

overlying part of the abdominal wall to which it was adherent could be removed in one piece. There were numerous adhesions between the gall-bladder and the omentum; these were not broken down, but the gall-bladder was freed by dividing the omentum between ligatures. It was then found that the growth had passed beyond the gall-bladder and had invaded the adjacent part of the liver, and accordingly a wedge-shaped piece was excised from the right lobe, its base measuring about two and a half inches. The wound in the liver was closed by means of catgut sutures. The subsequent progress of the case was uneventful with the exception of an attack of bronchitis which slightly retarded convalescence. The wound healed by first intention.

The specimen was composed of the gall-bladder and the adherent omentum, the overlying part of the liver, and part of the cystic duct. The walls of the gall-bladder were very much thickened and were obviously the seat of malignant disease which extended into the cystic duct. The growth projected into the cavity of the gall-bladder and partly filled it. There were no gall-stones in the gall-bladder or bile-ducts. Microscopically the growth was a columnar-celled-carcinoma.

Two similar cases have been reported. Lawford Knaggs<sup>3</sup> operated upon a woman, aged 69 years, in September, 1902. The gall-bladder was distended to the size of a fist and contained foul-smelling fluid with some pus. A single stone was felt in the cystic duct. This was squeezed back into the gall-bladder and was removed. The gall-bladder was very long and supple and not noticeably thickened; it was drained. The fistula persisted until the end of 1903, when it closed. Shortly afterwards the patient came under observation again on account of pain in the gall-bladder region which she thought was due to the closing of the fistula. Some thickening was felt under the scar of the old operation. On Jan. 23rd, 1904, a small incision was made over the closed sinus into the gall-bladder and some mucus and a little pus escaped. The mucous membrane was sutured to the skin. The patient ultimately died on Feb. 18th. At the post-mortem examination the walls of the gall-bladder were seen to be infiltrated with growth to the thickness of nearly half an inch, the growth extending to and involving the cystic duct. The growth involving the cystic duct had pressed upon and partially obstructed the commencement of the common duct. Above this stricture the ducts were markedly dilated and were the seat of suppurative cholangitis. No gall-stones were found. Microscopical examination of the growth showed it to be a columnar carcinoma.

Mayo Robson<sup>4</sup> performed cholecystotomy upon a woman, aged 57 years, in February, 1902. A stone was found in the cystic duct and was removed. In October, 1903, the gall-bladder and adjacent part of the liver were successfully excised. The gall-bladder was of the size of a small hen's egg and full of solid material. On incising it the swelling was found to be new growth which was infiltrating the adjacent parts of the liver.

The close connexion between carcinoma of the gall-bladder and gall-stones is now generally recognised, and Siegert<sup>5</sup> says that in 95 per cent. of cases of carcinoma of the gall-bladder and adjacent portions of the liver the malignant change is due to the chronic irritation of gall-stones. The frequency with which carcinoma of the gall-bladder has developed in connexion with gall-stones is often brought forward as one of the reasons for excising the gall-bladder in all cases when operating for gall-stones. On the other hand, when gall-stones by their irritation have given rise to carcinoma of the gall-bladder they are practically always found in the malignant gall-bladder, and it is extremely rare for carcinoma to follow cholecystotomy.

In April, 1905, G. R. Slade<sup>6</sup> published a paper containing some remarkable facts in connexion with gall-stones and malignant disease which he had observed while working in the Pathological Institute at the London Hospital. He particularly drew attention to the importance of chronic thickening of the wall of the gall-bladder, and pointed out that it should be viewed with the gravest suspicion and not lightly regarded as being due to chronic inflammation. In 12 cases the wall of the gall-bladder presented an appearance

which at the time of the necropsy was described as chronic inflammatory thickening. In five of these cases carcinoma was found on microscopical examination. The remaining seven unfortunately were not examined microscopically, but to the naked eye they presented an appearance exactly similar to that of the five cases which were proved to be carcinomatous. He added that since he began in all such cases to examine the wall of the gall-bladder as a routine, he had in no instance failed to find carcinoma.

