there were only 15 chromosomes (Fig. 2). One cell with 47 and 3 cells with 46 chromosomes which did not show a constant pattern were thought to be the result of technical error. The karyotype of this patient was thus thought to be of the 45/XO type.

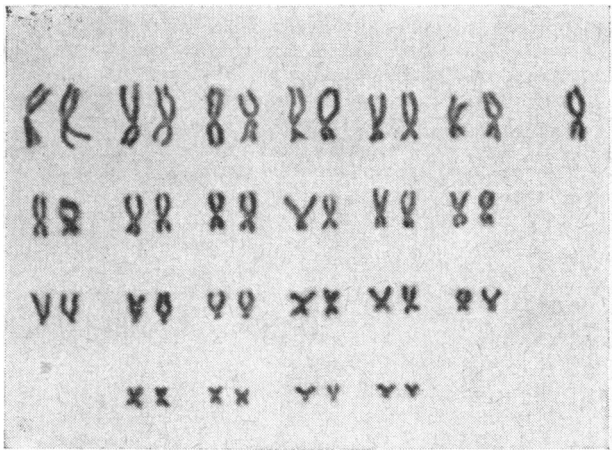

FIG. 2.—Karyotype of a metaphase cell from bone-marrow showing 45 chromosomes and XO sex chromosome constitution.

COMMENTS

Pseudohermaphroditism, regardless of the development of the somatic sex structures, has consistently revealed a chromosome sex constitution compatible with the type of gonad present. However, a case previously reported by us, in which one gonad was a testis and the other a "streak" commonly seen in Turner's syndrome, disclosed a 45/XO chromosome complement in bone-marrow cells (Bloise *et al.*, 1960). Except for the "streak," the case here reported is very similar and showed the same chromosome features. Noteworthy is the finding of a female sex chromosome complement in cells of cultured skin from a male pseudohermaphrodite (Shah *et al.*, 1961). Recently, a probable case of the so-called gonadal dysplasia with enlarged phallus showed 45 chromosomes and only one X chromosome. In addition, there was a "fragment" which could represent a portion of the Y chromosome (Vaharu *et al.*, 1961). We have studied a proved case of this last syndrome, and karyotype analysis revealed 45 chromosomes and an XO chromosome complement in bone-marrow cells (Epps *et al.*, 1962).

In view of the type of gonad present, all these male pseudohermaphrodites have different karyotypes from that expected. It is also true that all of them had the chromosomes studied in only one tissue. Thus the possibility of mosaicism is not excluded. An XO/XY mosaic could be present in those cases except for the subject reported by Shah *et al.*, who might be an XX/XXY mosaic. These reports show that male pseudohermaphrodites may have abnormal karyotypes and that the Y chromosome is not invariably present in persons with testicular tissue. Several cases of true hermaphroditism with XX sex chromosome constitution provide further support to this knowledge (Harnden and Armstrong, 1959; Hungerford *et al.*, 1959; Assis *et al.*, 1960; Ferguson-Smith *et al.*, 1960; Gordon *et al.*, 1960; Sasaki and Makino, 1960).

These findings suggest that gonadal differentiation may be brought about through several factors other than sex chromosome constitution alone. Further chromosome studies in more than one tissue, specially in testes, in similar cases may clarify the part played by the Y chromosome in the differentiation of the male gonad.

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Successful Treatment of a Case of Proteus Septicaemia

All forms of infection with species of *Proteus* are notoriously difficult to treat, and generalized infection with organisms of this group are usually fatal. It is therefore thought worth while to report briefly a case of *Proteus* septicaemia successfully treated with the help of a new synthetic drug.

"Trimethoprim" (2,4-diamino-r-(3,4,5-trimethoxybenzyl) pyrimidine) is a new drug which has been found by workers at the Wellcome Research Laboratories to be active against a wide variety of organisms, including all species of *Proteus*. Its activity is much influenced by both the composition of the medium and the size of the inoculum, but under optimum conditions 2 μg./ml. or less inhibits the growth of most common pathogens, only *Pseudomonas pyocyanea* and *Mycobacterium tuberculosis* being resistant. It has also been shown to act synergistically with sulphonamides: in a ratio of 1 part trimethoprim to 15 parts sulphadiazine, the minimum inhibitory concentration of each for a strain of *Pr. vulgaris* was reduced by one-eighth. The drug is absorbed from the alimentary tract, and a dose of 200 mg. four times a day gives blood-levels ranging from 3–8 μg./ml. with much higher urinary levels (S. R. M. Bushby, personal communication).

