the mischief in the tissues of the urinary tract. This is evident from the polymorphonuclear leucocytosis that occurs, and it is generally accepted that these infections are blood-borne or spread by lymphatics (Walker, 1922, 1930). This worker and others have demonstrated organisms and cellular infiltration in the tissues of the urinary tract. Of course the mischief may not be very deep-seated and the concentration of penicillin in the tissues of the urinary tract may be higher than elsewhere owing to the diffusion of that substance from the urine, but even if this is the case the tissue concentration must be lower than the urinary, though it may be greater than the blood. Thus we see that it is impossible to relate directly the urinary level and the sensitivity of the organism to penicillin *in vitro* and in this way determine whether a urinary infection is likely to respond to treatment with a certain dosage of penicillin; this argument will apply to any other drug. The final court of appeal, as always in this particular type of problem, will be clinical trial and error of various dosage systems given under standard conditions and related to the *in vitro* drug sensitivity of the organisms.

With ordinary doses it is practicable to maintain an average level of 200 units per ml. of penicillin in the urine, but theoretically there is no reason why 2 or more million units of penicillin should not be injected every three hours, though even under the best conditions this dosage would be inadequate for one-quarter of the *Bact. aerogenes* and nearly one-fifth of all the organisms in this series (as indicated by the extended penicillin sensitivities listed in the results). When penicillin becomes cheaper and even more readily available it may be possible to treat most Gram-negative urinary infections with it. In any event, it is already useful for treating urinary infections associated with Gram-positive organisms.

Of the coliforms examined 46 out of 50 (92%) resist 50 mg. of sulphathiazole per 100 ml. using the method described above. This is in approximate agreement with the findings of Neter and Clark (1944) but not with Strauss and Finland (1941), who used a synthetic medium. There do not seem to have been any published reports of the correlation of *in vitro* sensitivities with clinical results, but the figure seems high. Bearing in mind the possible site of action of the drug, one must pause to consider how much value the sulphonamides are in urinary infections with Gram-negative bacilli. However, Nathan (1947) reports favourably on them for treating paraplegic patients with suprapubic cystostomy.

Summary

Of 50 strains of lactose-fermenting coliform organisms isolated from infected urines of paraplegic patients 32 were *Bact. aerogenes*, 12 were *Bact. coli*, 2 were irregular types of *Bact. coli*, and 4 were unclassified. The incidence of *Bact. aerogenes* in this group does not differ greatly from that in other patients with urinary infections.

All the organisms were sensitive to streptomycin, and all but 4 resistant to 50 mg. of sulphathiazole per 100 ml.

Bact. aerogenes and the unclassified organisms were relatively resistant, and *Bact. coli* and its irregular types relatively sensitive, to penicillin. The high incidence of *Bact. aerogenes* and its undoubted resistance to penicillin does not favour the use of the drug at present in the routine treatment of urinary infections by Gram-negative bacilli. In this series it was concluded that at least one-fifth of all the organisms were too resistant for penicillin treatment in high dosages and three-quarters too resistant for ordinary dosages.

The results are discussed and their impact on the treatment of urinary infection considered.

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CARDIAC MURMURS IN INFANCY

BY

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Much has been written about cardiac murmurs in older children, but relatively little work has been done on their incidence and manifestations in infant communities. Von Reuss (1929) states that any definite murmur heard in a child who is quiet should be regarded as evidence of congenital heart disease and that murmurs at this age are very rare. On the other hand Holt (1940) states that 50% of all children have a functional murmur at some time. Lyon and others (1940) examined 7,000 newborn infants in the obstetrical wards of a general hospital and found that 147 (1.9%) had apical systolic murmurs; two of these died of congenital heart disease, and in 14 of the 88 who were re-examined six months later the murmurs were still present.

Since the Child Health Survey of the Institute of Social Medicine was initiated at Oxford three years ago 630 children have been enrolled, and the oldest have now been under observation for three years; 520 children remain in the survey at present, the 110 defaulters belonging chiefly to families which have moved to other areas owing to the housing shortage. The defaulters were followed up for periods varying from six months to two and a half years. It should be emphasized that this is not a hospital series but a sample of ostensibly healthy children drawn from all social classes, whereas the authors quoted either employed a hospital population or have not stated how their samples were obtained. Of the 630 children, 32 (5%) have been noted as having a murmur at some time. It was thought that it would be interesting to investigate the time of development of these murmurs and their subsequent history so far as at present observed.

