heart size of 2 cm. (Fig. 2, C and D). It is thought that this episode was due to pericardial effusion and not to heart failure.

Case 2

A boy of 10 was admitted four weeks after the onset of his first known attack of rheumatic fever. He had loud murmurs, and a skiagram showed moderate generalized enlargement and slight hilar congestion (Fig. 3, A). The temperature was 103° F. (39.4° C.), sedimentation rate 134 mm. per hour, and white count 19,000, with 80% polymorphs; the venous pressure was raised, the liver was enlarged, and there were rales at the lung bases. In view of the hilar congestion and the absence of radiological evidence of effusion, he was thought to have failure and was put on to digitalis. Four days after admission he developed a left pleural effusion. There was then some slow improvement in his general condition, but his venous pressure was still raised after eighteen days, when digitalis had to be stopped as there was electrocardiographic evidence of first-degree heart-block. His slow improvement continued despite stopping digitalis, and his venous pressure returned to normal seven days later.

A review of his chest skiagrams at this time showed that a pericardial effusion had developed during the first two weeks of admission; the heart size had increased by 2.5 cm. over 17 days (Fig. 3, A and B). There is little doubt that many of his abnormal signs had been due to this effusion and not to failure, and that this accounted for the high fever, raised sedimentation rate, and polymorph leucocytosis at the onset, and, later, the signs of fluid at the left base and failure to respond to digitalis. One week later he was put on to cortisone on account of persistent signs of rheumatic activity. On the eighth day of starting treatment he became dyspnoeic, the liver became enlarged, the venous pressure rose, and there were many coarse rales throughout both lungs; the sedimentation rate and temperature were normal and a skiagram showed marked hilar congestion but no change in heart size (Fig. 3, C).

A diagnosis of heart failure precipitated by sodium retention was made; he was given mersalyl at once and put back on to digitalis. There was a good response to mersalyl; 48 hours later the clinical signs of failure had disappeared and there was no radiological evidence of congestion, though the heart size remained unchanged. It was then possible to continue cortisone therapy, but he was kept on digitalis until 14 days after the hormone had been discontinued; at no time did any further signs of failure develop. Skiagrams later showed a gradual resolution of the effusion, and the heart returned to the same size and shape as it had been on admission (Fig. 3, D).

Summary and Conclusions

Heart failure in rheumatic carditis is thought to be less common than has been previously supposed; in many cases the signs of so-called heart failure are due to pericardial effusion. The ways of distinguishing between heart failure and pericardial effusion are discussed. Chief among them are high fever, raised sedimentation rate, and polymorph leucocytosis in effusion as compared with subnormal temperature, low sedimentation rate, and normal white blood count in failure; peripheral oedema, ascites, and sometimes liver pulsation in failure but not in effusion; rapid changes in heart size and shape in effusion but little change in failure; and a good response to digitalis and other treatment in failure and no response in effusion. Heart failure is rare except in patients with well-marked murmurs and cardiac enlargement who have often had long-continued preceding rheumatic activity, whereas effusion may occur when there is little or no other evidence of heart involvement and not infrequently within four weeks of the onset of a first attack.

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THE GENERAL PRACTITIONER AND THE CHILD WITH HEART DISEASE*

BY

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It has long been recognized that certain medical problems can be tackled more satisfactorily by a team than by a man working on his own. As early as 1888 the British Medical Association published the results of a collective investigation into acute rheumatism, and included an inquiry into the influence of home and social conditions (Whipham, 1888). The value of joint studies has also been recognized by the College of General Practitioners, which is actively fostering research and seeking to provide facilities for its prosecution.

With this encouragement it is tempting to face the challenge written in 1952, as a commentary on the first European Congress of Cardiology. "Judging by the papers at the Congress, cardiology is more concerned with 'ends' than with 'beginnings' of disease; for, apart from one paper on the inheritance of benign essential hypertension, aetiology was ignored. . . . If research were planned logically, then the major effort would centre round the aetiology and prevention of rheumatic heart disease, atherosclerosis, and hypertension" (*Lancet*, 1952). And, to quote from a more recent leading article on congenital heart disease, "Surgery has improved the chances of these patients; but even so the outlook is gloomy enough to make us want to know more about causation" (*Lancet*, 1953).

