accurate for routine use, besides having certain definite advantages. The possibility of pills remaining unabsorbed or being vomited was checked by a screening of the abdomen and radiological examination of any vomit. The dyes used had been the sodium salt of tetrabromophenolphthalein and tetraiodophenolphthalein prepared by Mallinckrodt of St. Louis, and in a few cases the sodium salt of tetraiodophenolphthalein prepared by Martindale of London; in all cases solutions were prepared a few hours before use and pills not more than ten days. Ill effects had been insufficient to cause any alarm, and in 20 per cent. of cases there was no reaction at all. In the oral cases the unfavourable sequels were limited to nausea, vomiting, and diarrhoea. Nausea was transient as a rule, but had once lasted for ten hours in a case where the gall bladder did not fill, and where three stones were found at operation. Vomiting was never severe and never exceeded three times. The largest vomit was in a case where the dye had been dissolved in 60 c.cm. of water. In no case was the vomit stained with the dye. For some time all vomits were x-rayed as a routine, and their density was compared with an equal thickness of tap water as a control, but without detecting the presence of any dye. Diarrhoea was limited to two or three loose motions and was never severe. No indication could be found to show which patient would have a reaction and which not. The impression gained was that the reaction was more likely to occur when the dye was old and in patients whose liver function was impaired. In no case had the test been omitted because of the general condition of the patient, and their experience as to ill effects was contrary to that expressed recently at a discussion in London. In practically all cases a small barium meal had been given at twenty-four hours; one film was taken with the patient lying on the left side and the tube in front of the patient working horizontally. In this way information was obtained as to pressure effects of the gall bladder on neighbouring hollow viscera and the mobility of the gall bladder was ascertained. With cholecystography they could determine in at least 90 per cent. of cases whether the gall bladder was healthy or not. There were some border-line cases, and only time and experience would settle the group into which these cases would fall.

Dr. Anderson showed slides to illustrate some findings confirmed by operation; in all cases the dye was given by the mouth.

Sir BERKELEY MOYNIHAN (Leeds), in congratulating Professor Graham on the great advance that had been made by the introduction of cholecystography, said that in their hands examination by Graham's method had given accurate results in 92 per cent. of cases. He disagreed with some of the observations as to the value of estimating the cholesterol content of the blood. In their early experience they found that as a rule in cases of cholelithiasis there was an increased amount of cholesterol in the blood; 85 per cent. of cases showed an amount above the mean normal, 65 per cent. over the high normal, and 2 per cent. an amount below the low normal. The presence of hypercholesterolaemia, especially when cholesterol crystals were found in the bile extracted from the duodenum, appeared to have a certain diagnostic value. In the last series of 81 cases they had extended their inquiries. They had examined both the cholesterol and the calcium content of the bile, the blood, the gall-bladder wall, and the stones; they had taken into close consideration the stage which the associated pathological conditions in the gall-bladder wall and in the stones themselves had reached. A short interval only elapsed between the examination of the patient's blood before operation and the examination of the gall bladder and its contents.

There was a clear difference between the conditions found in the early stages of cholelithiasis and those found in the late stages. In the early stage an excess of cholesterol was found in the blood, in the bile, and in the gall-bladder wall; there appeared to be a cholesterol "flood" or "high tide." The gall bladder had the property of abstracting cholesterol from the bile, which was heavily charged with it. If the gall bladder was removed early it might present the "strawberry" appearance which he had described

twenty years ago. This appearance was due either to a deposit of cholesterol crystals on the mucosa or to an excess of lipid in the wall of the gall bladder. If this state continued, and if it was preceded or accompanied by infection, the formation of gall stones occurred. These consisted at first almost entirely of cholesterol, as both chemical and radiological examination would prove. In a later stage of the disease, when the stones had caused injury to the gall bladder, which showed evidences of thickening and fibrosis, the conditions were changed. The flood of cholesterol had passed; the high tide was then followed by a low tide. There was no longer an excess of cholesterol in the blood, for the gall bladder, because its mucosa was destroyed, had lost its power of abstracting it from the bile. The chronic irritation of stones had caused the appearance of calcium in the bile, in the gall-bladder wall, and in the blood. Hypercholesterolaemia was changed for hypercalcaemia; and the stones removed from the gall bladder contained calcium. It was interesting to note that a large proportion of private cases fell into the early group, whereas a large proportion of hospital cases occupied the later group. If this view was correct, that the gall bladder extracted cholesterol from the bile, then removal of the gall bladder in patients with hypercholesterolaemia should result in a considerable reduction of the amount of cholesterol in the blood. This they found, on examining cases of cholecystectomy at periods of six months or more after operation, was invariable.

