with myxoedema or cirrhosis. The following case will serve to illustrate this complication:

Case 1.—Mrs. X, aged 50, entered hospital because of painless jaundice and abdominal distension. She gave a history of radical mastectomy and x-ray therapy for cancer of the breast eight years previously. Her prothrombin time was normal and her chest x-ray film negative. Additional laboratory data and x-ray examination were postponed because it was felt that she had metastatic disease, and a peritoneoscopy was done to confirm it. So it did. During the entire procedure the patient was very sleepy, and in the course of the next 12 hours her sleep became progressively deeper until she died. Mediastinal and abdominal metastases were found at necropsy. The liver was almost entirely replaced by malignant implants. The cause of death was the premedication ordered by the resident, consisting of 15 mg. of morphine and 0.2 g. of pentobarbitone.

Review of Peritoneoscopy in 390 Cases

Of the peritoneoscopies carried out, the diagnosis was established in 286 (73.3%) and coeliotomy was avoided in 273 (70%). The failures were: missed diagnosis in 9 (2.3%) and complications in 11 (2.8%); there were two deaths. The various types of complication are shown in Table I. The diagnoses obtained by peritoneoscopy are shown in Table II.

The failures are probably the most important aspect of our experience to discuss. One of the two deaths (Case 1) was the result of erroneous premedication in a case of carcinomatosis. The other (Case 2) was due to perforation of the gall-bladder.

TABLE I.—Complications Found in 390 Peritoneoscopies

Wound sepsis	2 cases
Ascitic fluid leak	4 "
Excessive premedication	1 case (death)
Perforated viscus	1 "
Reversible shock	2 cases "
Local haemorrhage	1 case

TABLE II.—*Diagnosis in 390 Peritoneoscopies*

Peritoneoscopic Diagnosis	No. of Cases
Metastatic carcinoma	114
Cirrhosis	88
Normal abdominal cavity	55
Medical jaundice	27
Ovarian and uterine tumours	26
Surgical obstructive jaundice	18
Pelvic inflammatory pathology	14
Tuberculous peritonitis	12
Retroperitoneal tumour	11
Adhesive peritonitis	9
Fatty infiltration of liver	7
Procedure impossible	6
Hepatoma	1
Acute pancreatitis	1
Neuroblastoma	1

Case 2.—Mrs. Y, aged 65, presented with severe anaemia and a history of massive haematemesis and melaena. By x-ray and laboratory data the diagnosis of portal hypertension was probable, but the aetiology was not certain. At peritoneoscopy we found minimal ascites, a rough-looking liver, and a distended gall-bladder. A biopsy specimen of liver was taken with a Franseen needle, about 2 cm. above the liver edge, at the level of the gall-bladder bed, in a region where the liver surface had a whitish appearance, so as to rule out the possibility of a local metastasis. As soon as the aspirating syringe was used a gush of bile came into it. We decided to continue with the aspiration until the gall-bladder appeared collapsed and no bile could be obtained through the needle. When the needle was withdrawn no blood or bile was seen coming out of the "biopsy site." The patient was kept in bed and watched closely. She showed no unusual or unfavourable symptoms or signs during the course of the next 48 hours. Then she gradually became unconscious and distended. Several massive haematemeses occurred and she died rather suddenly on the third day after peritoneoscopy. Necropsy was not performed, but an abdominal paracentesis yielded bile-tinged ascitic fluid. Although the patient's physician blamed the gall-bladder aspiration for the death, it was our opinion that such was not the case, but that death was due to severe gastro-intestinal haemorrhages. Nevertheless, it cannot be denied that the erroneous aspiration of the gall-bladder was a complication of the peritoneoscopic procedure and a contributing cause of the patient's death.

Although pathological proof of the diagnosis was obtained in 73% of our patients, it must be pointed out that a much higher success would be shown if peritoneoscopy were not carried out for academic reasons, as was often the case in our series. The fact that in 70% of our patients coeliotomy was avoided is to us the best argument in favour of peritoneoscopy. It has been pointed out by others (Ruddock, 1934; Narancio *et al.*, 1945; Benedict, 1951) that the cost of a peritoneoscopy is one-tenth that of an exploratory coeliotomy without undesirable sequelae. If one adds to this saving in time and money the lessening of pain and suffering, there is little doubt that peritoneoscopy is a desirable humane procedure.