Our surgical colleagues have made possible remarkable advances in the treatment of cardiovascular disease, but we must not allow their brilliant achievements to upset our sense of proportion. Only a small fraction of children with congenital heart disease can benefit from surgery. The same is true of patients with rheumatism. When 1,000 rheumatic children were observed for a period of 20 years, 117 developed mitral stenosis, but only 12 of these had significant pulmonary hypertension (Bland and Jones, 1951), and none needed valvotomy. The problem of rheumatism is medical, not surgical, for after 20 years 301 of the 1,000 patients were dead (87% of the deaths being directly or indirectly attributable to rheumatism) and another 139 were more or less severely crippled by their cardiac disability.

To the general practitioner heart disease seems to begin at 40, since until then defects of function are compensated by the body's powers of resistance; afterwards cardiovascular disease becomes increasingly manifest (R. J. F. Pinsent, 1954, personal communication). This is not wholly the result of essential hypertension and atherosclerosis, for the Registrar-General's returns

*A paper given before the Birmingham Division of the B.M.A. on February 16, 1954.

show that chronic rheumatic heart disease kills almost as many persons now (9,106 in 1952) as it did 10 years ago (10,459 in 1942). Quite a lot of the cardiovascular diseases of the forties is acquired in childhood. The child with heart disease is a challenge to us to find out what causes rheumatism and Bright's disease and congenital deformities of the heart.

Investigators all over the world have for years sought the solution to these questions. Perhaps some of the answers will be found, not by those who work in hospitals and laboratories, but by the general practitioner—in the homes of his patients.

Incidence

Little is known about the relative frequency of rheumatic and congenital heart disease in childhood. Any one practitioner is likely to count amongst his patients not more than five or six children with heart disease.

Rheumatic fever seems to be a dying disease. The wards of children's hospitals are no longer full of rheumatic children, and rheumatic schools are not now hard pressed to accommodate patients seeking admission. There has been a sharp decrease in deaths attributed to acute rheumatic fever and chorea—a decline of more than 60% between 1942 and 1952 (893 and 328 respectively). Nevertheless it is possible that we are being misled, and that the impression of a decline in rheumatism is false. Being less severe—like scarlet fever—it may be less readily recognizable, and if this be true the incidence of chronic rheumatic carditis will not necessarily decline. Patients with mitral stenosis often have such mild rheumatic fever that they deny ever having had the disease. Unfortunately there is no specific test for rheumatism, and there is no doubt that we sometimes fail to recognize the condition when we meet it.

Parkinson's (1945) plea that rheumatic fever should be compulsorily notifiable resulted in the introduction of local notification. The records obtained until the end of 1950 were analysed (Hewitt and Stewart, 1952), and the figures suggest that the annual incidence of rheumatic fever amongst schoolchildren in this country is now about 69 per 100,000. This compares with an American estimate of 31.5 per 100,000 for people of all ages (Collins, 1948). In 1939 2.6% of London schoolchildren had rheumatic heart disease (Bach *et al.*, 1939), and in 1952 it was calculated that in different parts of America between 0.1 and 6.0% of schoolchildren were afflicted (Schwentker, 1952). Each year between 3,900 and 5,000 children in England and Wales have their first attack of rheumatic fever (Conybeare, 1951; Hewitt and Stewart, 1952). Even though rheumatic fever may seem to be decreasing, it cannot be ignored.

The frequency of congenital heart disease is also difficult to determine with accuracy. Amongst Birmingham children

*Incidence of Heart Disease in Childhood in Toronto, 1948
(Modified from Keith, 1951)*

	0-5 Years	5-15 Years	Total
Children	56,000	74,000	130,000
Rheumatic heart disease	3 (1)	117 (4)	120 (5)
Congenital heart disease	139 (30)	151 (3)	290 (33)

Figures in parentheses refer to deaths.