Sir HUMPHRY ROLLESTON (Cambridge) referred to the possibility that although the normal gall bladder might have little, if any, function in the direction of contraction, it might so operate when it was the site of chronic inflammation and accompanying muscular hyperplasia of its walls. He suggested that the good clinical effects following the use of a diet in which cholesterol-producing foods had been reduced to a minimum might be due to some factor other than the cholesterol content. He was not optimistic enough to believe that medical treatment would be able, at any rate for a long time, to eliminate the need for cholecystectomy.

Professor EVARTS GRAHAM, in reply to a question as to the occurrence of "bad arms" at the site of injection, admitted that cases of thrombophlebitis were occasionally seen; he applied heat at once if pain was present. Such cases, however, were rare in skilled hands, and with a new preparation that he was now trying he hoped they might be rarer still.

THREE CASES OF CHANGED REACTION TO TUBERCULIN FROM POSITIVE TO NEGATIVE.

BY

ROBERT CARSWELL, M.A., M.B., Ch.B.,
WANDSWORTH.

In the literature of tuberculin comparative charts of the reaction before and after treatment are rare; indeed, specimens of negative charts alone are not common, owing no doubt to the widespread prevalence of latent tuberculosis making it comparatively uncommon to obtain negative reactions in practice. If it can be shown that a positive general reaction can be converted by specific treatment into a negative reaction, after a sufficient interval of time has been allowed to elapse to eliminate the immediate effect of tuberculin immunity, an important step will have been taken towards a valuation of the tuberculin test comparable to that of the Wassermann test in syphilis, and the diagnosis and treatment of tuberculosis will become practicable in the very earliest stage of all—that of infection with minimum pathological changes. The following three cases point in this direction. In the first case it seems fairly clear that the specific treatment was responsible for the conversion of positive to negative reaction. In the second, immunization was only carried to 0.4 c.cm. bacillary emulsion (2 mg. bacillary substance); and in the third, which was carried to 4 c.cm. (20 mg.), a long period

elapsed between the first positive test and the two subsequent negative tests. The tedious and laborious nature of these investigations, and the long intervals which must elapse in trials of this sort, will, I hope, justify the publication of only three cases in support of the above proposition.

Chart 1 was obtained in the case of a young man whose general health was reasonably good; the complaint for which he sought advice was a persistent, slightly painful, obscure affection of the wrist, apparently of no great importance so far as his general health was concerned. The decided positive constitutional reaction unexpectedly obtained led on careful physical examination to the discovery of slight but distinct physical signs at the right apex. Further importance was given to these facts by a history that the patient had suffered a few years previously from a run-down condition accompanied by a persistent cough, which was thought by his medical attendant to have "touched the lung," although a few months' residence in the country appeared to have re-established his health satisfactorily and cleared up the signs.

Acting on the assumption that this man harboured a tuberculous focus which for the time being was causing no disease in a clinical sense, a wide view was taken of the situation, and thorough treatment, specific and otherwise,

alterations in the living tissue at the time of the first chart had, by the time of the second, either been destroyed, or so encapsulated by fibrous or calcareous bounds as to be to all intents and purposes outside the body or out of organic relationship with it.

The same sequence of events is illustrated by Charts 3 and 4. The patient in this instance was a member of a family of which one sister was suffering from chronic pulmonary tuberculosis. The patient herself had drifted into a run-down condition accompanied by persistent cough, which, especially owing to a knowledge of her sister's disease, was giving rise to some anxiety. The tuberculin test,

which gave hardly a trace of reaction to the first injection (0.001 mg. T.K.), gave a distinct reaction to the second (0.002 mg.), and a pronounced reaction to the third (0.005 mg.). No physical signs were discovered in the chest, but, as before, importance was attached to the test; constitutional and specific treatment was carried out, the maximum dose on this occasion being 0.4 c.cm. (2 mg.), and after an interval of fourteen months from the conclusion of specific treatment the test was repeated, with the negative result shown in Chart 4.

