telorism, broad flat nasal bridge and rather highly arched eyebrows. Severe mental retardation, usually with an IQ below 50, is reported in all patients tested, with one exception who was normal at 15 months (Shapiro *et al.* 1970).

Short stature, hypotonia and skeletal anomalies are also found very frequently. The latter often take the form of radio-ulnar synostosis. The genitalia are hypoplastic, with a small phallus, underdeveloped scrotum and small testes, which are often undescended. Other features frequently found are intrauterine growth retardation, microcephaly, retarded bone age, a short neck and malformed ears. In some patients, as would be expected with an excess of X chromosomes, the total digit ridge count is reduced. Testis histology is often very abnormal, with scanty tubules and absent spermatogenesis. Five patients have had patent ductus arteriosus.

The Xg blood group, which is located on the X chromosome, may be helpful in determining the origin of the extra X chromosomes. In a few of these patients the mother and child have been found to be Xg (a−), and the father Xg (a+); the extra X chromosomes are therefore maternal in origin, and may arise as a result of multiple nondisjunction during oogenesis (Lewis *et al.* 1964, Race & Sanger 1968).

In two cases there have been other nondisjunctional events in the family. In one case of 49 XXXXY syndrome (Miller 1961), the father died of chronic lymphatic leukæmia, one of his sisters was a primary G trisomic Down's syndrome and another sister had a primary G trisomic Down's syndrome child. In a further case (Atkins *et al.* 1968) the brother, half-brother and father of the propositus carried a D/D centric fusion. In addition the brother also had a primary G trisomic Down's syndrome.

Of 43 cases where the maternal age was recorded, 28% were less than 25 years, 21% were more than 35 years and 51% were between 25 and 35 years.

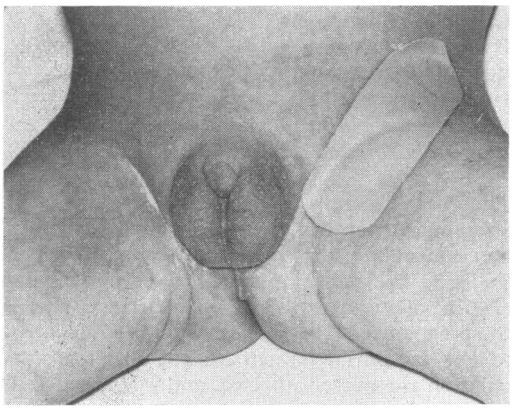

Fig 2 *49 XXXXY – hypoplastic genitalia*

It is interesting that the analogous situation in the female, 49 XXXXX, appears rare and only two cases have been recorded. Although these patients have similar facies, skeletal anomalies and are mentally retarded, there are no genital abnormalities. They may possibly not be recognized for this reason.

In the case of our patient, because of his mixed racial origin his abnormal facies was not considered significant, and the main features leading to the diagnosis were his abnormal genitalia and hypotonia. As far as can be ascertained this is the first case of 49 XXXXY syndrome to be diagnosed in the neonatal period.

Acknowledgment: We should like to thank Professor P Polani for his help and advice.

REFERENCES
Atkins L, Bartsocas C & Porter P (1968) *J. med. Genet.* 5, 314
Fraccaro M, Kaijser K & Lindsten J (1960) *Lancet* ii, 899
Fraccaro M & Lindsten J (1960) *Lancet* ii, 1303
Lewis F, Frøland A, Sanger R & Race P (1964) *Lancet* ii, 589
Miller O (1961) *Lancet* ii, 78
Race R & Sanger R (1968) Blood Groups in Man. 5th ed. Oxford & Edinburgh
Shapiro L, Hsu L, Calvin M & Hirschhorn K (1970) *Amer. J. Dis. Child*, 119, 79
Zaleski W (1966) *Canad. med. Ass. J.* 94, 1143

Melioidosis and Chronic Granulomatous Disease

M J Tarlow MB MRCP
(for June Lloyd MD FRCP)
(Hospital for Sick Children, Great Ormond Street, London WC1)

R A, boy aged 3. This patient is a non-identical twin, born in Singapore to healthy unrelated European parents. The case has been briefly discussed in a review of chronic granulomatous disease by Thompson & Soothill (1970).

History: Developed cervical adenopathy at age 10 months (not 18 months as stated by Thompson & Soothill 1970). Biopsy of affected lymph node taken two months later showed a chronic granulomatous reaction with caseous necrosis. Despite the absence of demonstrable *Mycobacterium tuberculosis* and negative Heaf and Mantoux tests, he was treated with antituberculous drugs (streptomycin, PAS and isoniazid) and the adenopathy cleared.

