THE POST-GRADUATE MEDICAL JOURNAL

VOL. II.

NOVEMBER, 1926.

No. 14.

CONTENTS

X RAYS IN THE DIAGNOSIS OF GALL-BLADDER LESIONS, WITH SPECIAL REFERENCE TO THE NEWER TECHNIQUE.

By ROBERT KNOX, M.D., M.R.C.P., D.M.R.E.—
(Illustrated) 17

ACUTE OEDEMA OF THE LUNGS.

By G. E. BEAUMONT, M.A., M.D., F.R.C.P.,
D.P.H. 23

ABDOMINAL TUBERCULOSIS IN CHILDREN.

By C. E. SUNDELL, M.D. 24

ERRORS OF REFRACTION, WITH SPECIAL REFERENCE TO SQUINT.

By A. F. MACCALLAN, C.B.E., M.D., F.R.C.S. . . 26

CLINICAL CASES AT THE CENTRAL LONDON OPHTHALMIC HOSPITAL.

By F. A. WILLIAMSON-NOBLE, M.B., F.R.C.S. . . 28

CORRESPONDENCE.

LECTURE-DEMONSTRATIONS IN PROVINCIAL TOWNS . . 29

EDITORIAL NOTES:—SPECIAL COURSES.—POST-GRADUATE WORK IN THE PROVINCES. 30

THE CANADIAN HOSTEL 22

THE POST-GRADUATE HOSTEL 32

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION:—OFFICERS, 1926-1927 . . 32

SPECIAL COURSES AND LECTURES 32

X RAYS IN THE DIAGNOSIS OF GALL-BLADDER LESIONS,

WITH SPECIAL REFERENCE TO THE NEWER
TECHNIQUE.*

BY

ROBERT KNOX, M.D. EDIN., M.R.C.P. LOND.,
D.M.R.E. CAMB.,

HON. CONSULTING RADIOLOGIST TO THE ROYAL NORTHERN
HOSPITAL; DIRECTOR, RADIOLOGICAL DEPARTMENT,
THE CANCER HOSPITAL (FREE).

X RAY DIAGNOSIS OF GALL-STONES.

THE first demonstration of the presence of a gall-stone by X rays was made by Carl Beck, of New York (1899). He detected two large stones in the gall-bladder, three similar ones in the liver, and one in the cystic duct.

In 1904 Kohler showed a large stone, the character of which he substantiated by repeated examinations. Kickuliez, in the year 1905, stated that he believed a positive result seldom obtainable; that observation is a reflection of the opinion held at that time by nearly all workers, and even to-day it still finds expression. In the following year Thurstan Holland published his first gall-stone case. He found a ring-like shadow in the right upper hypochondrium, but did not interpret it as a gall-stone, because he had never before seen anything similar. At operation two large gall-stones were found. Matthias and Felt reported two cases from Konigsberg.

At a meeting of the American Röntgen Society in 1910 Pfahler reported three positive diagnoses of gall-stones; Cole and Haenisch each reported

on the same occasion three cases. From then on more references were made to the possibility of demonstrating gall-stones. At the International Congress of Medicine, held in London in 1913, Case showed a wonderful series of negatives of gall-stones.

The claims made in America of a large percentage of successes in gall-stone demonstration by X rays excited a good deal of discussion throughout the world. In this country the possibility of demonstrating gall-stones was received with incredulity, and for a time progress was not made.

In order to prove the value of the method a number of experiments were carried out under the direction of the writer, showing that it was possible to demonstrate their presence in a considerable percentage of the cases examined in which gall-stones were afterwards found. At the conservative estimate of 38 per cent. of the Mayo Clinic the value of the X ray method is great.

The next important development in gall-stone diagnosis by X rays was made by Leonard and George, who indicated the indirect method. Briefly, this method depends upon the pressure effect of a distended gall-bladder upon adjacent hollow viscera, when the latter are made visible by an opaque material in their interior. George describes a half shadow, which is caused by pressure of the distended gall-bladder upon the duodenum in its first and second parts. Kirkland in a large measure substantiated the observations of Leonard and George.

