gastro-intestinal side-effects, preferred mecamlamine. This is probably partly attributable to freedom from injections, but also to the freedom from occasionally incapacitating episodes of hypotension.

Suggested Scheme of Treatment

Our results indicate that mecamlamine is an effective hypotensive substance. Although we have been unable to compare the effects of parenteral with oral administration, it is clear that mecamlamine is usually effective by mouth in smaller doses than other ganglion-blocking agents. However, it must be emphasized that, because of the long action, it is desirable to use caution in selecting patients for treatment with this substance. Where there is doubt about the safety of reducing the blood pressure, as in those with coronary ischaemia, cerebral vascular disease, or impaired renal function, cautious dosage with parenteral hexamethonium should be used until it has been established that the blood-pressure reduction is safe. In patients with impaired renal function, the action of mecamlamine may be extremely prolonged, so that a single daily dose, or occasionally a dose every two days, may be used. Other factors may also prolong the action: M. D. Milne (personal communication) has found that the excretion of mecamlamine in man is enhanced by the administration of ammonium chloride and diminished by the administration of alkalis or acetazolamide.

In general, however, the ideal dosage scheme seems to be the administration of two equal doses at 12-hour intervals. The initial dose should not exceed 2.5 mg. twice daily; increments of 2.5 mg. should be added until an effective hypotensive result has been obtained. We prefer not to increase the dose more frequently than at three-day intervals, for we have the impression that the full hypotensive effects of an increased dose may not become apparent for two to three days. In addition, severe gastro-intestinal effects seem less frequent when this dosage scheme is adopted. The dose range in our patients was from 2.5 to 50 mg. twice daily. In most cases the dose was between 10 and 25 mg. twice daily.

The treatment of hypertensive patients with mecamlamine can be readily instituted in out-patients, provided that facilities for measurement of the blood pressure over several hours in the standing position are available. When in-patients are treated it may be found that after discharge from hospital readjustment of the dose is necessary. In our experience out-patients usually required smaller doses than when they were in hospital.

The incidence of constipation is so high that we have found that prophylactic routine administration of laxatives is an advantage. We now give a nightly dose of pil. aloes, and a morning dose of a saline laxative, instructing the patient to adjust the dose until a daily bowel motion is obtained. The administration of parasympathomimetic drugs is sometimes helpful.

Combination with other drugs may help to reduce the incidence of side-effects. We have insufficient evidence to comment on this possibility.

Summary

The hypotensive action of a ganglion-blocking secondary amine, mecamlamine, has been studied in 45 hypertensive patients.

Oral administration leads to falls of blood pressure lasting for 12 hours or more. The hypotensive action seems predictable and acute hypotensive episodes are unusual.

Little if any tolerance occurs.

The side-effects, particularly alimentary, are also prolonged, and four patients preferred parenteral pentolinum.

Our experience suggests that in spite of the frequency of side-effects the advantages of oral administration, prolonged hypotensive action, and predictability of response make this substance the most convenient and reliable hypotensive agent so far available.

We are indebted to Messrs. Merck, Sharp and Dohme for generous supplies of mecamlamine, and to the physicians of Hammersmith Hospital for permission to study their cases.

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PERITONEOSCOPY

AN EVALUATION, WITH REPORT OF 136 CASES

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In some cases of abdominal disease the diagnosis remains in doubt even after the most detailed investigations, and the problem is solved only at laparotomy. Little is lost by operation in such cases if they prove to have a lesion amenable to surgery, but in medical or inoperable conditions unnecessary laparotomy carries a mortality and morbidity of its own. In certain lesions, particularly of the liver and peritoneum, peritoneoscopy offers the opportunity to look inside the abdomen without the risk of operation. It is the purpose of this paper to consider the place of peritoneoscopy in diagnosis and to analyse a short experience of 136 cases.

Peritoneoscopy consists in the inspection of parts of the peritoneal cavity with an instrument similar to a cystoscope, which is introduced through a cannula. In order to give the telescope "elbow room," air is introduced into the peritoneal cavity to form a "bubble," a litre or more in volume. It is only the structures which lie at the surface of this air bubble or project into it which can be seen. The position of the air bubble can be shifted by tilting the patient to bring into view different parts of the abdominal wall and different fixed organs (see Fig. 1). It is generally true to say that only the anterior surface of the liver, the parietal peritoneum of the anterior abdominal wall, and the omentum can nearly always be viewed. The gall-bladder and anterior surface of the stomach are often seen. An enlarged spleen is sometimes visible. By tilting the patient into a steep Trendelenburg position, the uterus and Fallopian tubes, and sometimes the ovaries, can be inspected. For other organs peritoneoscopy is not a useful examination, and the intestinal tract cannot be systematically searched for lesions, even though several coils of bowel may be in view.