He remained well for a year and then, at the age of 2, developed listlessness, fever and meningism. CSF examination was normal. Despite treatment with chloramphenicol and ampicillin in normal

doses, his condition deteriorated, and he developed bilateral psoas spasm. A laparotomy was performed which excluded intra-abdominal sepsis. The following day a greyish-white membrane was noted on the pharynx and pillars of the fauces, and from this *Pseudomonas pseudomallei* was cultured.

He was treated with tetracycline, to which the organism was sensitive *in vitro*, but failed to improve. Repeat sensitivity testing three weeks later showed diminished sensitivity to tetracycline. Abscesses on two toes and a finger appeared and these were shown radiologically to be associated with underlying osteomyelitis of the phalanges. Bone curettings from these abscesses grew *Ps. pseudomallei.*

Because of his failure to improve he was transferred from Singapore to England three months after the start of the illness. He was emaciated, dehydrated and anæmic on arrival. Three weeks treatment with intravenous chloramphenicol 100 mg/kg/day and kanamycin 15 mg/kg/day led to sufficient improvement to allow intramuscular therapy, and two weeks later the antibiotic regime was changed to oral sulphadimidine because of continued progress. Biopsy of a skin nodule five weeks after transfer, however, still grew *Ps. pseudomallei.* Recovery was interrupted by a urinary infection with *Strep. fæcalis* which responded to treatment with ampicillin.

For the last fifteen months, since recovery, he has been maintained on Septrin and has remained well.

He also has chronic granulomatous disease (diagnosed using the qualitative nitroblue tetrazolium test of Windhorst *et al.* (1967) and by a bacterial killing test modified from that of Quie *et al.* (1967)) and unexpectedly low immunoglobulin levels. After three months of chronic infection his IgG varied from 52% to 100%, IgA was 40–136% and IgM 112–156% of the MRC reference standards. Following clinical recovery IgG dropped to 44%, IgA to 52% and IgM to 40% of the MRC reference standards. Since his non-identical twin brother also has rather low immunoglobulins, this may be a familial abnormality unrelated to the chronic granulomatous disease, which is usually associated with high immunoglobulin values. It is surprising, however, that with defects in both leukocyte and immunoglobulin function, our patient has not had a more stormy clinical course.

Discussion

Melioidosis is a disease endemic in south-east Asia, and caused by the Gram-negative bacillus, *Ps. pseudomallei.* The organism is a widespread saprophyte and can be cultured from soil, drainage ditches and paddy fields in endemic areas. It is thought that the portal of entry is through minor skin abrasions, or by inhalation (Thin *et al.* 1970).

Melioidosis can be classified into three groups; subclinical, acute and chronic. The subclinical form has been defined immunologically by the detection of antibodies to *Ps. pseudomallei* occuring in the serum of otherwise healthy individuals in endemic areas (Nigg 1963). The acute disease presents with fever and pneumonitis accompanied by septicæmic spread of infection and has a high mortality. Chronic melioidosis has no specific mode of presentation, but may simulate disseminated fungal infections or tuberculosis. It seems likely that our patient was affected with the chronic form of the disease.

On reviewing the literature, the frequent occurrence of an underlying susceptibility to infection is notable. Whitmore (1912) first described the disease in morphia addicts and debilitated beggars in Rangoon, and many cases since have occurred in diabetics, alcoholics and patients with other infections. Because of this apparent rarity of clinical infection with an organism which is widespread in the region, our patient was investigated for an underlying susceptibility to infection, and chronic granulomatous disease was found. It is suggested that other patients with clinical melioidosis should be similarly investigated.

REFERENCES

Nigg C (1963) *J. Immunol.* **91**, 18

Quie P G, White J G, Holmes B & Good R A (1967) *J. clin. Invest.* **46**, 668

Thin R N T, Brown M, Stewart J B & Garrett C J (1970) *Quart. J. Med.* **39**, 115

Thompson E N & Soothill J F (1970) *Arch. Dis. Childh.* **45**, 24

Whitmore A & Krishnaswami C (1912) *Indian med. Gaz.* **47**, 262

Windhorst D B, Holmes B & Good R A (1967) *Lancet* i, 737

Cardiofacial Syndrome[1]

Cyril Chantler MRCP and Gerald McEnery MRCP
(for O D Fisher FRCP, A D M Jackson FRCP, H Jolly FRCP and M C Joseph FRCP)
(Queen Elizabeth Hospital and Brompton Hospital, London)

The clinical details of three children, with unilateral facial paralysis involving only the lower lip, and congenital heart disease, are summarized in Table 1. The family histories were negative and nothing of etiological significance occurred during the pregnancies. The cardiac lesion has given rise to no symptoms in patient A S but both the other children are severely affected, and F H has already

[1]Correspondence and requests for reprints should be sent to: Dr Cyril Chantler, Guy's Hospital, London SE1