(MacMahon *et al.*, 1953) the incidence has been shown to be at least 3.2 per 1,000 live births. Post-mortem studies (Brown, 1950) show a considerably higher incidence, amounting to 2% or more in childhood. There seem to be as many children with congenital heart disease as with rheumatic carditis. The Table shows the position as it was recently in the city of Toronto, where all forms of heart disease in childhood are notifiable (Keith, 1951). It might be expected that congenital heart disease would be commoner than rheumatic heart disease in children under

the age of 5, but it is not so widely recognized that congenital heart disease is as frequent as rheumatic heart disease in children of school age, and that throughout childhood it is a commoner cause of death.

Congenital Heart Disease

Congenital heart disease is almost always due to arrested foetal development during the period of organogenesis in the first three months of pregnancy. The hazards from an attack of maternal rubella in the first trimester have been amply confirmed since the first classic reports from Australia (Gregg, 1941; Swan *et al.*, 1943). Although the search for other agents was immediately stimulated, most investigations have been retrospective—looking back for a possible cause after an abnormal baby has been born.

There can be no reason to doubt that careful observation of pregnant women will disclose other aetiological factors, and that these are not necessarily infective. The mother's diet matters to the human foetus during the last three months of pregnancy, but less is known about dietetic requirements during the period of organogenesis. So far as I am aware it has never been proved that starvation increases the likelihood of congenital anomalies among human infants, but Warkany and Schraffenberger (1944) have shown that, in rats, a deficient diet increases the incidence of congenital deformities.

If reliable information is to be obtained about the effect of external influences on the foetus, the mother must be seen frequently during the early weeks of her pregnancy. Unfortunately a woman who is pregnant for the first time may be uncertain about her condition during the first three months, and she may hesitate to ask for confirmation. She is likely to be even more doubtful if she has regular small haemorrhages, and yet these may be an indication that foetal damage is occurring. No one has better opportunity of winning the confidence of his patients, and no investigator has such an excellent chance of observing the happenings of early pregnancy, as the family doctor. It is impossible to suggest what to look for; careful records should be kept, even of apparently trivial happenings, and at all stages of the pregnancy.

When MacMahon (1952) had shown that patency of the ductus arteriosus was relatively commoner in first than later pregnancies, he suggested that this might be due to prolonged labour, foetal distress, and asphyxia neonatorum. His colleagues (Record and McKeown, 1953), trying to confirm this suggestion, found that notes about the labour and the condition of the baby at birth were often quite inadequate for their purpose. To assess the effect of external factors, the observations of a considerable number of doctors will have to be pooled and correlated, and reliable results will depend on the accuracy with which records are kept.

In many cases, no doubt, foetal maldevelopment does not depend on the influence of external factors, but on genetic defects. Further information is needed about the familial incidence of all types of congenital defects.

The next problem is to recognize when a baby has congenital heart disease. The cases seen in hospital belong to a highly selective group, since most of these infants are referred because they have symptoms. The prognosis in this group of babies is poor, although there are some who can be cured by surgery, and others who, after a precarious first year, will improve spontaneously. This is not the occasion to consider how to distinguish between these various treatable conditions, or to consider methods of achieving an exact anatomical diagnosis. The point to be emphasized is that in hospital we get a wrong impression of congenital heart disease in infancy. Most infants with congenital lesions must have no symptoms and probably little in the way of signs. When symptoms occur they are apt to mislead, because if there is no cyanosis—and that is usually the case—the history is likely to direct attention to the lungs rather than to the heart. There may

be recurrent bronchitis, attacks of pneumonia, and shortness of breath, all of which are especially likely to occur when there is a large shunt of blood from left to right and consequent engorgement of the pulmonary blood vessels. The most readily recognizable sign is a murmur. This always awakens suspicion when it is heard, but often it is obscured, or even lacking, at first.

Like the pregnant mother, the infant must be examined often and regularly if an abnormality is to be detected. Because this precaution is neglected many of these children are first found to have a murmur, not in the neonatal period, but months or years later, when they are examined for some other reason—at a welfare centre, at the school clinic, or even at a Services medical board.