While the temperature record in Chart 4 is not entirely below 98.4°, it is to be noted that the time covered by the

CHART 1.

CHART 2.

CHART 3.

CHART 4.

was carried out for a period of twelve months. The specific treatment consisted in the subcutaneous injection of progressively increasing doses of Koch's bacillary emulsion, beginning with approximately 0.001 mg. and ending, in the course of about eleven months, with 4 c.cm. B.E. (= 20 mg. solid substance), and carried out more or less in accordance with Koch's final directions for this treatment. The remainder of the treatment was ordinary general care at home. A period of seventeen months from the conclusion of specific treatment having been allowed to elapse, the second test was undertaken for the purpose of comparison, when the completely negative Chart 2 was obtained.

Only when a complete explanation of the meaning of the tuberculin reaction is established will the full significance of these two charts in the medical history of this individual be appreciated. The view to which I adhere, but which for the time being I am not critically discussing, is that at the time of the first chart this patient was suffering from latent tuberculosis, probably at the site indicated by the physical signs, and possibly elsewhere, causing no distinct appearance of bodily ill health, but implying the presence of living tuberculous tissue in active relation with the body fluids, and capable of extension; while at the time of the second chart the negative result indicates that such living tuberculous tissue had been obliterated. That is to say, the tubercle bacilli formerly present and causing the usual

CHART 5.

CHART 6.

later part of the chart was pre-periodic, that event occurring on May 14th. Further, the record of 99° on June 1st was on the third day after the injection; the record of 99.8° on June 6th was also on the third day; that of 99.4° on June 10th was on the second day, and the full test dose of 0.01 mg. on June 13th was followed by still less appearance of disturbance.

Here again the assumption is that in June, 1906, this patient harboured tubercle bacilli in organic relation with the body tissues and fluids, capable of development, and entailing danger of the development of disease similar to that of her sister, while by May, 1908, this condition had been obviated and no such danger remained.

One more example of the same sequence of events is presented. Chart 5 shows a sharp reaction to a medium test dose of 0.005 mg. In this case there were no distinct focal signs of disease,

although there was certainly a depressed general condition of health. As in the other cases, enough importance was attached to the result of the test to cause steps to be taken to eradicate the infection indicated, which steps consisted in the administration of B.E. up to a maximum of 4 c.cm.

Chart 6 shows the result of a test undertaken after a period of thirteen months from the conclusion of treatment. Here the dose, which had previously caused a sharp reaction with a temperature of 102.6°, resulted on March 28th in a

temperature of only 99°, without constitutional disturbance, in marked contrast to the previous result, while the other test doses of the series were followed by no temperature disturbance at all. This test was repeated twelve months later, with five-day intervals between the injections, instead of two as on the previous occasion (Chart 7).

On this occasion likewise there was nothing approaching a reaction; a temperature of 99.2° on June 3rd was on the fifth day after the first injection and previous to the administration of the second one. A temperature of 99° on June 10th was on the second day after the third injection, and neither of these, nor any of the other

CHART 7.

injections, was accompanied by other than quite trivial symptoms.

The points intended to be brought out in this communication are the striking changes in reactivity to tuberculin in the above cases, together with the means whereby these changes were brought about, and the inferences to be drawn therefrom.

A positive general tuberculin test is a matter of very great practical importance as it is capable of revealing disease at a time when it can be comparatively easily dealt with, and when specific treatment with large doses of tuberculin is easy, safe, and effective.

HEART DISEASE IN CHILDREN.

BY

G. ARBOUR STEPHENS, M.D., B.S., B.Sc.LOND.,
CONSULTING CARDIOLOGIST, KING EDWARD VII WELSH NATIONAL
MEMORIAL ASSOCIATION.

THE results of an investigation into one series of 30 cases of heart disease in children are given in the hope that they will be of some service to those who are interested in this important subject. The cases were sent to the clinic with the object of allowing me the opportunity of determining to what extent there were certain conditions common to those children who were suffering from carditis.

