24 of the patients had arthralgia and arthritis, 22 swelling of the hands and fingers, many with skin changes of scleroderma, 21 Raynaud's disease, 18 myositis, 17 lymphadenopathy, and 20 hypergammaglobulinaemia. Several had skin rashes typical of dermatomyositis, and of the 22 patients on whom cine-oesophograms were performed 17 showed abnormal motility such as found in scleroderma. Histopathology entirely confirmed these clinical findings. Thus six out of 10 skin biopsies were characteristic of scleroderma and seven out of eight muscle biopsies showed inflammatory infiltrates, so confirming the presence of myositis already indicated by typical electromyograms and raised levels of creatine phosphokinase. Only four patients had an erythematous rash similar to that of systemic lupus, and, of especial significance, only one patient developed a renal lesion of indeterminate nature despite the length of follow-up, which ranged from 8 weeks to 8 years.

In support of the hypothesis that mixed connective tissue disease is an entity distinct from the hitherto recognized diseases of the connective tissues is the presence in all 25 patients of an antibody to an extractable nuclear antigen, which in its purest form so far obtained is an RNA protein of molecular weight greater than 20,000. The specific antibody is readily detected by tanned cell agglutination, and in these patients it was detected at dilutions betweeen 1 in 1,000 and 1 in 1,000,000. The only other conditions in which a similar antibody was found was systemic lupus erythematosus, but that antibody could be readily distinguished from the one in mixed connective tissue disease because of its much lower titre and because the agglutination of the coated cells was resistant to the action of RNAse.

The response of these patients to high doses of prednisone, 1 mg/kg body weight daily, was usually good, and the majority required little or no maintenance therapy. Even the sclerodermatous changes, in contrast to classical scleroderma, responded in a satisfactory manner.

Should mixed connective tissue disease be regarded as distinct from the other recognized diseases of the connective tissues? Since it can be differentiated from them on both clinical and serological grounds, and since it carries a more benign prognosis, with clear-cut therapeutic requirements, the differentiation would appear to worth making.

[1] Dubois, E. L., Chandor, S., Friou, G. J., and Bishel, M., *Medicine*, 1971, 50, 199.
[2] D'Angelo, W. A., Fries, J. F., Masi, A. T., and Shulman, L. E., *American Journal of Medicine*, 1969, 46, 428.
[3] Tuffanelli, D. L., and Winkelmann, R. K., *Archives of Dermatology*, 1961, 84, 359.
[4] Sharp, G. C., Irvin, W. S., Tan, E. M., Gould, R. G., and Holman, H. R., *American Journal of Medicine*, 1972, 52, 148.

Renal Radiology

Recent advances in the treatment of renal disease have been accompanied by equally impressive progress in the histopathology, immunology, bacteriology, and physiology of the kidney. Radiology has not lagged behind. Originally the intravenous pyelogram, as its name implies, was used mainly to examine the kidney's drainage system, but now as much attention is paid to the nephrogram, and it would be more correct to refer to it as an intravenous urogram. Furthermore, radiology no longer provides only a static picture of renal structure; it has become an important tool in the dynamic study of functional disturbance in disease. The current edition of the *British Medical Bulletin*,[1] which is devoted to renal radiology, provides a timely review of the clinical status and potential for research in the field.

Undoubtedly the most important practical innovation has been the recognition that the use of high dosage of the contrast media enables a useful urogram to be obtained in patients with severe renal failure. Since obstruction of the urinary tract can often be excluded by this means, the need for the more difficult and hazardous retrograde pyelography has been lessened. The excretory urogram is of value even in the differential diagnosis of oliguric acute renal failure. For example, acute tubular necrosis characteristically produces an immediate, dense, and persistent nephrogram with little or no pyelogram, an appearance which has been observed in only one other condition—acute suppurative pyelonephritis. In addition this observation has helped our understanding of the pathogenesis of acute tubular necrosis, since it supports the theory of continuing glomerular filtration with almost complete reabsorption of tubular fluid. I. K. Fry and W. R. Cattell have been pioneers in the dynamic interpretation of the excretory urogram, and in the *British Medical Bulletin* they analyse in detail the nephrographic pattern in various disorders. The safety of the contrast media is fundamental to their use in high dosage, and from a comprehensive account of their toxicity by R. G. Grainger it is reassuring to learn that with simple precautions, especially against dehydration, the present-day agents are remarkably safe.