Rheumatic Carditis

When local notification of rheumatic fever was introduced the diagnostic criteria adopted were one or more of the following occurring in a person under the age of 16 years—rheumatic pains or arthritis accompanied by a rise in temperature, rheumatic chorea, rheumatic carditis, valvular disease of the heart of rheumatic origin.

It is widely believed, but not universally accepted, that when a child has rheumatic fever the heart is always damaged, although not necessarily so severely as to be recognizable by clinical methods. Even when, in the initial attack, a child has such evidence of heart damage as enlargement, an obvious murmur, pericardial friction, or congestive failure, there is a 30% chance that there will be no detectable abnormality 20 years later (Bland and Jones, 1951).

Rheumatic Activity

If such a result is to be obtained and permanent damage restricted to a minimum, a child needs rest when carditis is active. The difficulty is to recognize activity, for rheumatic carditis can be a remarkably quiet process. As already mentioned, many patients with mitral stenosis deny ever having had rheumatism. Likewise, that cardinal sign of rheumatic activity the Aschoff node may be found in heart muscle biopsies of patients who have no evidence whatsoever, either laboratory or clinical, of acute rheumatism (McKeown, 1953).

Sometimes it is easy to recognize active carditis: its presence should certainly be assumed when a child with rheumatic heart disease has chorea, subcutaneous nodules, erythema marginatum, arthritis with temperature, a sore throat, or an increased blood sedimentation rate. At other times symptoms of activity are less obvious and may amount to little more than an unnatural tiredness which makes the child fractious and irritable, easily provoked to tears, and disinclined to play. The child is often pale, has a poor appetite, and complains of ill-defined muscular, joint, or abdominal pains. Active carditis is suggested also by a pulse which is rapid during sleep, by heart sounds and murmurs which alter in quality, by pericarditis or heart failure, and by a changing electrocardiographic pattern.

Children with acute rheumatism should be treated in hospital, where rest is more readily secured and where salicylates can more easily be given in adequate dosage. On the whole cortisone and A.C.T.H. have proved no more effective than salicylates, and, although the first effects may be spectacular, the action is "apparently purely suppressive, and relapse will often occur after stopping therapy unless in the meantime the disease has burnt itself out spontaneously" (Cope, 1953).

Cause of Juvenile Rheumatism

Perhaps the most important reason for sending the child to hospital is to get him away from the home which probably played a part in initiating his illness. Presumably certain factors in the environment are essential to the development of rheumatic fever, but our knowledge of the subject is limited. The disease certainly tends to run in families (Read *et al.*, 1938), and it has been argued that this is due to an inherited susceptibility (Wilson, 1940).

More recent studies have failed to confirm that a Mendelian mechanism is, in fact, operative (Stevenson and Cheeseman, 1953); and, despite suggestive evidence, it is not even certain that the aggregation of cases in families is determined by heredity. The occurrence of rheumatism in several members of a family might be due to a common environment. Since it is only claimed that susceptibility is inherited, and since the susceptible subject can be recognized only after he has been exposed and has acquired the disease, it becomes extremely difficult to determine the relative importance of heredity and environment.

The B.M.A. inquiry (Whipham, 1888) drew attention to the relative immunity of the "upper classes," and all later investigations have shown that rheumatic fever is a disease of the relatively poor, who usually come of large families and from overcrowded rooms in city slums. Overcrowding matters more than poverty, damp, or undernutrition. Overcrowding increases the chance of acquiring respiratory infections.

While there is no doubt about the importance of the home environment, yet it is one of the strange things about the disease that a child rarely develops rheumatism until after starting school. Again, despite the importance of being at home, it is in August, during the school holidays, that the smallest number of fresh cases occur. Fresh cases reach a peak in September and again in January—times which "may correspond to the reassembly of children for the autumn and spring terms" (Hewitt and Stewart, 1952).

It has long been known that rheumatic fever often follows a sore throat and that the likelihood of attacks is perhaps greater after two infections at a relatively short interval. Although the respiratory infection may be so mild as to be symptomless, immunological tests will confirm that there has been infection with a Group A haemolytic streptococcus. When there is a marked difference in the incidence of rheumatic fever in different parts of a country, the frequency is related, not to climatic factors, but to the incidence of other streptococcal infections such as scarlet fever (Schwentker, 1952). Infection with a haemolytic streptococcus is a factor of proved significance in the production of the rheumatic state.