The next advance, and perhaps the greatest of all, is due to Graham, Cole, and Copher, who used a compound of tetrabromphenolphthalein. This is opaque to X rays, and when injected in a vein is evacuated in the bile; accumulating in the gall-bladder it shows an outline of that organ. The tetraiodophenolphthalein is more suitable, and is now generally used. These salts, or a compound, can be used intravenously or by the mouth—the oral method.

* Read at the Cancer Hospital, July, 1926; also in part at a discussion on *Etiology and Diagnosis of Gall-stones*, Medical Society of London.

METHODS OF EXAMINATION AND TECHNIQUE.

There are, therefore, now three recognised methods for the investigation of gall-bladder conditions. Of these the oldest and best known is :—

(1) The *Direct*.—That is the demonstration on a photographic film of a shadow of the gall-stones. The percentage of accuracy claimed varies from 38 per cent. at the Mayo Clinic to between 80 and 90 per cent. by Leonard and George. The latter, however, use the direct and the indirect methods.

(2) The *Indirect*.—This was first advanced by Leonard and George, and confirmed to a large extent at a later date by Kirkland. The principal feature in this method is the demonstration of a pressure effect upon the adjacent parts of the stomach and duodenum and the colon. This effect is produced by the distended gall-bladder exerting a pressure deformity. This may be seen sometimes in the colon without the aid of opaque material (Fig. 7), but as a rule it is necessary to fill the stomach and duodenum and colon with opaque material before it can be seen.

(3) The use of an opaque salt administered (a) intravenously, or (b) orally, and evacuated in the bile.

HISTORY OF DEVELOPMENT OF THE NEW METHOD.

Abel and Rowntree, working on the pharmacological actions (1910) of some of the phthaleins and their derivatives, showed that many of them were evacuated in large part in the bile. Hence they had been used as a means of determining the functional capacity of the liver. It occurred to Graham, Cole, and Copher that it might be possible to obtain X ray shadows of the gall-bladder if substances were used which were opaque to the rays, and contained a nucleus identical with, or closely allied to, phenolphthalein, with which iodine or bromine atoms had been combined. Experiments were begun by these workers in the summer of 1923. The first substance used was tetraiodophenolphthalein of the following formula (Fig. 1) :—

FIG. 1.

The free acid and the sodium salt were both used. Experiments on dogs followed, and it was shown that cholecystography was possible. In 1924 pure tetraiodophenolphthalein was used with less disturbance than with the earlier and impure compounds, and then it was used on the human subject by intravenous injection. A large group of compounds has been experimented with by the authors, but finally they selected the tetrabromophenolphthalein and tetraiodophenolphthalein

compounds for a standard technique. This was used in the first experiments by intravenous injection of the salts.

FIG. 2.

Normal gall-bladder. Oral method.

SUMMARY OF THE PAPER BY GRAHAM, COLE, AND COPHER.

1. Cholecystography, a new principle in the diagnosis of lesions of the biliary tract, has been introduced, consisting of the use of substances which, after entering the blood stream, are largely evacuated in the bile, and render the gall-bladder opaque to the rays.

2. At present the most satisfactory substance for clinical use is sodium salt of tetraiodophenolphthalein. The technique of its use is described. There are many other substances which are capable of rendering the gall-bladder opaque.

3. This principle may be capable of application to the roentgenologic visualisation of other organs, if opaque substances, which are specifically secreted by such organs, can be found.

4. The method of cholecystography owes its chief value as a diagnostic agent to the fact that it is a sensitive test of the functional activity of the gall-bladder.

5. As a method of diagnosis it has been found to be correct in 96.23 per cent. of the 80 patients, upon whom it has been possible to test by means of an operation.

Pharmacology.—This was carefully worked out in regard to the reactions of the two substances. Doses of about half the tetraiodo give relatively the same shadow as the tetrabromophenolphthalein. This practically eliminates the toxic effect.