In the course of the main health survey a full physical examination is made at regular intervals; first at the age of 6 weeks or less, then at 3, 6, 9, and 12 months, with subsequent examinations at six-monthly intervals. It has not always been possible to adhere strictly to the exact intervals owing to illnesses or other difficulties. Three observers, working in succession but observing the same routine as closely as possible, have carried out examinations on children first seen at infant welfare centres or at mothercraft clinics. All the children have had their chests examined radiographically, first at the age of 6 months and

thereafter at six-monthly intervals, except in a few instances where some unforeseen occurrence has prevented this.

Development of the Murmurs

The 32 children with murmurs have been grouped according to the age at which the murmurs were first noted; the murmurs have been described as "transient" if heard at only one examination and not subsequently; "temporary" if heard at more than one examination and then apparently disappearing; "persistent" if heard at more than one examination and persisting up to the most recent examination.

Table Showing Development of the Murmurs

Age in Months when Murmur First Noted	Transient Murmur	Temporary Murmur	Persistent Murmur	Present for First Time and Not Yet Re-examined
0-2	3	1	1	0
3-4	1	1	1	1
6-7	0	0	1	0
9-10	3	0	2	1
12-13	1	0	2	2
18	1	1	6	0
24	2	0	1	0

The murmurs recorded were all systolic in time, and it may be noted that Owen and Kingsbury (1924) state that a diastolic murmur is never heard in a newborn infant. The murmur was often heard best when the child was lying down, and was usually loudest at the apex; it was most commonly conducted over the whole praecordium, but in some cases it was confined to the left border of the sternum. Three murmurs were specifically described as cardio-respiratory.

Some of the following data may prove relevant to the presence or absence of murmurs, but the cases are as yet too few to allow any conclusions to be drawn.

The ante-partum health of the mother was good in 21 cases, in the remainder the illnesses recorded were cystitis 1, ulcerated mouth 1, anaemia 1, ante-partum haemorrhage 1, toxæmia 1, vomiting 1, and giddiness 1; in three the health was recorded as "only fair." The birth weight of one of the children was only 4 lb. (1.8 kg.); the others varied between 6 lb. and 9 lb. 2 oz. (2.7 and 4.1 kg.). The sex distribution was unequal—23 boys and 9 girls. The general physical condition of the children was noted as "only fair" or "poor" in 13 out of the 32, without any specific diagnosis being attached. According to the Registrar-General's classification of social groups which depends upon the father's occupation, one of the 32 children was in social group 1, four were in social group 2, 21 in social group 3, three in social group 4, and three in social group 5. Group 3 has been the predominant single class from which the babies have been enrolled.

Haemoglobin estimations were made in only six of these children, and these gave figures of 60%, 82%, 85%, 88%, 96% and 106%. The haemoglobin estimations were discontinued because we were anxious not to undermine the confidence of the children, and those subjected to the test seemed to remember their visit unfavourably; furthermore, the mothers were not always very willing to consent to the taking of blood samples, and in a long-term survey such as this it is especially important not to risk the default of any more babies than can be helped. The child with the lowest recorded haemoglobin (60%) was treated with iron, and when last seen, while still under treatment, the murmur had become very much fainter.

The x-ray examination of the chests in 20 out of 29 of the children showed considerable variation in respect of size or shape of the mediastinal shadow, which my colleague Dr. F. H. Kemp commented upon; but whether the variations are significant or whether they are within the wide range of normal variability manifest at this age has yet to be determined. The mediastinal shadow in infancy shows wide variations not only as between one baby and another but also in the same baby in

successive radiographs taken at intervals of only a few seconds. Three of the children in this series were not radiographed.

Discussion

A long follow-up of these cases should provide further clinical data on the significance of the cardiac murmurs observed, and this report can be regarded only as preliminary. The knowledge that a murmur has been present since infancy may be of value to the individual, as it will assist in the differential diagnosis from rheumatic carditis at a later age, and in the absence of other signs or symptoms it may then be possible to allow normal activity, which might not otherwise seem justifiable.

It is apparent from the material studied that some murmurs are present from birth and others appear later. Those already present at the first examination and disappearing later may be due to the changes taking place during the adaptation from foetal to post-natal life. Transient or temporary murmurs may also accompany anaemia or may be exocardial in origin. Persistent murmurs either may be due to relatively insignificant congenital defects or may accompany the more important lesions.

