symptoms have been markedly reduced and the radiographic results no less valuable, if not quite so striking. An injection of 4 grams for a stout subject and 3 grams for one of slender build, in each case dissolved in 40 to 60 c.cm. of distilled water, may be reckoned a perfectly safe dose. We have been unable to recognize any particular benefit from special preparation, or from the regular dosage with alkalis, which was followed scrupulously in our earlier cases. We have as yet had no opportunity to test the newer drug, phenol-tetra-iodo-phthalein, which, in Graham's clinic, is found to be less toxic than the tetra-iodo-phenol-phthalein.

Conclusions.

Cholecystography is a method of real clinical value in the diagnosis of diseases of the gall bladder. Not only does it show whether the gall bladder is functioning, but also how well or how ill it is functioning. It will frequently disclose the presence of gall stones which do not show in the ordinary radiogram. It may, by showing the relation of the gall bladder to an abdominal tumour, give strong presumptive evidence as to the site of the growth and the possibilities of surgical treatment.

Using pure sodium tetra-iodo-phenol-phthalein in a dose not exceeding 4 grams, freshly dissolved, and injected intravenously very slowly, no disturbing toxic symptoms need be feared. X-ray films made twelve hours after injection and six hours later, after a meal containing fat, should give reliable evidence as to the functional capacity of the gall bladder.

The method has its limitations, and an apparently normal cholecystogram does not exclude the possible presence of a small cholesterol stone or mild degrees of infective cholecystitis.

CHOLECYSTOGRAPHY.

THE RESULTS OF 125 CONSECUTIVE CASES EXAMINED
BY THE ORAL ADMINISTRATION OF THE SALT.

BY

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THE existence of such divergent views as to the relative values of the intravenous and oral methods of cholecystography has led us to believe that our results will be of interest.

The difficulty of oral administration appears to be due to the fact that the compound is decomposed by the hydrochloric acid of the stomach, converting the soluble salt into the insoluble free acid, which acts as an irritant and may be vomited. Endeavours were made, therefore, to provide for its passage through the stomach and liberation in the small intestine, where it would be absorbed and carried by the portal system directly to the liver. Stewart¹ of New York reported recently that he had obtained successful cholecystograms by enclosing the dye in keratin-coated gelatin capsules and using x rays twelve hours later. Other observers, however, do not seem to have met with the same success, and presumably their difficulties have been due to the unreliability of the preparation used, and also to the unsuitable nature of the capsule and its coating. In many cases the drug appears to have been liberated in the stomach, and vomiting has ensued, or the coating has been so resistant to the digestive juices that the capsules have been passed on into the colon intact.

In our early cases the results were similar. A British preparation of sodium tetraiodo-phenolphthalein, made into capsules by the manufacturers, was used. The capsules were not dissolved, as many as eight and even fourteen being seen in the large bowel next morning. We next obtained capsules of the iodine salt prepared in the United States. The results obtained were good but the cost exces-

sive. Finally, an American preparation of sodium tetraiodo-phenolphthalein made up into capsules by the dispenser of the hospital seemed to be the most suitable. Different coatings were tried, but the best results were obtained by the following method.

Preparation of the Capsules.

The drug used is the sodium tetraiodo-phenolphthalein obtained from Messrs. Kodak, Ltd.; 0.3 gram of the salt is placed in a gelatin capsule, which is then given three coats of a keratin solution, made (using Merck's keratin) according to the *British Pharmaceutical Codex* formula. The capsules are allowed to dry in the air after each coat without heating. They are now prepared by a Liverpool firm of wholesale druggists from the salt supplied by Messrs. Kodak.

It is important (1) that the salt be obtained as fresh as possible and carefully stored, and (2) that the capsules be made up freshly. If capsules are kept for more than seven days the coating is not dissolved readily in the small bowel.

Technique Employed.

Twenty-four hours before administering the drug the patient is given an aperient, preferably one ounce of castor oil. On the day preceding the examination the patient takes an ordinary diet containing fats. No food is allowed after 6 p.m. and no further aperient is given. Between 9 and 9.30 p.m. the capsules are swallowed whole with sips of water. (For an average patient fifteen capsules are taken—that is, 4.5 grams of the salt.)