Technique

Fig. 2 illustrates the appearance of the peritoneoscope and shows its resemblance to a cystoscope. The examination is

done in an operating theatre, under either general anaesthesia or local analgesia, though the former is preferable. The patient's abdomen is prepared and towelled as for a laparotomy. An incision $\frac{1}{4}$ in. (6 mm.) long is made in the skin, in the midline and close to the umbilicus, and a small trocar and cannula are pushed into the peritoneal cavity. The requisite amount of air is then introduced, preferably with a pneumoperitoneum apparatus, and the small trocar and cannula are withdrawn. The large trocar and cannula, illustrated in the lower half of Fig. 2, are then thrust into the peritoneal cavity. The trocar is withdrawn and the sheath into which the telescope has been introduced is passed through the cannula. The electrical lead is fitted on, and the examination conducted.

This brief description of the technique is not meant for those who intend to perform the examination for the first time; it has been expanded elsewhere (Handley, 1955).

FIG. 1.—Field of view of the peritoneoscope.

Indications

Peritoneoscopy is of most value in diseases of the liver, particularly with hepatomegaly or jaundice, and for ascites of unknown cause. It is sometimes useful for deciding the operability of malignant disease in the abdomen, particularly in the stomach, where a demonstration of hepatic or peritoneal deposits from a primary growth which is not causing much distress will contraindicate laparotomy. Peritoneoscopy may also be useful in the diagnosis of abdominal masses. In doubtful ectopic pregnancy, in pelvic tumours, in tuberculous peritonitis, and in splenomegaly it is sometimes of help. As Ruddock (1949) has pointed out, peritoneoscopy should not be done without a definite indication and the procedure should not be expected to accomplish more than the purpose for which it is done.

Personal Series of Cases

In the past nine years peritoneoscopy has been done on 136 patients. The examination as a technical exercise failed in four cases and in eight others a satisfactory view was not obtained because of adhesions or obesity. In 124 the procedure was technically successful. There was no mortality and the only complications met with were minor ones—a haematoma of the abdominal wall in one patient, continued leakage of ascitic fluid in four patients, and implantation of carcinoma in the puncture in a patient with malignant ascites. In two cases in which the examination failed, laparotomy was done because a perforation of the bowel was suspected, but it was not in fact found.

Grouping.—The 136 examinations have been grouped according to the part which peritoneoscopy played in establishing the diagnosis, as follows: (1) Where diagnosis was uncertain and was made by peritoneoscopy (38 cases). (2) Where the clinical diagnosis was confirmed (45 cases). (3) Where peritoneoscopy was helpful—for example, in excluding or confirming metastasis from a diagnosed primary tumour (18 cases). (4) Where a faulty but firm clinical

FIG. 2.—The upper instrument is the sheath of the peritoneoscope. It carries the lamp; and the fore-oblique-vision telescope which is illustrated below it fits inside it. Below are the large trocar and cannula. Through the latter the sheath and telescope are introduced into the peritoneal cavity.

diagnosis was altered by peritoneoscopy (7 cases). (5) Where the examination was unsuccessful or unhelpful (21 cases). (6) Where the examination was misleading (7 cases).

Table I amplifies this grouping and shows the conditions for which peritoneoscopy was performed. It will be seen that the examination was useful in over three-quarters of all cases, or in nearly 90% of those in which it was a technical success.