It is noteworthy that 23 out of the 32 murmurs were not detected until the age of 9 months or later, and that six of those appearing at 18 months have persisted. One child who had a murmur first detected when she was 9 months old is now 2½ years old and has a loud persistent murmur with a faint palpable thrill over the pulmonary area, but no symptoms. It is possible that increased activity with crawling and walking may bring out defects not previously detectable.

In only one case in the series was cyanosis observed. It was noted at birth, a murmur was detected soon after delivery, and the mother was informed that the child had a congenital heart lesion. The cyanosis lasted only a few hours, but the murmur was present and clearly audible at each routine examination until the age of 1 year, when it was hardly perceptible. The child has been particularly healthy and active since she came under observation. In view of the fact that murmurs do disappear and that there may be no associated symptoms, it would seem advisable not to alarm mothers unduly. In the case described the mother had waited 12 years to have a child and was then given the impression that the child would be a permanent invalid. One other child showed some suggestion of dyspnoea on exertion. Except in the case of the child with anaemia, who had been suffering from diarrhoea for several weeks, there was nothing to suggest that the development of a murmur was ever a consequence of a specific illness. All the other children with murmurs appeared healthy, and no obvious congenital abnormalities were found affecting other structures.

Summary

In a routine periodic examination of the heart in 630 infants systolic murmurs were detected in 32 (5%).

Some were present at the first examination—i.e., before the sixth week—and later either disappeared or persisted; others appeared for the first time at the second or subsequent examinations, some of these disappearing and others persisting.

In 22 cases the murmur was not detected until the age of 9 months or later.

With the exception of one case in which a thrill in the pulmonary area subsequently developed, and another in which there was some suggestion of dyspnoea on exertion, no associated symptoms or signs were recorded.

No correlation between clinical findings and radiographic appearances could be established.

I am indebted to Prof. J. A. Ryle, to Drs. Allen-Williams and Helen Morley (my predecessors in the survey), and to all my colleagues in the Institute of Social Medicine for their assistance and

advice. Thanks are also due to the medical officers and health visitors of the Oxford City Health Department for their co-operation, and to all the mothers for their participation in the survey.

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Medical Memoranda

Acute Lymphatic Leukaemia Presenting with Skin Lesions and Mastoiditis

It is exceptional for skin lesions to appear as the first or even as an early sign of leukaemia, although examples have been reported by Ketron and Gay (1923), Boardman (1928), and Wintrobe and Mitchell (1940). The paucity of published literature on this subject prompted the recording of the following case.

CASE REPORT

A woman aged 65 was admitted to hospital on Nov. 7, 1946, with a history of pains in the ears and deafness for three weeks and a more recent history of bilateral otorrhoea. Despite difficulties owing to deafness and her critical state it was ascertained that her health had been failing for some time and that within the previous three months she had developed a rash over her body.

On admission she was gravely ill with pronounced anaemia and slight icterus. Her gums were hypertrophied and bled readily, and there were scattered loose stumps of carious teeth in both jaws—accounting for the presence of pathologically enlarged submental and submaxillary nodes. There was evidence of bilateral mastoiditis. Over the trunk and proximal regions of the limbs there were numerous brown-grey plaques varying in size from 0.25 to 3 cm. in diameter. The majority projected above the skin surface, and though some were deeply situated none were adherent to bone. The papules were not painful, did not itch, and were not tender. There was some bruising of the legs, but purpura was absent until shortly before death. Apart from a marked thoracic kyphoscoliosis and a small plaque on the right fundus physical examination was negative.

A blood count showed: haemoglobin, 48%; red cells, 2,500,000; white cells, 1,300; platelets, 67,500. A biopsy revealed lymphadenitis cutis, a lymphatic leukaemic deposit in the skin. Sternal puncture verified the diagnosis of acute lymphatic leukaemia in an aleukaemic phase.

The patient went steadily downhill and died on Nov. 23. Necropsy was carried out, but revealed no evidence of leukaemic infiltrations except in the skin. There was no involvement of any of the nodes in the various groups throughout the body.