Tetrabromphenolphthalein has a molecular weight of 634, and it contains about 50.4 per cent. of bromine. In contrast with this the tetraiodophenolphthalein has a molecular weight of 634, and it contains about 61 per cent. of iodine. The difference is due to the fact that the atomic weight of iodine is 127, while that of bromine is 80, and it is because of this fact that equally good shadows can be obtained with much smaller doses of the iodine compound than with the bromine compound. Practically the entire bromine content of tetrabromphenolphthalein can be recovered in the bile after injection.

Experimental work on dogs led to these conclusions: 1. Injections into the venous system are followed by a transient fall in blood pressure of about 15 mm. of mercury in the dog. 2. Both substances are non-irritating when applied to the skin; in any considerable concentration, however, they will produce necrosis when injected into the subcutaneous or muscular tissues. 3. Shadows of the gall-bladder may also be obtained after the administration of the substance by the mouth. This has been elaborated by Dr. Stewart and Dr. Ryan, of New York, who have published several papers on their work. [By the courtesy of Dr. Stewart a number of slides from their cases were shown.]

Technique.—Opinions vary in regard to the preliminary technique, but the majority of workers prefer to have the patient prepared for the examination by a mild

the stomach and the duodenum may be completely empty. The injection is made between 8.30 and 9 A.M. The pulse, respiration, and blood pressure are taken; if the latter is below normal, add 0.5 c.cm. of a 1 in 1000 solution of adrenalin chloride to the tetraiodo solution. If the pressure is high, do not examine the case until it is brought down to the normal.

It is customary to use 0.045 g. of tetraiodo per kilo of body-weight in a 2 per cent. solution in freshly distilled water. The solution is sterilised for 15 minutes in a hot-water bath, and then allowed to cool to a temperature at which the intravenous injection can be made immediately.

Radiograms are taken at 4, 8, 24, and 36 hours after the injection.

6. The unpleasant toxic effects have been practically eliminated.

THE ORAL METHOD.

The oral method is not quite so reliable as the intravenous, but it is practically free from any of the disadvantages of the latter; for example, it is a fairly safe method for the investigation of patients in the out-patient department, while the intravenous is a purely hospital procedure.

FIG. 3.

FIG. 4.

Multiple small gall-stones, showing change of position of the stones in two negatives, 3 and 4.

aperient, such as castor oil (40 to 50 g.) 48 hours before the examination. The following morning a warm linseed enema, at 45° Centigrade, is given with a rectal tube, and repeated 24 hours later. The diet is light porridge of cereal (wheat, rice, oatmeal, &c.), beginning these 48 hours before the test. Stewed fruit and black coffee are permissible. Milk and other proteid foods are suspended.

This regimen is kept up until 10 o'clock of the night before examination, after which the patient is allowed nothing at all to eat up to the hour of the injection, in order that

Dr. Stewart and Dr. Ryan have published papers which show clearly the advantages of the oral method. They indicate simple preparatory methods, and give liquorice the night before the examination, followed by a simple enema on the next morning. A preliminary examination in the usual way is next made about 10 A.M. The usual lunch is allowed. At 6.30 P.M. the following meal is

allowed: A thick soup, creamed chicken, baked potato, bread-and-butter, and a glass of milk. The abundance of fat in this meal will completely

FIG. 5.

Multiple small gall-stones.

empty the gall-bladder in one to two hours. It is then in a receptive condition for the opaque bile. Commencing at 9 P.M. two capsules containing 5 gr. of tetraiodophenolphthalein are given with a wine-glass of water, every 15 minutes until eight capsules are taken.

The patient reports at the department 12 hours later, at 9 A.M. the following morning, with an empty stomach, no breakfast being allowed. A series of negatives are taken. Four hours later, at 1 P.M., the examination is repeated. Regular lunch is allowed at 1.30 P.M., followed by re-examination an hour later. The patient reports on the following morning for a final examination.

Up to the present they have examined 147 cases. In not one has there been a severe reaction.