The variety of diagnoses established must be enlarged to include those reported by others (Ruddock, 1934; Benedict, 1944b, 1951): Boeck's sarcoid, arsenical hepatitis, haemachromatosis, ectopic pregnancy, lymphoma, von Gierke's disease, etc.

The following three cases are unusual enough to warrant short descriptions.

Case 3.—A man of 45 presented with severe epigastric pain. There was abdominal rigidity, but x-ray examination showed no free air under the diaphragm. He had no history of gall-bladder or ulcerative disease, but acute cholecystitis, acute pancreatitis, and perforated ulcer were regarded as good possibilities, and it was decided to carry out a peritoneoscopy. Uncountable pale yellowish implants were found on the parietal peritoneum and falciform ligament.

One of these was taken for biopsy; the pathologist reported it as typical fat necrosis. The patient was treated conservatively and recovered satisfactorily.

Case 4.—A 3-year-old child was admitted to hospital because of dyspnoea and jaundice. Liver enlargement and fluid in the chest and abdomen were found on physical examination. A diagnosis of kwashiorkor with superimposed infectious hepatitis was made. In spite of his age and dyspnoea, a peritoneoscopy was carried out uneventfully. The liver was found to contain a greyish mass which contrasted with the colour of normal liver. A biopsy showed a neuroblastoma, and the child died from it after a gradual downhill course. At necropsy the peritoneoscopic diagnosis was confirmed. His tumour had spread and metastasized extensively.

Case 5.—A man aged 73 had previously had a diagnosis of cirrhosis established clinically and by liver biopsy. He had recently become emaciated, and his ascites did not respond to medical treatment. Instead of a repeat blind liver biopsy, we recommended peritoneoscopy, and this showed a discrete bulging in the right lobe of the liver close to the midline. Biopsy showed a typical hepatoma. The patient was discharged for terminal care.

Conclusions

We have found that peritoneoscopy fulfils a useful role in the diagnosis of intra-abdominal pathology. It is a simple, economical, essentially painless, and harmless procedure, but its usefulness and accuracy are in direct relation to the ability and experience of the peritoneoscopist. He should know its limitations, indications, contraindications, and dangers.

Because it is important to make macroscopic evaluations during the inspection of the abdominal cavity, it seems logical to recommend that peritoneoscopies be carried out by an active abdominal surgeon, but it is indispensable that he should have the correct attitude regarding this procedure: he must be wise and avoid conclusions without solid proof (which might deprive a patient of a desirable coeliotomy); he must be patient, adroit, and anxious to save the patient from a fruitless abdominal exploration. A physician will usually have the correct philosophy regarding the procedure, but he may lack the useful experience of daily intra-abdominal inspection.

It is our experience that the pathological study of the liver is more accurate and satisfactory when a needle aspiration biopsy is carried out under peritoneoscopic guidance than with the standard bite biopsy and electrocoagulation instrument.

Except in very rare instances, peritoneoscopy should not be carried out in uncooperative patients (this includes children and psychoneurotic adults); nor should it be carried out on patients *in extremis*, in cases of peritonitis, in the presence of hypoprothrombinaemia, or of obliteration of the abdominal cavity by adhesions.

An experienced peritoneoscopist will prove to be a most important member of the hospital staff. His useful contributions will cause him to be regarded by physicians and surgeons as the endoscopist *par excellence*.

Summary

The experiences with peritoneoscopy in 390 cases are presented.

The benefits to the patient and to the hospital have proved the usefulness of peritoneoscopy for the establishment of certain intra-abdominal diagnoses without exploratory coeliotomy.

The information obtained by the endoscopist depends directly on his experience, and his knowledge of the limitations, indications, and contraindications of peritoneoscopy.

For the evaluation of hepatic disease we prefer needle aspiration biopsy under peritoneoscopic guidance to biopsy with biting forceps and electrocoagulation.

A hospital is considered to be not completely equipped if it lacks a peritoneoscope and a peritoneoscopist.