At 9.30 the following morning the first radiogram is taken, using the Potter-Bucky diaphragm, the patient being in the prone position. The patient returns at 12.30 p.m., and the second radiogram is taken. If the gall bladder appears normal at both these examinations the patient is told to take a meal containing fat and to return between 3 and 4 p.m. for a third radiogram. Should the gall bladder be empty or nearly so the examination is concluded. If it has not emptied, the patient is asked to return the following day. But in those cases where there is no suggestion of a gall-bladder shadow on both the 9.30 a.m. and 12.30 p.m. radiograms the examination is carried no further and a "pathological gall bladder" is reported.

If the gall bladder is normal a definite shadow is visible on the radiogram taken twelve hours after administering the dye. At the end of fifteen hours the shadow is denser and usually smaller. The radiogram taken two or three hours after the meal containing fat shows either no gall-bladder shadow or one very much reduced in size. If the gall bladder is not markedly smaller the patient is examined the following day.

Using the method outlined above cholecystography is as satisfactory as with the intravenous method, and it has the advantage that the preliminaries are very much simpler. Though the shadow with the oral method appears a little later, it is equally dense and yields equally satisfactory evidence of the form and function of the gall bladder.

It is important to realize the theoretical considerations involved in the use of this test. It demands a liver capable of secreting the dye into the bile capillaries, a patent cystic duct to allow of its passage into the gall bladder, and, finally, a mucous membrane sufficiently healthy to concentrate it by the reabsorption of water. It follows, therefore, that the normal gall bladder yields the densest shadow. At the same time it is obvious that a variety of conditions—adhesions and tumours pressing on the cystic duct or gall bladder, infections of the mucous membrane interfering with its power of concentration, thick tenacious debris in its interior—in addition to stones either in the cystic duct or gall bladder itself, can cause all degrees of variation from the normal density to complete absence of shadow. In actual practice, however, as seen from Table I, a definite and unequivocal complete absence of shadow occurs in 77 per cent. of the cases reported as pathological. Probably the only contraindications to cholecystography by this method are (1) advanced disease of the liver—for example, cirrhosis, secondary carcinoma—and (2) pyloric stenosis. Both these conditions, however, should be discovered by other methods, and there is little likelihood of their being present to confuse the issue in the type of case in which this investigation is being carried out.

Toxic Effects.

In our own series of cases we have seen no severe reactions. In two instances there was a slight rise of temperature, but in neither did it reach 100° F. Eight patients complained of nausea lasting a few hours, but only one of them actually vomited. This patient stated that she had vomited "purple material," but subsequent radiograms demonstrated a normal gall bladder which was unusually well defined on the x-ray film. Two somewhat

nervous patients vomited almost immediately after taking the capsules, which were returned whole, but this can hardly be attributed to any toxic effect of the drug. In one other case there was slight diarrhoea, the bowels acting three times during the night. All the other patients were apparently quite unaffected by the drug, and in no single instance did a patient fail to appear at the appointed time for the first x-ray examination.

TABLE I.

Group 1. Normal gall bladder outlined ...	56
Group 2. No shadow ...	53
Group 3. Irregularity or deformity ...	3
Group 4. Non-opaque stones ...	8
Group 5. Delay in emptying... ..	5

Number of cases reported abnormal ... 69

Total number of cases examined by the oral method 125

TABLE II.—Operative Findings.

Group 1:	
Confirmed as being normal	3
Contained stones	1
	4
Group 2:	
Contained stones	19
Cholecystitis without stones	2
Adhesions around gall bladder	2
Tumour involving gall bladder and ducts	1
Gall bladder found normal	1
	25
Group 3:	
Inflammatory mass at the pylorus	1
Group 4:	
Contained stones	4
Group 5:	
Dense mass of adhesions at neck of gall bladder... ..	1
	35
Total cases operated on	35
Total cases where x-ray diagnosis was confirmed ...	33
Total cases where x-ray diagnosis was not confirmed ...	2
Percentage of cases where x-ray findings were correct ...	94.3

Comments on the X-Ray and Surgical Findings.

The cases here reported were consecutive, arising in private and hospital practice, and have not been selected in any way. It will be observed that in a large number a normal gall bladder was outlined on the x-ray films. An interesting example in this group was seen in the case of a patient in whom a normal gall bladder containing three opaque stones was visualized; concentration occurred in the usual way and it also emptied after the fatty meal had been taken. From this it would appear possible for the gall bladder to function in a perfectly normal way despite the presence of stones. The patient's only symptom was occasional nagging pain under the right costal margin. The instance in this group where the x-ray diagnosis was not confirmed at operation was one of our earliest cases. Only a faint shadow was shown, but owing to our inexperience of the oral method it was interpreted as being normal. A similar finding now would undoubtedly be reported as pathological.