A few weeks after the appearance of Slade's paper H. A. T. Fairbank<sup>7</sup> briefly reported a case which had been operated upon by Mr. Stanley Boyd. Two gall-stones were impacted in the neck of the gall-bladder, which was kinked. Cholecystectomy was performed as it was thought to be the most satisfactory way of dealing with the case. The wall of the gall-bladder was thickened to a uniform degree. On microscopical examination it proved to be carcinomatous.

In an excellent chapter on cholecystectomy, Moynihan,<sup>8</sup> in pointing out that one of the arguments for cholecystectomy as opposed to cholecystotomy is based on the fact that gall-stones are responsible for so many cases of primary malignant disease of the gall-bladder, says that it must be shown that carcinoma of the gall-bladder has occurred after cholecystotomy, and this the cases reported by Lawford Knaggs, Mayo Robson, and myself certainly appear to do. It is remarkable that each of these three cases should have come under notice at about the same interval after the primary operation—viz., 15, 20, and 21 months respectively, and it raises the question whether early carcinomatous changes could have been already present in the gall-bladder at the primary operation. If so, the general rule that carcinoma of the gall-bladder does not occur after cholecystotomy holds good; but even if the gall-bladder were free from carcinoma at the time of the primary operation these three cases are in such an extremely small ratio to the cases which have not developed carcinoma after cholecystotomy that they cannot be regarded otherwise than as exceptions to the general rule. They cannot alter the generally accepted indications for cholecystectomy, but only serve to accentuate the importance of carefully examining the gall-bladder in every operation for gall-stones, and of regarding cholecystectomy as an operation of necessity and not of choice if there is any thickening or ulceration of its wall, or if its appearance or consistency is in any way suspicious.

I am much indebted to Mr. C. W. Mansell Moullin and Mr. Jonathan Hutchinson, jun., for whom I was acting when these two cases were admitted to hospital, for permission to record them.

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## A CASE OF VASCULAR DEGENERATION: A STUDY IN CARDIAC ARRHYTHMIA.

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THE patient, a German, aged 66 years, from whom the accompanying tracings were obtained, went to the Westminster Hospital complaining of general weakness, of dyspnoea on exertion, and of pain in the chest. On examination he was found to be a feeble man of spare habit, whose radial arteries were decidedly atheromatous, while the pulse was very irregular. It was noticed that there were frequent "intermissions" and that at times the rate of the pulse was infrequent and at other times of normal frequency, the less frequent rate being exactly half the more frequent. The chest was emphysematous and the heart was somewhat overlapped by lung. The apex beat was about half an inch outside the normal position. On auscultation the first sound was shorter than normal but there was no added sound. Not infrequently an extra-systole could be heard—i.e., a premature feeble systolic sound followed by a long pause. Beside these there were numerous pauses or intermissions during which no feeble sound was heard. During auscultation the halved rhythm did not happen to occur. The case was diagnosed as general vascular degeneration affecting the coronaries as well as other arteries. It was considered that owing to insufficient blood-supply to the cardiac walls

<sup>3</sup> THE LANCET, April 16th, 1904, p. 1054.

<sup>4</sup> Diseases of the Gall-bladder and Bile-ducts.

<sup>5</sup> Virchow's Archiv, Band cxxxii., Heft 2, 1893.

<sup>6</sup> THE LANCET, April 22nd, 1905, p. 1062.

<sup>7</sup> THE LANCET, June 3rd, 1905, p. 1542.  
Gall-stones and their Surgical Treatment.

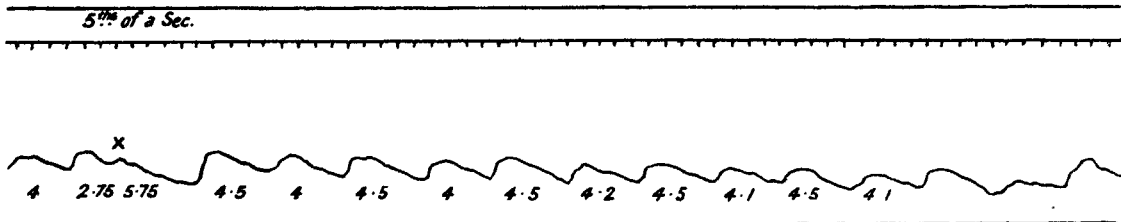


Fig. 1.  
Alternating action.