In our opinion peritoneoscopy proved its worth in the diagnosis of liver disease. There were in our series 58

TABLE I.—Value of Peritoneoscopy in the Light of the Final Diagnosis in 136 Cases

Final Diagnosis	No. of Cases	Value of Peritoneoscopy					
		Helpful (108 = 79.4%)				Unhelpful (28 = 20.6%)	
		Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Secondary carcinoma of liver	34	13	13		3	2	3
Cirrhosis of liver	24	10	8		4	2	
Secondary carcinoma of peritoneum	18	9	6			1	2
Carcinoma of stomach	15	1	4	8		2	
Carcinoma of pancreas	14	1	11			2	
Cholecystitis	5		1	2		2	
Carcinoma of ovary	4	2				2	
Cystic liver disease	3						1
Polycythaemia	3			2		1	
Carcinoma of colon	2		2				
Carcinoma of gall-bladder	2			2			
Steatorrhoea	2			1		1	
Abdominal pain	2					2	
Myeloid leukaemia	1						1
Miscellaneous	7			3		4	
Total	136	38	45	18	7	21	7

patients with cirrhosis or secondary carcinoma of the liver. In 23 of these the true diagnosis was in doubt until peritoneoscopy demonstrated cirrhosis in 10 and secondary carcinoma in 13. In seven other cases of hepatomegaly, three were shown to be due to secondary carcinoma when cirrhosis had been the firm clinical diagnosis, and in four cirrhosis was revealed after secondary carcinoma had been diagnosed. In a further 21 cases peritoneoscopy confirmed the clinical diagnosis.

There were 18 cases of peritoneal carcinomatosis, and the diagnosis was made or confirmed in 15 of these. In only one case of carcinoma of the stomach was the diagnosis made by peritoneoscopy, when an unsuspected primary tumour was seen; but in 12 others confirmatory evidence of the primary growth or its spread was obtained, in eight the primary tumour actually being seen. The evidence elicited in the cases of carcinoma of the pancreas was necessarily indirect (because the pancreas cannot be seen) and was confined to verifying or diagnosing enlargement of the gall-bladder, obstruction of the liver, and the presence of secondary deposits: in one case it made the diagnosis and in 11 yielded confirmation. In diseases of the gall-bladder peritoneoscopy was not particularly helpful. In five cases of cholecystitis and two of carcinoma of the gall-bladder, the latter was not seen in five cases owing to the presence of adhesions. The numbers of the remaining conditions in Table I for which peritoneoscopy was done are too small to require comment.

Of the 28 failures of peritoneoscopy, 12 were technical and have already been mentioned. Of the 16 remaining, no helpful information was obtained in nine, and in this category are included cases where clinical hepatomegaly was verified but no further light shed on its cause. In seven patients the information obtained by peritoneoscopy proved to be false. Of these, three had liver metastases and two had peritoneal deposits which were not seen at peritoneoscopy. One patient with polycystic disease of the liver was misdiagnosed as having cystic new growth, and the remaining error was to regard white mottling of the spleen as due to tuberculous peritonitis when in fact it was a manifestation of myeloid leukaemia. The two latter mistakes were errors of interpretation and due to the observer, not the instrument.

In Table II peritoneoscopy is considered under its main clinical indications. This table shows that hepatomegaly, jaundice, ascites, and an abdominal mass were the main

TABLE II.—*Value of Peritoneoscopy in Relation to its Main Clinical Indications. Some Patients Showed More than One Clinical Indication*

Indication for Peritoneoscopy	No. of Cases	Value of Peritoneoscopy		
		Helpful	Unhelpful	Misleading
Hepatomegaly (all causes) ..	49	40	5	4
Jaundice	28	24	4	
Ascites	24	17	7	
Abdominal mass	14	10	2	2
Assessment of operability ..	34	31	3	
Total ..	149	122	21	6

indications for which the examination was done, and, since some patients showed more than one of these signs, they are listed under more than one heading, and thus the numbers do not tally with those in Table I.

In the estimation of operability in 34 patients with malignant disease, peritoneoscopy showed widespread metastasis in 13 and thus saved a needless laparotomy. In 21 the absence of widespread deposits encouraged the surgeon to operate, though in fact three patients were then discovered to have liver metastasis which had not been seen through the peritoneoscope. In two of these the deposits lay deep in the liver substance and were recognizable only by palpation.

We have performed a peritoneoscopic biopsy in eight cases, taking tissue from the parietal peritoneum in two

and from the liver in six. All specimens have yielded a satisfactory histological diagnosis. In one patient the peritoneoscopic appearances suggested a low-grade peritonitis, but the peritoneoscopic biopsy showed invasion of the affected areas by undifferentiated carcinoma. There have been no complications due to biopsy.