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TUBELESS GASTRIC ANALYSIS WITH AZURE A AND BETAZOLE HYDROCHLORIDE

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The ability of the stomach to secrete hydrochloric acid (Prout, 1824) is often a crucial observation in the differential diagnosis of diseases affecting the alimentary tract. In an attempt to overcome the unpleasant necessity for intubation, Segal *et al.* (1950a, 1950b) introduced the method of "tubeless gastric analysis" which depends on the dissociation of a cation exchange resin by the hydrochloric acid in the stomach. This cation is absorbed and appears in the urine, where it is simple to estimate the quantity of cation excreted.

The first exchange resin used contained quininium ("diagnex"), which requires an ether-sulphuric-acid extraction of the urine and is thus rather inconvenient for routine use. More satisfactory is the dye azure A, which is present in considerable quantities in commercially available methylene blue (Segal *et al.*, 1955). This is used in diagnex blue ("azuresin"). Dilute hydrochloric acid displaces the dye from its carbacrylic exchange resin "amberlite RXE-96," and examination of the urine in a comparator block indicates the quantity of the dye excreted, release of which both *in vivo* and *in vitro* starts at pH 3.2 and is maximal at pH 1.5. Segal *et al.* (1950a, 1950b, 1955) had used 500 mg. of caffeine benzoate as parietal-cell stimulant, but after the successful clinical trials by Kirsner and Ford (1955) of the histamine isomer betazole hydrochloride [3-(2- β -aminoethyl) pyrazole] ("histalog") as gastric stimulant, Segal *et al.* (1959a, 1959b) replaced the caffeine with 50 mg. of betazole hydrochloride given orally or subcutaneously.

We are now in agreement with the extensive American experience which suggests that the azure A test combined with betazole hydrochloride is a useful and reliable procedure for indicating the presence of acid in the stomach and deserves wider clinical application. In this paper we record our further experiences with this test, which we use routinely in screening patients for achlorhydria. In many instances the results of the tubeless analyses were confirmed by comparison with the augmented histamine test of Kay (1953).

Present Study

Selection of Patients.—We studied 182 patients, of whom 50 were out-patients. A high incidence of achlorhydria was expected, for most of the patients selected suffered from diseases thought to be more commonly associated with achlorhydria, such as pernicious anaemia, iron-deficiency anaemia, rheumatoid arthritis, thyrotoxicosis, myxoedema, and polycythaemia vera.

Test Procedure.—This was essentially the same as that reported earlier from this department (Denborough *et al.*, 1958). After an overnight fast the bladder was emptied, the urine was discarded, and the patients were given either 500 mg. of caffeine or 50 mg. of betazole hydrochloride diluted in a glass of water. One hour later the bladder was emptied again and the "control" specimens were collected. Immediately afterwards 2 g. of the granules containing the dye azure A were given by mouth and the patients instructed not to have anything else until two hours later, when the bladder was emptied and the "test" specimens were obtained.

Method of Estimation.—Like Gilbert *et al.* (1957), we accepted as indicating the presence of acid only those tests in which the colour of the urine matched or was darker than the 0.6-mg. standard; less colour indicated achlorhydria. It was found that the estimation could be simplified in two ways without lowering the accuracy of the interpretation. Dilution of the urine specimens to 300 ml. was not necessary. Instead of heating aliquots suspected of containing reduced dye in a water-bath for 10 minutes, the specimens, to which one drop of Benedict's reagent and one drop of 6 N hydrochloric acid had been added, were heated gently over an open flame until the maximum colour had developed. They were then cooled under running water and compared with the standards supplied by the manufacturers.

Test of Comparison.—The results of the tubeless tests were correlated with the augmented histamine test carried out in the manner described by Kay (1953), but we used only 50 mg. of mepyramine maleate as the antihistamine and we collected specimens for one hour after the injection of histamine. Titration was carried out with decinormal NaOH to pH 7.4 in a direct-reading pH meter, and the results were expressed as the total milli-equivalents of acid secreted in one hour (mEq/hr.) after the injection of histamine (Bock, 1961a). The normal range for men would appear to be 15–30 mEq/hr. (mean 22.4 mEq/hr.) and for women about 5 mEq/hr. less (mean 14.6 mEq/hr.) (Bruce *et al.*, 1959).

Results

In the 77 subjects given caffeine as gastric stimulant the azure A test indicated the presence of acid (positive result) in 51 and apparent achlorhydria (negative result) in the other 26 (Table I). None of the positive results