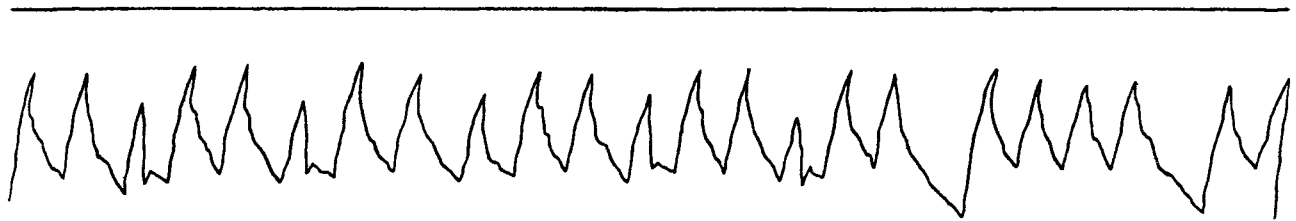


Fig. 2.  
Delayed beat after every second normal beat.

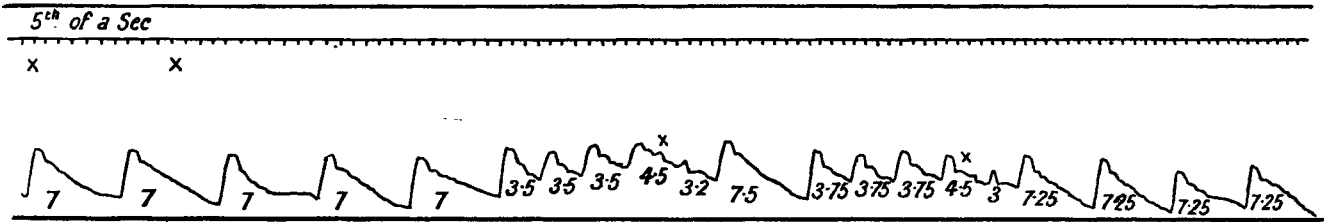


Fig. 3  
Halved rhythm.

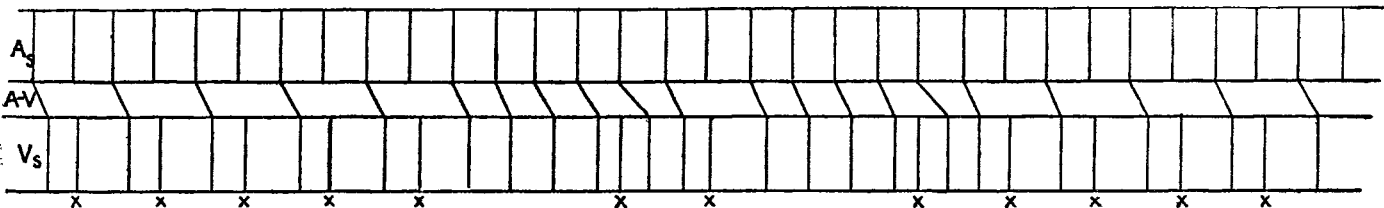


Fig. 3a  
Diagrammatic representation of Fig. 3.

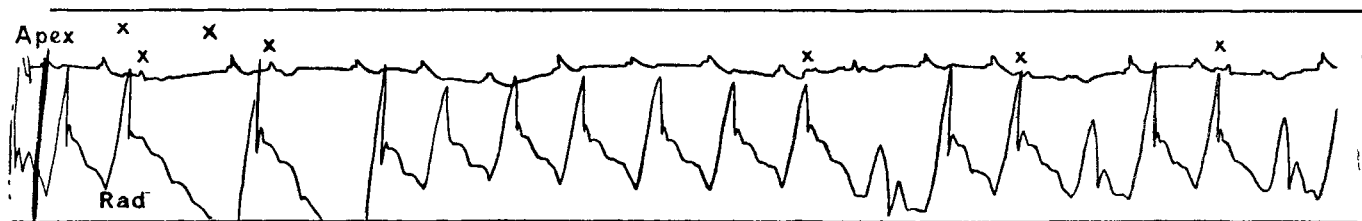


Fig. 4.  
Delayed small beats preceded by smaller beats.