Wilkie and Illingworth, of Edinburgh, report a series of 63 cases by the intravenous method, and also state that they have noticed no severe reaction. Dr. Roberts, of Liverpool, has also published a paper on the results obtained with the intravenous method. Dr. McLean, of Glasgow, and Dr. Brailsford, of Birmingham, have shown some excellent results obtained by the intravenous method.

EFFECTS OF THE DRUG.

The following symptoms may occur after the administration of the drug: (1) a fall of the blood pressure; (2) headache; (3) nausea; (4) vomiting; (5) pain in the back; (6) diarrhoea. The iodophenolphthalein in the dose usually given appears to cause less disturbance than the tetrabromophenolphthalein.

The new method, which we owe to American workers, is full of promise; its chief use will be for the demonstration of the functional activity of the liver and gall-bladder. In this field there exists a wide range for research on physiological lines. Future developments may indicate methods for the investigation of other organs, such as the kidney.

The demonstration of the presence of gall-stones is aided by the use of the dye, for it will be seen that stones, not previously detected, may be shown when the opaque material is in the gall-bladder. The negative shadow described by a number of workers in the past becomes more readily shown.

The use of the method will be of great service in determining the presence of malignant disease.

FIG. 7.

Gall-bladder, showing pressure deformity of the first part of the duodenum. Note large gall-stone at the distal end of the gall-bladder. A, gall-stone; B, remains of gall-bladder; C, duodenal cap.

in the gall-bladder. Imperfect filling of the gall-bladder, with marked irregularity of the outline of the opaque shadow, should rouse suspicion of the condition.

INTERPRETATION OF RADIOGRAMS.

If the technique has been carefully carried out, a normal gall-bladder will show the following reactions. Usually about the fourth to the seventh hour after the injection a faint but definite outline of the gall-bladder appears, which is seen to have the contour of the normally shaped organ, but to be somewhat larger than the normal gall-bladder usually seen at laparotomies (Fig. 2). At the end of 24 hours the shadow is much more distinct, but contracted down to about half the earlier size. From then on until the forty-eighth hour the shadow diminishes in size and fades gradually. Abnormalities reveal themselves in various ways. A failure to obtain, after carefully following the prescribed technique, a shadow of the gall-bladder has invariably indicated the presence of a definite pathological condition of the biliary tract.

In our zeal to adopt the new method, we must not, however, overlook the

FIG. 6.

A large gall-bladder, showing gall-stone (A) impacted at cystic end of gall-bladder and non-opaque gall-stone (B). C, fundus of gall-bladder; D, deformity of colon—adhesions between gall-bladder wall and colon; E, gas-distended colon.

(A)

FIG. 8.

(B)

FIG. 8 (A).—Radiogram of gall-bladder containing gall-stones after removal. A, typical gall-stone shadow; B, non-opaque stone (negative shadow); C, pultaceous opaque material at fundus.

In Fig. (B) the non-opaque stone has been forced upwards by pressure. Note the effect of pressure upon the shadow at the fundus.

great value of the direct method. At the low estimate given from the Mayo Clinic of 38 per cent., the value of the method is incontestable. With advancing technique it is possible that a greater percentage may be recorded. Leonard and George, for example, claim up to 80 per cent. of successes. My own figures approximate to those of the Mayo Clinic.

It is hoped that if a moderate advance in technique could be made, at least 50 per cent. of the cases in which gall-stones are present will be demonstrated. In support of this claim, a number of cases in which the diagnosis has been made by the direct method are shown (Figs. 3, 4, and 5). The diagnosis was proved to be correct by operation.

The cases are selected to show the types of gall-stones recognisable by a careful examination and scrupulous technique. If radiologists would apply themselves to the technique, and most carefully scrutinise the films, they would find an increasing percentage of accurate diagnoses.

The new method will be most useful in the more difficult cases, in which non-opaque gall-stones are present; these, by the ordinary method, only show signs when the stomach, duodenum, and colon are filled with opaque food, and these signs are at the best not very reliable. The pressure deformity shadow described by Dr. George is an example of the type in which the visualisation of a pathological gall-bladder should at once prove the value of this observation.