Of the cases falling into Group 2—that is, those where no shadow is seen—the x-ray and surgical findings point definitely to a non-functioning gall bladder. Although the x-ray finding is a negative one it is most valuable, and, if the preliminaries have been carefully carried out, can be definitely relied upon. Where the clinical signs have not been very suggestive of cholecystitis, it has been our practice to repeat the examination in those cases where no shadow was seen at the first examination. In two such instances a normal gall bladder was outlined at the second x-ray examination, the explanation in one case being that the patient had taken a breakfast of bread-and-milk before the 9.30 a.m. film was taken—the radiologist was not informed of this at the time. We were unable to account for the failure in the other case. Of the twenty-five cases falling into this group which were operated upon, the gall bladder was found to contain stones in 76 per cent.; in a further 8 per cent. there was marked cholecystitis, while in another 8 per cent. adhesions around the gall bladder were the most obvious pathological finding. In one of these latter cases, where the adhesions were merely divided and the gall bladder was allowed to remain, the dye test was repeated a fortnight later and a perfectly normal gall

bladder was revealed. In one case only of this group the gall bladder was found to be normal at operation; it was not removed, and this patient's symptoms were not relieved.

It is well known that a considerable degree of cholecystitis and even stones can exist undiscovered until the gall bladder is opened and examined, either *in situ* or after removal, and in view of this we consider it the surgeon's duty to remove the gall bladder when the x-ray evidence points definitely to disease being present in the organ, even though its external appearance seems normal.

Of the three cases occurring in Group 3 there was one example of an hour-glass gall bladder, and one where the gall bladder filled slowly and had an irregular outline. The third filled and emptied normally, but was abnormal in shape and position. The patient was operated upon and found to have a pyloric ulcer with adhesions to the gall bladder, to account for the x-ray findings.

Of the eight cases in Group 4 where a shadow indicative of non-opaque stones was seen, four patients were operated upon and the x-ray diagnosis was confirmed. Usually the stones are very definitely outlined by the dye, and in Stewart's¹ opinion this is the most positive finding of all. But in a later paper² he expresses a warning against the diagnosis of stones by mottling alone, giving his reason that small circular bubbles of gas in the duodenum often overlap the gall bladder and closely resemble non-opaque stones.

It is in Groups 3 and 5, as Graham points out, that most errors of diagnosis occur. Among our cases which fell into the latter group the gall bladder was still outlined at periods varying from eighteen to thirty-four hours, although several fatty meals had been taken by the patients. In the case of the patient operated upon there was a dense mass of adhesions at the neck. It seems probable that a similar condition will be responsible for the delay in emptying in the case of the remaining instances of this group.

It is perhaps worthy of mention that only in six instances out of our series of 125 cases were opaque gall stones seen on the x-ray films.

Conclusions.

1. The success of the oral method depends on obtaining a reliable salt, careful coating and preparation of the capsules, which must be freshly used, together with first-class x-ray technique and intelligent co-operation on the part of the patient.

2. Cholecystography by the oral method is easier than the intravenous so far as the preliminaries are concerned, and yields equally satisfactory results from a radiographic point of view.

3. The proceeding is devoid of risk, and the toxic effects are practically negligible.

4. The surgical findings confirm the x-ray diagnosis in 94.3 per cent. of the cases.

We wish to thank Dr. R. E. Roberts for allowing us to include some of his private cases, and Mr. D. Douglas-Crawford and Mr. O. Herbert Williams for permission to use the findings in the cases operated on by them.

REFERENCES.

- ¹ Stewart: *Amer. Journ. Roentgen.*, 1926, xvi, p. 234. ² *Idem, ibid.*, 1925, xiii, p. 259. ³ *Idem, ibid.*, 1926, xvi, p. 224.

EPIDEMIC ENCEPHALITIS: THE PROPORTION OF PERMANENT RECOVERIES.*

BY

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I THINK it may be said that, after the passing of the earliest outbreaks of epidemic encephalitis of which this generation of physicians has had experience (six to ten years ago), the percentage of complete recovery was estimated by most writers on the subject at 20 to 30. Later writers express a more guarded opinion and generally record a much lower complete recovery rate. My own experience has been that in every outbreak the complete

* Abstract of a paper read before the Ulster Medical Society on January 27th, 1927.