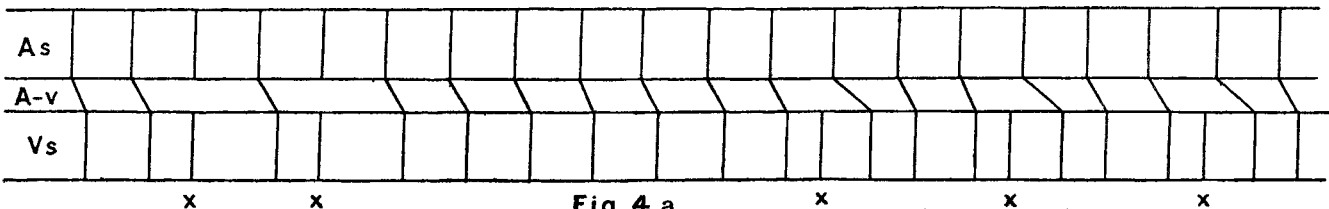


Fig. 4 a  
Diagrammatic representation of Fig. 4.

there was fibrosis of the heart and loss of contractile power in its muscle. The pain in the chest, which was partly constant, partly paroxysmal in character, brought on by exertion, was regarded as being of the nature of angina pectoris. This view was confirmed by the relief afforded by nitroglycerine.

Numerous tracings were taken from the patient, and these were interesting from the complicated nature of the irregularity of the rhythm and the difficulty in arriving at a correct interpretation of its causes. It was found necessary to take the tracings when the patient was sitting up in a chair, as the irregularity completely disappeared when he was lying down. No tracing could be obtained from the jugular vein except in the horizontal position and then not a satisfactory one; this, however, showed that the auricles were beating in their normal relation to the ventricles and that the interval between the auricular beat and the ventricular was of the normal length. Owing to the emphysematous condition of the lungs it was very difficult to get a tracing from the apex, and a cardiogram was only obtained after the patient had been under observation for several weeks. Thus at first the only tracings showing the irregularity were those obtained from the radial artery alone. From these it was possible to draw certain conclusions, but there were many doubtful points which were only cleared up by the cardiogram.

To begin with, the tracings showed a fair number of extra-systoles. In some of these the compensatory pause was complete, in others it was incomplete, which means that some of the extra-systoles were of the ventricular type, others of the auricular. The majority had, however, a complete compensatory pause, and so were of ventricular origin. An example is shown in Fig. 1, where the premature systole *x* is followed by a pause of such length that the sum of the intervals before and after it was equal to the period (8.5 fifths of a second) occupied by two normal beats. On looking at Fig. 1 another irregularity may be noticed. The beats are alternately large and small, but the pause before each small beat is longer by one-tenth of a second than that after it. The small beat here cannot be an extra-systole, since extra-systoles are always premature, whereas here the small beat is delayed. This is, then, a true alternating action of the heart, the beats occurring at regular intervals, but being alternately larger and smaller. The delay in the occurrence of the small beat in the radial is due to the fact that a feeble contraction takes longer to open the aortic valves than a strong one and takes longer to travel to the periphery; at the heart the beats occur at equal intervals of time. In animal experiments an alternating action of the heart has been shown to be due to loss of the contractile power of the muscle, and Hofmann and Wenckebach give the following explanation of its occurrence:—"Each beat of the heart destroys the contractility of the muscle and after the beat this contractility is gradually restored, but reaches its full extent before the arrival of the next beat. Slight variations in the length of the diastole make no difference in the size of the subsequent beat. Where contractility is depressed it takes longer to recover and has not fully recovered before the commencement of the next systole. Under these circumstances any increase in length of the diastole will be followed by a larger beat owing to the better recovery of the contractility; any decrease of diastole will be followed by a smaller beat. A large beat encroaches on the subsequent period of rest since it is not only larger in size but lasts longer. Hence after a large beat there is a shorter period of rest which, with depressed contractility, will cause the next beat to be small: the period of rest after this would be longer and so the next beat larger and the next pause shorter. Thus there would be alternately large and small beats occurring at regular intervals once this abnormal rhythm is started."