It must not be overlooked that occasionally a normal gall-bladder, if full of bile at the time of the examination, does show in a good-class radiogram. If such a bladder is again examined by the new method, the value of the previous observation will be strengthened.

The value of the new method is indicated by the following case. A diagnosis was made by clinical methods, and on examination by X rays no evidence of gall-stones was found. Tetraiodophenolphthalein given orally showed a distended gall-bladder, with, near the cystic end, a number of small "negative" shadows in the general opacity of the gall-bladder shadow. A positive diagnosis of gall-stones was made. At operation this was confirmed; the gall-bladder with the stones was removed. The doctor in charge of the case kindly supplied me with a description of the conditions found. "Thirteen or fourteen small gall-stones were removed. Several of the largest measured one-twelfth of an inch in diameter."

There can be no doubt, when all the methods available are used with a careful technique, aided by skill in interpretation, that the diagnosis of diseases of the gall-bladder and bile-ducts has been placed upon a surer foundation, and that few cases in which pathological conditions exist should now escape our notice. It is for the clinician to help us in the investigation of the interesting points which are at present obscure.

CONCLUSION.

In conclusion, allow me to illustrate the value of the X ray method by quoting a case recently examined. The patient was sent for an examination of the colon, with a suggestion of possible obstruction in that organ. A barium enema was given. The hepatic flexure showed in the area adjacent to the gall-bladder a deformity with irregularity of the outline. Above this area, and well away from the barium shadow, a rounded shadow was seen. This was diagnosed as a gall-stone. A tentative diagnosis of a colon lesion was given, and a request made for an examination of the whole tract by an opaque meal (Figs. 6, 7, and 8).

The duodenal cap on its outer surface showed a very definite pressure deformity, typical of a

gall-bladder pressure effect. In the centre of the gall-bladder area a negative shadow was detected. This clearly indicated the presence of a non-opaque gall-stone. Continuing downwards from this stone was an irregularly shaped shadow of considerable density, the lower limit of its outline defined the fundus of the gall-bladder. It was seen distinctly that the colon adjacent to it was deformed, the half shadow described by George being beautifully seen. Near the cystic duct the definite outline of the gall-bladder stone referred to above was seen.

It was thought that this stone was impacted in the cystic end of the gall-bladder, and was probably occluding the opening of the cystic duct; to prove this point a dose of tetraiodophenolphthalein was given orally. At the examination no opacity due to the dye getting into the gall-bladder was seen.

The diagnosis was now fairly established: (1) gall-stone impacted near the cystic duct; (2) pressure deformity of the duodenal cap; (3) pressure deformity of the hepatic flexure of the colon and probably adhesions between the colon and the fundus of gall-bladder; (4) the presence of a non-opaque gall-stone.

Mr. Ernest Miles, who operated on the patient, kindly sent on the gall-bladder, and notes of the operation stated that there was an adhesion between the gall-bladder and the colon. The gall-bladder was X rayed before opening it. The shadows seen in the radiograms in vivo were shown distinctly.

This might be described as a classical case, in which the points ascertained by the X ray examination were typical of the value of the direct and the indirect methods, and further it indicated the value of the new method, in so far as it demonstrated that the opening of the gall-bladder was obstructed.

THE CANADIAN HOSTEL.

On Oct. 30th another addition to the hostel system in Paris came into action in the Canadian Students' Hostel. This is situated in the south of Paris near the Parc Montsouris, adjacent to the Hostel for Belgian Students and to the French Students' Hostel, which was started in the summer of 1924. As we understand negotiations are in progress for the building of other hostels for workers from other countries, including the United States, all of which, it is anticipated, will be grouped in the same district.

The Canadian Hostel is intended not only for medical post-graduates, but also for those following, among other things, law, literature, and theology. The building has three storeys containing 45 rooms, all suitably fitted. On each floor there are several bath-rooms and on the ground floor there is a large hall, also a restaurant.