Some families seem peculiarly susceptible to disease of the upper respiratory tract. I know a family in which, early in life, each child in turn has suffered from recurrent otitis media; as they grew older the children have had sore throats and perhaps scarlet fever; the parents have had repeated tonsillitis or sinusitis. The pattern of disease in each individual seems to change with the passage of the years, but there can be very little doubt that it is due to a haemolytic streptococcus. We know very little about the natural history of this infection, especially in infants—yet it is common enough. Rantz and his colleagues (1952), for example, showed in an urban out-patient practice that 6% of infections during the first year of life were due to this organism.

The spread of streptococcal infections in the home is already being investigated by general practitioners (E. Tuckman, 1953, personal communication), but there is room for more work in this field. If we could learn how to recognize the clinical manifestations of mild streptococcal infections in persons of different ages it would be possible to compare the behaviour of streptococcal infections in rheumatic and non-rheumatic families, and to see whether infection of a pregnant woman has any bearing on the susceptibility of her child to rheumatic fever. Taran (1953) maintains that the susceptible child in a rheumatic family can be recognized even in infancy, because it takes unusually long to throw off upper respiratory infections, it is pale, and it is difficult to interest in food. It gets attacks of abdominal pain and is capricious and irritable, particularly towards the end of the afternoon. But this is a picture of almost any city infant.

To be able to recognize streptococcal infections by clinical methods would be a big step towards the elimination of rheumatic fever and of acute nephritis.

Prevention of Rheumatic Fever

The prevention of rheumatic fever needs to be considered under two headings—the prevention of the initial attack and the prevention of relapses in those who have had rheumatism.

In a rheumatic family, children not yet affected by rheumatism can be protected by antistreptococcal agents such as sulphadimidine or penicillin, given either continuously in small doses or in larger doses at the time of exposure to infection. Continuous administration has its disadvantages—the danger of toxic reactions and the emergence of organisms resistant to the drug. On the other hand, intermittent therapy demands (what may still be impossible) the early recognition of streptococcal infections and the immediate and vigorous treatment of all affected members of the household.

Once rheumatic heart disease has been acquired it tends to be progressive. It has not yet been established that control of streptococcal infection will prevent this progress once it has started, although it may well be that it does. Certainly it is reasonable to use treatment known to prevent streptococcal invasion of the nasopharynx and, for a child with rheumatic carditis, to accept the risks of continuous use of sulphonamides in doses of about 0.5–1 g. daily (Coburn and Moore, 1939; Hansen *et al.*, 1942), or penicillin (Gale *et al.*, 1952; Rammelkamp *et al.*, 1952). For this purpose injection of a repository preparation such as benzathine penicillin has much to recommend it, given in a dose of 600,000 units once every two to four weeks during the autumn and spring terms (Fletcher and Knappett, 1953). Continuous therapy depends for its success on the intelligent co-operation of the parents, and the first sulphonamide trial conducted in Birmingham by Dr. K. D. Wilkinson was abandoned. Oral penicillin (benzathine penicillin) should be given in curative doses, 300,000 units five times a day, for at least five days after the start of a respiratory infection or exposure to a sore throat.

Subacute Bacterial Endocarditis

The other important use for antistreptococcal agents in children who have rheumatic or congenital heart disease is to prevent subacute bacterial endocarditis. This is almost always due to *Streptococcus viridans*, which enters the blood stream from diseased teeth. The dangers of the condition require no emphasis; it is extraordinary that there should be such reluctance to advise dental extractions. The deciduous teeth of children with Fallot's tetralogy are especially liable to decay. In children with heart disease the milk-teeth must not be allowed to rot. In my experience subacute bacterial endocarditis is quite often due to infection in the deciduous teeth. If conservative methods fail to stop the spread of caries, extractions should be advised, using penicillin cover. For this purpose 300,000 units of procaine penicillin should be injected on the day of extraction and for the next four days. The child should then be seen at least once a month for six months; sweats, tiredness, pallor, and general malaise should be regarded with deep suspicion.