It is not surprising that an alternating action is specially prone to start with the large beat that occurs after the long compensatory pause after an extra-systole, as is the case in Fig. 1. An alternating action of the heart is thus a valuable sign of depressed contractility in human beings and its presence in this case confirms the view that the contractile power of the cardiac muscle is deficient.

In other tracings from the patient, as in Fig. 2, a small delayed beat is found after every second normal beat instead of there being an alternating action. Theoretically, it is difficult to account for this small beat as being due to

depressed contractility unless there were some outside influence—e.g., nervous—which rhythmically lessened the contractility. Vagus influences are known to depress contractility, and Mackenzie<sup>1</sup> has recorded cases where small beats from depressed contractility occur quite irregularly. There is, however, another difficulty with regard to this interpretation of Fig. 2; the delay before the small beat is exceptionally long, longer than would be expected from the comparative slowness of its transmission to the wrist. In Fig. 2 are also shown some pauses, double the length of the normal pulse period, which might possibly be due to the small beat being too small to reach the wrist or to the small beat being entirely left out. In other tracings (see Fig. 3) there is a halved rhythm which one might explain as an alternating action where the small beat was either left out or too small to reach the wrist. Such a halved rhythm can be obtained with depressed contractility in animal experiments, being preceded by an alternating action in which the small beat gradually gets less and less. In human beings cases have been recorded of isolated intermissions of the pulse apparently due to loss of contractile power in the cardiac muscle, but so far no case of a halved rhythm due to this cause has been described, although its possibility has been acknowledged. Against this interpretation it might be urged that to produce a halved rhythm the contractility would have to be very gravely depressed, and yet my patient was capable of walking about. In two places marked *x* in the tracing Fig. 3 it will be noticed that a delayed small beat occurs and that in the first of these there appears to be another small beat before the delayed one. This is, however, not certain. The numbers below the tracing indicate the pulse periods in fifths of a second.

Fig. 4, in which a tracing from the apex was at last obtained, clears up all obscurities. Here several examples of delayed small beats appear and in each case the cardiogram shows that the small beat is preceded by another smaller beat, which is not large enough to produce a wave at the wrist. These beats, marked *x* in the apical tracing, are evidently interpolated extra-systoles. Interpolated extra-systoles are rare, but Mackenzie has shown that they do occur, particularly in senile hearts. The reason for the delay in the beat after these interpolated extra-systoles is that the conductivity has not fully recovered in the auriculo-ventricular bundle, so that the stimulus takes longer to pass across it, while the small size of this next beat is due to the contractility not having fully recovered. In the early part of Fig. 4 are two apparent intermissions. The apex tracing shows that here also an extra-systole is present, but this is later in its occurrence than the interpolated extra-systoles. Still the extra-systole is too small to give a wave at the wrist. Owing to the comparative lateness of this extra-systole the next stimulus from the great veins and auricles finds the properties of the ventricular muscle insufficiently recovered for a response to take place and a beat is left out, there being a full compensatory pause as usually occurs in ventricular extra-systoles. These points can be perhaps better appreciated from the diagrammatic representation of Fig. 4 given in Fig. 4a, where *A*s represents the auricular systole, *A-V* the auriculo-ventricular interval, and *V*s the ventricular systole. Here the marked lengthening of auriculo-ventricular interval after the interpolated extra-systoles is well shown. This tracing favours Mackenzie's view that extra-systoles start from the primitive cardiac tissue (i.e., the auriculo-ventricular bundle and its continuations) and that the cause of the compensatory pause after a ventricular extra-systole in man is that in these cases the conductivity of the bundle is depressed and has not sufficiently recovered to let the next stimulus through. It is just possible, however, in this case that the compensatory pause may be due to the contractility of the ventricles not having sufficiently recovered after the extra-systole. The explanation of the halved rhythm in this patient is evidently that it is in reality a bigeminal action of the heart, the second of the coupled beats not being large enough to reach the wrist. This is shown in the diagrammatic representation of Fig. 3 given in Fig. 3a.