Arteriography is a well-established technique for the investigation of the major renal vessels and of renal tumours and cysts, but little attention has been paid to the smaller vessels. Macro-angiography, however, enables vessels as small as the interlobular arteries to be visualized, and M. E. Sidaway describes characteristic patterns in diseases such as hypertension, chronic pyelonephritis, and polyarteritis nodosa. J. P. Lavender and T. Sherwood give other examples of the use of radiology in pathophysiological research with their studies of the renal microcirculation in experimental haemorrhagic hypertension in the dog. Bone disease in uraemia, formerly little more than a pathological curiosity, has increased in importance with the advent of long-term haemodialysis, for it has crippled many otherwise rehabilitated patients. Separation of the various radiological patterns is necessary for the rational choice of treatment, and these are detailed, together with a correlation with bone histology, by F. H. Doyle and his colleagues.

Other articles deal with the techniques of videocystography, topographical scintigraphy, and ultrasonic and isotopic diagnostic methods. Any clinician or radiologist with a special interest in renal diseases will find this issue of the *Bulletin* a useful progress report in a rapidly advancing field.

[1] *British Medical Bulletin*, 1972, 28, No.3.

Pertussis in Adults

If a doctor has spent a large part of his life working in the whooping-cough wards of an infectious diseases hospital, he will probably have seen a few cases of whooping-cough in adults. No doctor will have seen many, for whooping-cough is a disease of early childhood. But no age group is immune.[1-3] Second attacks may occur, though very rarely.[3 4] And immunization does not confer life-long immunity.[5]

An attack in the adult may be typical or atypical. In the

typical attack the patient first suffers a febrile, catarrhal illness for 10 days to a fortnight and then passes into the stage of spasmodic coughing. Because they do not expect whooping-cough in the adult, both patient and doctor may regard this stage for some time as an unusually severe form of bronchitis, but it may become so distressing that eventually they suspect the true diagnosis. The whoop is not usually so pronounced in the adult as in the young child, and the adult often learns to control it. Vomiting, too, is less common in the adult, but when cough, whoop, and vomit all occur there can be little doubt about the nature of the illness. In atypical attacks the adult patient suffers simply from the early febrile catarrhal illness or from a respiratory illness indistinguishable from acute bronchitis. In such cases the true diagnosis is likely to be missed, even when there has been close contact with children with whooping-cough, unless the doctor is aware that the disease can occur at any age and with symptoms very unlike the classical cough, whoop, and vomit of young children.

The difficulty of the diagnosis in adults is well illustrated by the report of two outbreaks among hospital staff of a paediatric unit in Denver, U.S.A.[6] In one, a house officer developed a mild respiratory illness after contact with a child with whooping-cough. He infected his wife, a ward clerk, and two children whom he saw as outpatients. A nurse caught the infection from one of these children, and she infected her husband and two other nurses. In the second outbreak a graduate student caught whooping-cough from children she attended in their homes. She infected another student, who in turn infected a nurse and a third student. Two of the adult patients had severe cough and loss of weight, and one of them had paroxysmal cough on effort for more than three months. Except for these severe attacks the other milder respiratory illnesses and the chain of infection from adults to children might have gone unrecognized, and this is epidemiologically important because it is in the early, non-paroxysmal, catarrhal stage that whooping-cough is most infectious. As it was, diagnosis was confirmed by culture and fluorescent antibody examination of nasopharyngeal swabs, and titration of sera for rise in pertussis agglutination titres.