Some Points in Management

Exercise.—Children with congenital heart disease are more likely to suffer from too much restriction than from too much freedom. Recently we admitted a child of 8, still on the bottle and not allowed to walk. This was corrected while she was in hospital and operative treatment was highly successful. She then went for a year to a residential home, where activity was encouraged and progress was rapid. Shortly after the child returned home the almoner called and found her once more confined to bed by a mother who was unwilling to relax restrictions for which there had never been any need. These children will stop exerting themselves when they have had enough; there is usually no need to set limits for them. The case is different for children with rheumatic heart disease. A boy who has been well until his attack at the age of 10

has already learnt to enjoy the element of competition which is part of school life. For him restrictions will be needed, and a year in a residential rheumatic school, where return to activity is carefully graded, will introduce him in a more pleasant way to what may have to be a life-time of restriction.

Education.—Children with congenital heart disease are of average intelligence, although they may seem stupid because they have never been given a chance to learn. No doubt it is because both parents and teachers expect these children to die suddenly that it may be difficult to convince them that school is a good thing, and that, as a general rule, the childhood infections will be surmounted with little disturbance. The children should attend an ordinary school if it is at all possible, for they will depend on their mental powers for a livelihood. They may not be able to play games; but only if they are greatly limited in their exercise tolerance should they be sent to a school for physically handicapped children before first being tried at an ordinary school. If operation is going to be necessary, it is an advantage to get it over before serious schooling begins. When a child is confined to bed for a long time learning is still important, and the education authority can sometimes provide the services of a home teacher.

Conclusions

This has been a sketchy review of a vast subject. I have attempted not so much to give information as to stimulate an interest in what is not yet understood. Progress has been made towards discovering the cause of heart disease in childhood, but much remains to be done. Because the problems are those of the home—the mother and her family, the infant, and the young child—no one should be better able to find the answers than the general practitioner.

What is the relative incidence of congenital heart disease and juvenile rheumatism? What more can be learnt about pregnancy and the cause of heart disease in children? What part does heredity play? What are the clinical manifestations of streptococcal infections? How should the spread of streptococcal infection be controlled? Can anything further be done to reduce the incidence of heart disease in childhood?

Because these are unanswered problems no guidance can be given to those who aspire to solve them. No one can tell what to look for or what is important. Perhaps something might be discovered by the joint efforts of general practitioners, making regular monthly visits to selected homes—not a hurried coming and going, but with leisure to sit and talk, to make friends, to discuss, to help and to learn, and especially to observe and to record. Observations might be so indefinite as to be valueless, but perhaps after analysis and correlation they might point to some new factors at present unrecognized, and there would at least be the satisfaction of taking more interest in the "beginnings" and not merely the "ends" of heart disease.

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A NEW TABLET TEST FOR BILIRUBIN IN URINE

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This paper describes a simple method for the detection of small amounts of bilirubin in the urine. Bilirubin is first concentrated by adsorption on a special test mat and then allowed to react with a stable diazonium compound incorporated in a tablet. Results obtained with urine from normal and jaundiced subjects have been compared with those using two standard routine methods for urinary bilirubin, Fouchet's test and the iodine ring test.

Methods

The *tablet test* is performed as follows: (1) Place 5 drops of urine on the test mat, which is 19 mm. square and 2 mm. deep, and is composed of a mixture of asbestos and cellulose fibres. (2) The tablet is placed on the centre of the moistened area of the mat. It contains a stable diazo dye (*p*-nitrobenzene diazonium *p*-toluene sulphonate) and also sulphosalicylic acid, sodium bicarbonate, and boric acid. (3) Two drops of water are allowed to flow on the tablet. (4) The colour developing on the mat is recorded within 30 seconds. The bilirubin is concentrated on the test mat. The diazo dye is taken into solution by the water, aided by the effervescence caused by the presence of sulphosalicylic acid and sodium bicarbonate in the tablet; the boric acid is a vehicle. If bilirubin is present in the urine the mat around the tablet turns purple and the amount of bilirubin is roughly proportional to the speed of development and intensity of the colour. Any colour developing after 30 seconds is ignored. It is found that the most satisfactory colour reaction is given if the first drop of water is allowed to remain on the tablet for a few seconds before the second drop is put on to wash the fluid on to the test mat.