Discussion

There is no doubt that peritoneoscopy is a less dangerous and less uncomfortable procedure than diagnostic laparotomy. McHardy, Browne, and Edwards (1947) recorded a mortality of 12%, and Cayer and Sohmer (1955) 19%, for diagnostic laparotomy in patients with severe liver damage. In contrast to this, 4,606 peritoneoscopies collected from papers by Ruddock (1949), Anderson, Dockerty, and Waugh (1950), Benedict (1951), and Hegstrom, Zoeckler, and Keil (1953) showed a total of 10 deaths (0.2% mortality). Although these figures are not strictly comparable because the peritoneoscopy patients would not all have had severely damaged livers, the contrast between them is very striking. Peritoneoscopy also has a great advantage over laparotomy as a diagnostic procedure in that the patient occupies a hospital bed for a much shorter time. Against these advantages of safety and saving of time must be set the more limited information which can be obtained, because in practice only the liver and parts of the peritoneum can be readily seen, and even then they cannot be palpated.

The chief dangers of peritoneoscopy are from perforations of bowel and from haemorrhage. It might be thought that pushing a large trocar into the peritoneum must often result in perforation of the bowel, but this is not so unless the bowel is anchored to the abdominal parietes by adhesions. The adhesions which cause the mishap also limit the spread of intestinal contents, and Ruddock had no mortality from the eight bowel perforations which he records in his 2,500 examinations. In the selection of a site on the anterior abdominal wall through which to pass a peritoneoscope it is clearly desirable to avoid old scars. A patient known to have many adhesions in the peritoneal cavity is likewise unsuitable for peritoneoscopy, not only from the danger of introducing the instrument but also from the very limited view likely to be obtained inside. It will have been noted that perforation did not occur in our series.

Haemorrhage does not constitute much of a hazard unless biopsy is added to peritoneoscopy. Biopsy greatly enhances the value of peritoneoscopy, but it is a dangerous business in unskilled hands because of the difficulty in checking haemorrhage. Though more dangerous than needle biopsy, peritoneoscopic biopsy has the great advantage that the tissue for examination may be selected under direct vision and a piece of adequate size removed. In jaundiced patients the prothrombin time must be known to be normal, and this is especially important if biopsy is contemplated.

Air embolus, though known to occur in therapeutic pneumoperitoneum, seems to have been recorded only twice after peritoneoscopy, with one fatality (Jernstrom, 1951; Mullarky, 1952).

Of the 10 deaths in the 4,606 cases already quoted, biopsy was responsible for seven. Six of these patients died as a result of haemorrhage from the biopsy site and one died from biliary peritonitis following liver biopsy. Of the three deaths following straight peritoneoscopy, one was due to peritonitis, one to perforation of bowel in tuberculous peritonitis, and one to improper selection of a patient with advanced heart and lung disease. In the latter connexion it is obvious that a seriously ill patient is unfit to undergo the strain of having a litre or more of air put rapidly into the peritoneum because of the embarrassment caused to the heart and lungs. If a patient's general condition forbids the use of the general anaesthetic which we employ for peritoneoscopy, that patient is unfit for peritoneoscopy even under the local analgesia which some use.

Conclusions

Our experience with peritoneoscopy leads us to believe that it is a safe, and minor, procedure which, if employed with due regard to its limitations, will give information that could otherwise be obtained only by laparotomy.

Obesity and abdominal adhesions are contraindications to peritoneoscopy because no useful information is likely to be obtained. Peritoneoscopy is unnecessary if the patient certainly needs an operation for treatment, but it may indicate the necessity for operation when this is in doubt.

Peritoneoscopy is most successful in the diagnosis of liver disease, ascites, and abdominal masses, and in estimating the spread of abdominal malignant disease. When employed for a definite indication peritoneoscopy achieves its purpose in nearly 90% of technically successful cases. Peritoneoscopic biopsy has been used in very few of our cases, but its value is unquestioned. We shall continue to use it with caution because of its dangers.

Summary

The results of peritoneoscopy in 136 patients are reported. There was no mortality, and only minor complications were encountered.

In 79.4% of all cases, and in nearly 90% of the technically successful examinations, useful diagnostic information was obtained by peritoneoscopy.

Peritoneoscopy has its chief value in diagnosing the nature of hepatomegaly and ascites. In suitable cases it saves the need for laparotomy, and is much safer, more comfortable, and more rapid, both in performance and in recovery of the patient.