This patient was evidently suffering from fibrosis of the heart, probably associated with atheroma of the coronaries. In consequence of this the contractile force of the muscle

<sup>1</sup> Mackenzie: Diseases of the Heart, p. 210

was deficient, leading to the pulsus alternans and to the attacks of angina pectoris. The fibrosis had probably invaded the *a.-v.* bundle, causing an increased irritability and hence numerous extra-systoles arising in the primitive tissue of which the bundle is composed. An important point to observe is the difficulty of the interpretation of the radial tracing alone, whereas when a simultaneous tracing was obtained from the apex to compare with the radial, the causation of the irregularity became quite clear.

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## SOME APPLICATIONS OF THE PRECIPITIN REACTION IN THE DIAGNOSIS OF HYDATID DISEASE.<sup>1</sup>

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AND

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*Results previously obtained.*—In January, 1908, two of us<sup>2</sup> published an account of our experience with the precipitin reaction in hydatid disease, and quoted nine consecutive and unselected cases of hydatid invasion in all of which a well-marked precipitin reaction was obtained. In eight of these cases blood from the hydatid patient was collected in sterile glass pipettes on the morning of the day of operation; the hydatid fluid or cysts were obtained in sterile flasks in the afternoon; the patient's serum and the hydatid fluid were allowed to stand overnight in a cool chamber; and the test was made next morning about 24 hours after the blood had been collected. Control sera from healthy persons were taken at the same time as the sera to be tested and were kept in the same manner. From six to 12 drops of serum were shaken up with one cubic centimetre of clear hydatid fluid, precautions to minimise bacterial infection being taken, and the tubes were allowed to stand for 24 hours at room temperature before the precipitates were read. In these circumstances, with one exception, the patient's serum never failed to give a positive reaction with the hydatid fluid removed from his tissues. The single exception, however, yielded a precipitate when the patient's serum was tested with the hydatid fluid obtained from another patient. While this was our usual procedure, we also tested the serum of some of the patients, collected before operation, with hydatid fluids taken from other patients, and we obtained positive precipitin reactions in cases in which subsequent operation revealed undoubted hydatid invasion, and negative precipitin reactions in doubtful cases in which at operation hydatid cysts were not found. Notwithstanding our small series of cases, the fact that in every case the presence of the reaction corresponded with the presence of hydatid cysts, and the absence of the reaction with the absence of cysts, led us to the conclusion that in the precipitin reaction we had a valuable aid to the diagnosis of hydatid disease. We must, however, emphasise the fact that this striking evidence of the correlation of a specific precipitin reaction with hydatid invasion was obtained in the most favourable conditions of experiment, since usually the serum and the hydatid fluid were taken from the same patient and tested within 24 hours, or, when the serum and the hydatid fluid were obtained from different patients, the hydatid fluid had not often been kept for more than a few days.

*Object of the present paper.*—It was obvious, however, that if the test was to be of general value as a means of diagnosis we must have a method of storing for considerable periods of time hydatid fluid in such a form that it would be capable of giving a well-marked reaction with the sera of patients suffering from hydatid disease, and that it would not yield any reaction with sera obtained in other conditions of disease. Our present communication, which is of the nature of a progress

report, deals mainly with the interactions of hydatid fluids (*a*) not derived from the patient whose serum was being tested, (*b*) of longer standing than those used in our first series of cases, and (*c*) subjected to various methods of treatment in order to preserve them in a sterile condition for many months. The conditions of experiment were, therefore, less favourable than in our first series of cases, and we may at once state that in this second series the amount of the precipitum in positive cases was on the whole smaller than in our first series, and that some cases of hydated invasion failed to give a satisfactory reaction with the hydatid fluids employed by us. Nevertheless, in no single instance did we obtain a positive reaction where hydatid invasion was afterwards proved not to exist, and we were able to give a positive diagnosis in some cases in which the clinical evidence was on the whole opposed to the probability of hydatid disease, our diagnosis being confirmed by subsequent operation.