During a study by one of us (P. M. W.) of the action of combinations of antibacterial drugs, using the "cellophane" transfer technique, the combination of

trimethoprim and polymyxin B was shown to be bactericidal to all species of *Proteus*, although under the conditions of this test trimethoprim alone was bacteriostatic only and polymyxin B had no effect (see Garrod and Waterworth, 1962). In view of this observation the patient was treated with this combination.

Case History and Clinical Course

On March 26, 1962, a married woman aged 19 was admitted to St. Andrew's Hospital, Billericay, Essex, under the care of Dr. I. Gilbert, with a seven-day history of pyrexia, headache, and vomiting, associated with an exacerbation of chronic discharge from the left ear. She was seen by Mr. J. Littlejohn, E.N.T. surgeon, who made a diagnosis of acute/chronic mastoiditis with thrombophlebitis of the internal jugular vein. At operation foul-smelling pus under pressure was found as the cortex of the mastoid bone was removed. The lateral sinus was found to be full of septic thrombus, extending for 1½ in. (3.8 cm.) on the cephalic side of the lateral sinus. A swab from this grew *Pr. mirabilis*.

In spite of treatment with penicillin and sulphonamide, followed by chloramphenicol, the temperature failed to settle and the jugular vein was tied on April 3. The vein was found to be an abscess cavity and contained no blood, and bacteriological examination again revealed *Pr. mirabilis*.

In spite of further treatment with methicillin and streptomycin she developed pneumonia and pleurisy and became very ill, with a temperature up to 105° F. (40.6° C.), and a blood culture taken on April 5 grew *Pr. mirabilis*.

On April 6 treatment with trimethoprim and sulphatriad was started, in doses of trimethoprim 200 mg. four-hourly and sulphatriad 1 g. four-hourly. There was an immediate clinical improvement and drop in temperature. Next day methosporin (polymyxin methane sulphonate), 500,000 units six-hourly, was added to the treatment regime. The general improvement and fall in temperature were maintained, but on April 13 there was a rise in temperature associated with a local abscess in the neck. This was drained on April 16, and the swab again grew *Pr. mirabilis*. The patient, however, was well and blood culture at this time was negative.

After this the patient made an uninterrupted recovery, and on May 7 the mastoid was re-explored, the lateral sinus and jugular bulb were covered with firm granulation tissue, the middle ear was cleared of debris, and primary skin suture was obtained. The patient is now very well.

Bacteriological Findings

The minimum inhibitory concentration of trimethoprim for the *Pr. mirabilis* isolated from the blood was found to be 2 μg./ml. in normal urine containing 0.5% glucose and 0.12 μg./ml. in normal human serum, and trimethoprim and polymyxin B were bactericidal when tested by the cellophane transfer technique, though in some experiments there were one or two survivors. Viable counts showed that in urine 4 μg./ml. trimethoprim had little bactericidal effect, and if the inoculum was large growth occurred overnight. If 100 μg./ml. sulphathiazole was added growth was always prevented (this amount of sulphathiazole alone is inhibitory to a small inoculum), and a small inoculum (4,000 bacilli/ml.) was sterilized overnight. The addition of 8 μg./ml. polymyxin B to 4 μg./ml. trimethoprim usually sterilized a small inoculum in six hours, but, if large, the count fell sharply in two hours but survivors subsequently multiplied. These organisms and those growing in trimethoprim alone showed an 8–16-fold increase in resistance.

On the other hand, in normal serum 4 μg./ml. trimethoprim alone killed a small inoculum overnight and prevented growth from a large one. The addition of 100 μg./ml. sulphathiazole made little difference to the bactericidal effect, but if 8 μg./ml. polymyxin B was added the inoculum was always killed overnight, often in two to four hours.

We wish to thank Dr. I. Gilbert, Consultant Physician, and Mr. J. Littlejohn, Consultant E.N.T. Surgeon, for their permission to publish this case. Our thanks are also due to the Wellcome Foundation for the supply of trimethoprim.

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