COMMENTARY

The skin lesions associated with leukaemia may be subdivided into (1) non-specific—sometimes known as leukamids—including such conditions as herpes zoster, purpura, prurigo, etc., and (2) lesions specific for the disease and composed of infiltrations by the cell types. Forkner (1938) states that the second group conforms to the following types. In myelogenous leukaemia the lesions consist of macules, papules, or plaques, sharply circumscribed, brownish to bluish in colour, and chiefly involving the trunk. The lesions are not painful and do not itch. Ulceration with local loss of tissue and possibly haemorrhage may occur. The lesions associated with lymphatic leukaemia are: (1) Erythrodermia (l'homme rouge), which is characterized by subacute or chronic progressive reddening of the skin spreading gradually to involve a large area of the body surface. This may be accompanied by a sensation of chilliness owing to increased loss of heat, and itching may be a prominent feature. Scaling is found and regional or generalized lymph-node enlargement is not uncommon. (2) Universal leukaemia of the skin, which is an exaggerated generalized form of the above. (3) Circumscribed leukaemia of the skin, where the lesions are usually well-defined maculae, or are slightly elevated,

with a wide variation in size and colour from yellow to bluish-red. These are most commonly found on the face, neck, and dorsum of hands and are rarely numerous. Apart from slight burning, subjective sensations are absent.

The circumscribed skin lesions associated with myelogenous and lymphatic leukaemia differ only in their distribution, and the distribution of the lesions in the above case conforms more to the myeloid type. Lewis (1919) published a similar case, with mastoid disease and the blood picture of lymphatic leukaemia, as chloroma. Brannan (1926) states that this term cannot be used correctly unless green pigmentation is present in the tumour, and Kandel (1937) defined the term as being applicable to any tumour which is green when fresh. Jones (1939), in an extensive review of the literature, decided that chloroma presented itself in two clinical forms: (1) affecting children and characterized by rapidly growing bone tumours, and (2) an adult type in which a progressive anaemia and signs of leukaemia are more prominent. He believed, however, that in both types the two essential features are leukaemic changes in the blood and green tumour deposits in the bones. The term "chloroma" should therefore be confined to conditions with lesions which have a frankly green colour, and is not applicable to my case.

I am indebted to Dr. John Craig for permission to publish this case, to Dr. H. W. Fullerton for the haematological findings, and to Dr. W. M. Davidson for the necropsy report.

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Severe Reaction after Penicillin

The following report of a severe reaction following penicillin injections may be of interest.

CASE REPORT

A Regular Army officer aged 32 was hit on the left ankle while playing hockey on Sept. 17, 1947. He consulted me ten days later for pain and swelling of the ankle, and feeling generally out of sorts. On examination his temperature was 101° F. (38.3° C.), and he had an obvious infected haematoma just above the left external malleolus. He was given an intramuscular injection of 100,000 units of penicillin (sodium salt, yellow) immediately and a further 100,000 units that night. The next morning the haematoma was incised under local analgesia and about 1 oz. (28.4 ml.) of thick pus evacuated. He was given two injections each of 100,000 units of penicillin on this day. On Sept. 29 he was given one further injection of 100,000 units. His general condition was now good. Locally much of the pain and swelling had disappeared. The leg was healed and normal by Oct. 5.

On the night of Oct. 10-11 he developed a severe widespread urticarial eruption with intense itching. He was seen in the morning and given "benadryl" capsules to take four-hourly. This controlled the irritation but made him feel so ill that the drug was stopped and ephedrine substituted. On Oct. 13 the urticarial condition was unchanged. He complained of anorexia and indigestion and vomited in the evening, when his temperature rose to 100° F. (37.8° C.).

On Oct. 14 his condition was worse. In addition to the previous symptoms he then complained of stiffness and aching in all his joints. Curiously, if he could provoke an urticarial reaction by rubbing or scratching his skin the joint symptoms were temporarily relieved. Ephedrine was without effect on his joints. Next day he became so stiff that he could hardly move; nor could he move his jaw to eat solids. The aching pain was very severe and was only partially relieved by tablets containing aspirin, phenacetin, and codeine. His evening temperature still rose to about 100° F. This was his worst day, and he slowly improved until by Oct. 21 he had completely recovered.

J. F. L. WALLEY, M.B., B.Chir.

The Ministry of Health reports that about 17,500 doctors and 16,000 nurses attended 506 showings of the film entitled "The Early Diagnosis of Acute Poliomyelitis."