*Data on which paper is based.*—Exclusive of control observations, this paper is based on 50 precipitin reactions tested in regard to 36 patients known or suspected to harbour hydatid cysts. Of these patients 20 were definitely proved to be infested by hydatids and 30 precipitin tests were carried out in regard to them in addition to the usual controls. The analysis of these 30 reactions, the nature of the hydatid fluids employed, and the results obtained constitute the substance of our paper. We may note, however, that of the other precipitin tests 11 were conducted with the serum of ten patients from whom hydatids were in all probability absent, since an operation, or the subsequent history, revealed the presence of some other condition (new growth, suppuration, calculus, &c.) sufficient to account for the symptoms. In all of these cases the precipitin reactions were negative. The remaining nine precipitin tests were made with the serum of six patients in whom an operation, or the progress of the case, was inconclusive as regards the presence or absence of hydatid invasion. Of these doubtful cases two gave a slight positive reaction and four a negative reaction. Since the diagnosis was doubtful we have not dealt further with this group of cases.

### List of 20 Cases Investigated in which Conclusive Evidence of Hydatid Invasion was Obtained at Operation or Otherwise.

- Case 1.—Male, 23 years; large single cyst of liver with clear contents.
- Case 2.—Female, 40 years; multiple suppurating cysts of liver.
- Case 3.—Female, 24 years; hydatid of liver.
- Case 4.—Male, 39 years; multiple cysts in muscles of back; cysts densely matted and packed with minute secondary cysts.
- Case 5.—Female, 12 years; multiple cysts of kidney.
- Case 6.—Female, 26 years; large single cyst of liver with clear contents.
- Case 7.—Male, 26 years; multiple cysts in kidney of at least ten years' duration.
- Case 8.—Male, 69 years; multiple small cysts in liver.
- Case 9.—Male, 39 years; cyst on under surface of liver compressing portal vein and simulating cirrhosis of liver.
- Case 10.—Female, 18 years; large cyst of liver with clear contents.
- Case 11.—Male, 31 years; cyst behind liver.
- Case 12.—Male, 11 years; suppurating hydatid in left iliac region.
- Case 13.—Male, 42 years; large cyst of liver with clear contents.
- Case 14.—Female, 50 years; large, shrunken, degenerated cyst of liver with caseous, bile-stained contents.
- Case 15.—Female, 28 years; medium cyst of liver with clear fluid contents.
- Case 16.—Male, 42 years; hydatid of liver.
- Case 17.—Male, 35 years; hydatid of lung (?); no operation was performed, but patient coughed up a piece of hydatid membrane.
- Case 18.—Female, 12 years; cyst of liver with clear fluid contents.
- Case 19.—Female, 49 years; multiple cysts of liver, spleen, and peritoneum.
- Case 20.—Male, 22 years; large cyst of liver with clear contents.

*Analysis of the precipitin reactions obtained with various hydatid fluids tested with the sera of the patients in whom the presence of hydatid cysts was conclusively proved.*—The tests may be arranged in the following groups according to the nature of the hydatid fluid employed in the interactions.

*Group I.*—In this group of seven tests we repeated the methods adopted in our previous investigation of allowing the serum of the patient to interact with the fresh untreated hydatid fluid taken from the cysts harboured by himself, or with similar fluid collected from another patient. In every instance but one definite evidence of a precipitate was obtained in 24 or 48 hours at room temperature. In two cases the precipitate was very slight, but distinct in comparison with the control tubes; in two cases the precipitate was well marked; and in two it was massive. In one case of long-standing hydatid invasion, Case 7, the reaction was indeterminate.

1. One cubic centimetre of fresh hydatid fluid from Case 4 interacting with nine drops of serum from the same case taken just before operation gave a well-marked precipitate.

<sup>1</sup> Communicated to the Australasian Medical Congress, Melbourne, October, 1908.

<sup>2</sup> Welsh and Chapman: Australasian Medical Gazette, 1908, and THE LANCET, May 9th, 1908, p. 1338.