Similar incidents have been reported,[5] but they are probably not common. They may occur when perhaps the strain of *Bordetella pertussis* is unusually invasive or the level of adult immunity unusually low, convenient assumptions for which there is no epidemiological evidence. To advocate serum antibody titration in all who have to look after children with whooping-cough and to immunize those who appear to lack immunity might be getting things out of proportion. But one should be aware of the risk. Doctors, nurses, and other attendants who develop coughs and colds when looking after children with whooping-cough should be investigated bacteriologically and isolated till results are known. In the early catarrhal stage antibiotics such as the tetracyclines or erythromycin may help to eradicate the organism and modify the clinical attack. In the paroxysmal stage antibiotics have no effect on the illness, but by then the patient is rapidly becoming non-infectious.

[1] Mannerstedt, G., *Journal of Pediatrics*, 1934, 5, 596.
[2] Morse, S. I., *Annals of Internal Medicine*, 1968, 68, 953.
[3] Christie, A. B., *Infectious Diseases: Epidemiology and Clinical Practice*, p. 699, 1969. Edinburgh: Livingstone.
[4] Horner, F. A., *New England Journal of Medicine*, 1962, 266, 470.
[5] Lambert, H. J., *Public Health Reports*, 1965, 80, 365.
[6] Kurt, T. L., Yeager, A. S., Guenette, S., and Dunlop, S., *Journal of the American Medical Association*, 1972, 221, 264.

Some Problems of Acute Osteomyelitis

Antibiotics have had an increasingly important role in the treatment of acute osteomyelitis in children. Indeed, without them the control of the infection would be almost impossible. But over the years resistance to the original antibiotics has developed, and in 1970 N. J. Blockey and J. T. Watson[1] reported on it in a review of 113 children who were treated for acute osteomyelitis between 1961 and 1968. Organisms were cultured from blood and pus in 79 patients, and in 68 of them (86%) *Staphylococcus aureus* was found. In 1946 14·1% of staphylococci were resistant to benzylpenicillin, and by 1970 this had increased to 93%.[2] The resistance of *Staph. aureus* was almost exclusively confined to penicillin, streptomycin, and tetracycline. Blockey and T. A. McAllister[2] showed that, though resistance to penicillin has increased, staphylococci resistant to penicillin were always sensitive to cloxacillin, though they consider that *Staph. aureus* resistant to cloxacillin and methicillin will be found in acute osteomyelitis of children. They concluded that careful choice of drugs should prevent the development of resistance, provide a broad spectrum of activity, and show synergy, and suggested fusidic acid and erythromycin. They decided that from January 1969 children with acute osteomyelitis should initially receive fusidic acid and benzylpenicillin, and, if there was evidence of resistance to penicillin, erythromycin should be substituted. From January 1969 to May 1970 this antibiotic combination was given to 38 patients. It was found that fusidic acid gave slightly better results with erythromycin or benzylpenicillin (10·5% failures) than cloxacillin and benzylpenicillin in a previous series (14·5% failures). In addition to antibiotic therapy rest by immobilization of the affected limb is important, though it is apt to be overlooked. The Thomas splint is very suitable for the lower limb, for it allows the affected area to remain exposed for an examination. For the upper limb plaster-of-Paris slabs should be used.

In arriving at a diagnosis careful palpation is important, and if pain is severe a general anaesthetic may be necessary. The bulky muscles round the thigh and knee may make it difficult to detect an abscess, and in some regions such as the hip it may be impossible to detect it by palpation even with an anaesthetic. In these circumstances the area should be explored with an aspirating needle and syringe, and aspiration should include the hip joint. It is also worth bearing in mind that osteomyelitis may involve the scapula and pelvic bones.

Surgery should not be undertaken unless there is clear evidence of a superiosteal abscess, and even then drainage by incision or aspiration is not proved to be essential in the treatment of osteomyelitis. Drilling of the metaphysial region has in the past been advocated, but most surgeons now regard it as unnecessary at any stage, and it may even be harmful.

Successful primary treatment was defined by Blockey and Watson[1] as cure of the symptoms and signs within four weeks of the first admission to hospital, with no complication attributed to local bone disease appearing thereafter. In all 21 cases in which treatment failed by these criteria the bone infection disclosed itself within seven months of leaving hospital. It would seem therefore that the correct treatment for this condition has not yet been decided. We do not know if the use of a powerful antibiotic is sufficient without drain-