Our thanks are due to the Clinical Research Committee of the Middlesex Hospital for a grant to one of us (A. W. N.), during the tenure of which the information in this paper was assembled; and to Miss Hewland, artist to the Middlesex Hospital, for the drawings.

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The National Old People's Welfare Council's *Progress Report* for the year ending March 31, 1956, records a satisfactory year. The various organizations which form the council have continued to co-operate to help the elderly, and the public has become more aware of the problem. The number of letters asking for information has increased, and the press and B.B.C. are constantly passing on to the council the inquiries they receive about elderly people. When these inquiries are frequently on the same subject the council prepares a special memorandum giving basic information. During the year a memorandum on the night attendance, home bathing, evening visiting, and laundry services for the elderly has been prepared; those on housing and chiropody have been revised. The *Progress Report* includes a list of the council's publications and their price. Boarding-out information is included in the quarterly *Bulletin*, which has now reached a distribution of 15,730. The number of local Old People's Welfare Committees is 1,205, and the whole country is covered by them on an area, regional, county, or local basis. There are now 5,000 clubs throughout the country, and no lonely elderly person need be without a friendly caller if he or she so wishes. The *Report* also includes a financial statement, list of represented organizations, and addresses of county committees. There is also a form of bequest for those who might wish to contribute. The *Report* is obtainable from the council, 26, Bedford Square, London, W.C.1, price 1s. 6d.

NEODYMIUM 3-SULPHO-ISONICOTINATE AND BLOOD COAGULATION

BY

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It has been known since 1930 that some of the rare earth metals affect blood coagulation both *in vitro* and *in vivo* (Guidi, 1930). Salts of lanthanum, cerium, praseodymium, and neodymium were found to prolong the clotting-time of whole blood on intravenous injection in animals, and to have an irreversible anticoagulant effect *in vitro* on whole blood and recalcified plasma (Dyckerhoff and Kuerten, 1936; Dyckerhoff *et al.*, 1936; Vincke and Oelkers, 1937). All the compounds used were very toxic until Vincke (1947) reported that neodymium nicotinate could be given to animals in sufficient dosage to prolong the clotting-time of whole blood without toxic effects. It was later found (Vincke and Sucker, 1950) that neodymium 3-sulpho-isonicotinate was water-soluble, neutral, and could be sterilized in ampoules; its toxicity in cats was low; and it prolonged the clotting-time of whole blood in rabbits in a dose of 50 mg. per kg.; the full effect did not become evident for six hours, and lasted for 18–24 hours. It was claimed by these workers that this compound acts by interfering with circulating prothrombin and that it may also, in very high doses, precipitate fibrinogen. The newer knowledge and improved techniques in the study of blood coagulation have enabled us to examine afresh the mode of action of neodymium 3-sulpho-isonicotinate.

Experiments

We have confirmed the observation that the compound administered intravenously to dogs, rabbits, and mice in a dose of 50 mg. per kg. greatly prolongs the clotting-time of whole blood. It also prevented coagulation when added to blood immediately on withdrawal, so that it is active both *in vitro* and *in vivo*. Intravenous injection of protamine sulphate failed to restore the clotting-time to normal in neodymium-treated animals, and the addition of thrombin in various concentrations to various dilutions of normal and neodymium-treated plasmas gave similar results. The drug, therefore, does not interfere with the thrombin-fibrinogen reaction.

In all these experiments, in spite of a great prolongation of the whole blood clotting-time, the one-stage "prothrombin" time (Quick test) showed only a moderate prolongation of 6–12 seconds, and prothrombin measured by the two-stage test (Biggs and Douglas, 1953a) was normal. The most striking abnormality was in the generation of intrinsic blood thromboplastin (Biggs and Douglas, 1953b), which was grossly impaired in the treated animals, the deficiency affecting both the plasma factor (antihaemophilic globulin) and the serum factors concerned in the reaction.

A dose of 50 mg. per kg. is far too high to be either practicable or safe for human use, and in clinical studies we gave doses that had been reported from Germany as having favourable clinical results—namely, 250–375 mg. by intravenous injection. The results were consistent, and in some important respects quite different from the results obtained in animals with much larger doses. In all instances (more than 50 injections) the clotting-time of whole blood remained normal. Once again the thrombin-fibrinogen reaction was unimpaired.