From the accompanying case notes it will be observed that there is a marked liking for acids, especially vinegar, amounting oftentimes to a perversion of appetite. Together with this partiality for acids there is in many cases a great dislike for milk. The aggravation of the choreic movements said to take place in Case 1 after partaking of acids is very strikingly direct. Puffiness of the gums is also a very common factor pointing to a constitutional disturbance closely associated with the alimentary canal. Many of the children are in the habit of biting their nails—a habit indicative of an irritable state of the nervous system, and one which might be said to be preliminary to a choreic condition.

In connexion with these results it may be useful to draw attention to some statistics I collected from the schools under the Swansea Education Committee, of which I have the honour to be chairman.

No. of children examined	...	8,638
No. who disliked milk	...	944=10.9%
No. of nail-biters	...	3,154=36.5%
No. of acid takers	...	5,469=63.3%
No. of those whose gums bleed on cleaning	...	2,392=27.6%

Amount of milk available=0.34 of a pint per head of population.

It will be seen that the condition of a large number of these children can hardly be said to be satisfactory; in fact, such a large amount of nail-biting and gum-bleeding might be described as factors closely associated with a predisposition.

One item in the case notes—namely, “Cardioscope 1— $\frac{1}{2}$ ” —must be defined. The usual chest-piece of a stethoscope is barely an inch in diameter, and covers a limited part of the cardiac area. I use a chest-piece nearly 3 inches in diameter, and as a result I find the sounds in a healthy child almost of the same quantity, which I mark “1—1.” When the second sound varies and the quantities are unequal, I mark them accordingly “1— $\frac{1}{2}$ ” or “1— $\frac{1}{4}$ ” as the case may be. Sound quantity is much easier to estimate than sound quality unless the observer has a musical gift. The assumption that medical students are gifted musically is responsible for a wrong conception of

1. Taken with 1-inch receiver from patient sitting up.
2. Taken with 1-inch receiver from patient lying down.
3. Taken with 3-inch receiver from patient sitting up.
4. Taken with 3-inch receiver from patient lying down.

heart sounds on the part of medical men generally. The instrument with this large chest-piece I call a “cardioscope.” That such a variation in size of chest-pieces produces different results the accompanying cardiographic diagrams amply testify.

Heart Cases Examined at the Clinic.

1. Aged 9. Had a fall in January, 1925, followed by a rash, and six days later by chorea. She is fond of acids and every time she takes any the chorea is aggravated. She dislikes milk. Left tonsil enlarged and chest narrow. There is no diaphragmatic breathing, and the heart is displaced outwards; no murmur. Cardioscope 1— $\frac{1}{2}$.
2. Aged 5. Tonsils enlarged, adenoids present, and a discharge from both ears. Can take milk, but is very fond of oranges. Heart thrill and mitral murmur present. Cardioscope 1—.
3. Aged 10 $\frac{1}{2}$. Is stated to have had chorea in November, 1924, when “the movements were slight and the heart sounds rough.” Complains of pains and aches in legs and feels tired. Is fond of vinegar, lemons, and salt. The gums are puffy; there is no heart murmur. Cardioscope 1— $\frac{1}{2}$.
4. Aged 13 $\frac{1}{2}$. In November, 1924, the first sound was stated to be “rough.” Is fond of vinegar. Gums are puffy; he bites his nails; chest moves badly during respiration. After exercise the first sound is rough. Cardioscope 1— $\frac{1}{2}$.
5. Aged 8. When examined in July, 1924, and February, 1925, she is stated to have had a “loud systolic bruit.” She gets no milk or proper food. Gums puffy; loud systolic murmur. Cardioscope 1—.
6. Aged 8. In 1922 had chorea and in 1923 had chorea and rheumatic fever. Takes no milk but is fond of vinegar. Complains of pains in legs. Bites nails; gums puffy; systolic murmur. Cardioscope 1—.
7. Aged 10. Stated to have had chorea in 1922, when “the first sound was coarse.” In July, 1924, heart normal. Is fidgety about her food. Gums puffy; tonsils and cervical glands enlarged; no murmur. Cardioscope 1— $\frac{1}{2}$.
8. Aged 7. Stated to have had a “soft systolic murmur” in February, 1924, and March, 1925. Very fond of vinegar. Gums puffy; marked mitral murmur. Cardioscope 1—.