Fouchet's test is performed by adding 2 ml. of 10% barium chloride to 10 ml. of urine, filtering and adding Fouchet's reagent to the filter paper. A positive result is indicated by a green colour.

The *iodine ring test* is performed by layering 2 ml. of tincture of iodine diluted 1 in 4 with water on to 10 ml. of urine in a test-tube. A positive result is indicated by a green ring at the interface.

A *modification of the tablet test* has been employed, using 5 drops of urine on the test mat as before, but replacing the tablet with 1 drop of Fouchet's reagent. A positive result is indicated by the development of a green colour on the mat.

Quantitative urinary bilirubin estimations were performed by the method of Golden and Snively (1948). Urinary urobilin and urobilinogen were tested qualitatively by Schlesinger's test with alcoholic zinc acetate and by Ehrlich's aldehyde reagent. Serum bilirubin levels were estimated by the method of King and Coxon (1950).

Materials

Samples of urine from 100 non-jaundiced patients picked at random from the wards of a general hospital and 200 urines from jaundiced patients were tested. Thirty-six urines containing urobilin or an excess of urobilinogen but no bilirubin were also studied. In 92 instances the serum bilirubin level was estimated at the time of testing the urine.

Specificity

The 100 urines from non-jaundiced patients were tested to determine whether false-positive reactions might result from the administration of drugs or from the presence of other abnormal substances in the urine. The patients were receiving many varied forms of treatment and suffering from a wide range of disorders. In no instance did the urine give a positive tablet reaction, and it therefore seems unlikely that false-positive reactions occur owing to the presence of commonly administered drugs in the urine. Sometimes there was seen on the mat a faint orange-brown colour which became more conspicuous after the mat had been standing for some time. This colour did not interfere with the reading of the test, and was presumably due to the presence in the urine of diazotizable non-bilirubin chromogenic material.

The presence of urobilin or an excess of urobilinogen in the urine does not give a false-positive result, for 36 urines with a positive Ehrlich or Schlesinger reaction were negative both by the tablet test and by Fouchet's method.

These results agree with those previously reported with the tablet test. Free and Free (1953) tested approximately 2,000 urine samples from general-hospital patients and failed to find any substance giving false-positive reactions. They also tested 100 urine samples from normally healthy adults; 99 gave negative reactions and one an unexplained trace reaction. Klatskin and Bungards (1953) found two false-positive tablet reactions in a series of 478 urines, and in both these instances there might have been some hepatic dysfunction. Giordano and Winstead (1953) found that the presence of increased amounts of urobilinogen in the urine did not mask the colour reaction as it did in the Harrison spot test, in which Fouchet's reagent is used.

Sensitivity

Of the 200 urines tested which gave either a positive Fouchet or a positive tablet reaction, 185 were positive for both methods; 192 gave a positive Fouchet and 193 a positive tablet reaction, while only 135 were positive with the iodine method.

Ninety urines giving a positive tablet reaction were also tested with the modification using the test mat and replacing the tablet by Fouchet's reagent: 58 gave a positive result and 32 a negative one.

These results suggest that the tablet test and Fouchet's method are of about equal sensitivity and are considerably superior to the iodine ring test and to the modification for the detection of bilirubin in the urine. Other workers found that the tablet test was more sensitive than methods using Fouchet's reagent (Klatskin and Bungards, 1953; Giordano and Winstead, 1953).

Quantitative analysis of bilirubin in urine is made difficult by the presence of interfering substances. However, an attempt was made to compare the quantitative urinary bilirubin values with the results for the qualitative tests. Eighteen urines were analysed and then diluted serially, and the lowest concentration giving a positive qualitative reaction was recorded (Table I). Although the results varied, the tablet test could usually detect bilirubin between 0.1