Both the 48,XXYY and the 47,XY chromosome anomalies are now well-recognized conditions following the first reports by Muldal and Ockey (1960) of the XXYY genotype, and Sandberg et al. (1961) who described an XYY male.

This paper presents the findings in 2 patients with 47,XY/48,XXYY mosaicism, and one patient with the 47,XY anomaly, discovered among 250 men in a comprehensive hospital for the mentally subnormal in which there are no special security facilities. They had been selected for the investigation because of their outstanding tallness and their histories of antisocial and delinquent conduct in association with mental retardation.

**Clinical Features**

**Case 1.** This man, aged 22, is an illegitimate child adopted at the age of 4 months. No details of his parents are available. He walked at the age of 2, talked at 3, and achieved clean habits at 5. He has had no serious illnesses. After attending an ordinary school to the age of 7 he went to special schools until 15, when he was excluded for indecent behaviour and admitted to hospital, where he started a fire in his ward. Intermittently he has shown evidence of psychosis. On the Wechsler Adult Intelligence Scale his full scale intelligence quotient is 53, and he is classified as subnormal. On examination, he is tall, height 182 cm., weight 60 kg. His head appears small, with a cranial circumference of 52 cm. He is myopic and of asthenic physique, with small testes, gynaecomastia, and scanty pubic and axillary hair. Skull x-ray shows a bulky mandible and prominent supraorbital ridges; the pituitary fossa is normal. Electroencephalography reveals no abnormality. His excretion of 17-ketosteroids is 1 mg./24 hr., and excretion of 17-hydroxycorticosteroids less than 1 mg./24 hr. (normal ranges: 17-ketosteroids, 5–28 mg./24 hr.; 17-hydroxycorticosteroids, 5–21 mg./24 hr.). Dermatoglyphs show axial triradii on both palms in a more proximal position than normal, with narrow atd angles of 35° on both hands. His finger-print patterns are ulnar loops except for whorls on the left ring finger (iv) and on the right index (ii), middle (iii), and ring (iv) fingers.

**Case 2.** This man, aged 31, was born of non-consanguineous parents when his mother was 29 and his father 32. He is the youngest of three. His two brothers, aged 36 and 37 respectively, are normal. Neither parents nor sibs were said to be unusually tall. He walked at 2 years, talked at 3, and developed clean habits at 9. He had meningitis at the age of 3. He went to special schools until he was excluded at 14 to attend a training centre. There he was described as having a violent temper, was a gang leader, and a frequent

![Skull x-ray showing the bulky mandible (Case 3).](image)
absconder. He has a tendency to wander, has been guilty of breaking and entering and larceny, and he has been known to inflict injuries on himself. He has a full-scale intelligence quotient of 55 (Wechsler Adult Intelligence Scale), and is classified as subnormal.

He is tall, height 189 cm., and his weight is 77 kg. His cranial circumference, 58 cm., is normal. His testes are small; he has scanty pubic and axillary hair, but no gynaecomastia. Both eyes show optic atrophy. His skull x-ray shows a bulky mandible, with prominent supra-orbital ridges and a normal pituitary fossa. His electroencephalogram reveals no specific abnormalities. Excretion of 17-ketosteroids is 8 mg./24 hr., and of 17-hydroxy-corticosteroids 5.5 mg./24 hr. His dermatoglyphs show axial triradii on both palms in a more distal position than normal with atd angles of 52° on both hands. A hypothenar pattern, a carpal loop, is present on the right palm only. The finger-patterns are mainly ulnar loops with whorls on both thumbs and the right ring finger (iv), and a radial loop on the right index finger (ii).

Case 3. This man, aged 22, was born of non-consanguineous parents when his mother was 26 and his father 31. The parents were not said to be unusually tall. He is the eldest of three. His two sisters, aged 12 and 20, are normal. He walked at 2 years, talked at 3, and had clean habits at 4. He has had no serious illnesses. He attended special schools and was admitted to a hospital for the mentally subnormal at the age of 15 after being found guilty of indecent assault. His full-scale intelligence quotient (Wechsler Adult Intelligence Scale) is 49 and he is classified as severely subnormal.

He is tall, height 188 cm., and he weighs 77 kg. His cranial circumference is 56 cm. His testes and hair distribution are normal and he has no physical abnormalities except for flexion deformities at the proximal interphalangeal joints of the middle, ring, and little fingers on both hands. He is myopic. Skull x-ray shows a flattened occiput, a bulky mandible (Fig. 1), and prominent frontal protruberances; the pituitary fossa is normal. Electroencephalography reveals no abnormalities. 17-ketosteroid excretion is 6.5 mg./24 hr., and 17-hydroxycorticosteroid excretion is 6 mg./24 hr. Dermatoglyphs show proximal axial triradii on both palms with narrow atd angles of 38° on both hands. His finger-print patterns are ulnar loops except for an arch on
the right index finger (ii), and a radial loop on the left ring finger (iv).

**Cytogenetic Findings**

Samples taken from the three patients included buccal smears, a plain blood film and venous blood for chromosome analysis.

Blood cultures prepared from separated leucocytes were set up according to a modified technique of Moorhead et al. (1960) and incubated for 72 hours. Microcultures were also set up using 0·25 ml. of whole blood. The results of these studies are summarized in the Table.

**TABLE**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Chromosome Count</th>
<th>Total No. of Cells Examined</th>
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<tr>
<td></td>
<td>46</td>
<td>47</td>
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<tr>
<td>1</td>
<td>1</td>
<td>22</td>
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<tr>
<td>3</td>
<td>6</td>
<td>28</td>
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<tr>
<td></td>
<td>1</td>
<td>33</td>
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**Case 1.** 42% of cells in the buccal smear were chromatin positive. Seven drumsticks were counted among 300 neutrophils in the blood film.

Blood culture revealed 2 cell-lines, one with 47 and one with 48 chromosomes. Detailed karyotypic analysis of 10 metaphases of the 47 cell-line showed two Y chromosomes together with 15 chromosomes in the C group, the extra one presumed to be an X chromosome (47,XYY) (Fig. 2). Analysis of 10 cells of the 48 cell-line showed the presence of two Y and two X chromosomes (48, XXYY) (Fig. 3 and 4).

One cell had a modal count of 49 and analysis revealed a probable sex chromosome complement of XXXYY. It is possible that this cell represents a third stem-line.

**Case 2.** 12% of cells in the buccal smear were chromatin positive. Among 500 neutrophils in the blood film, 5 drumsticks were counted.

Blood culture again showed two cell-lines of 47 and 48 chromosomes. Karyotypic analysis of 10 cells of each of the cell-lines showed a chromosome complement of 47,XYY and 48,XXYY respectively, as in Case 1 (Fig. 5 and 6). Analysis of the six cells with 46 chromosomes
showed that the missing chromosome varied in each cell, and these cells were presumed to be artefacts.

The proportion of cells with the karyotype of 48,XXYY (about 50%) may be reflected in the relatively low buccal and blood smear counts.

**Case 3.** No cells in the buccal smear showed sex chromatin, and among 300 neutrophils in the blood film no drumsticks were observed. Of the metaphases examined from the blood cultures, 33 had a modal count of 47, and analysis of 10 of these revealed a chromosome complement of 47,XYY (Fig. 7).

In all three cases the Y chromosomes were easily distinguished from the G group, being somewhat larger and having parallel long arms.

**Discussion**

The patients described in this paper were found when a special survey was conducted in the hospital on all the male patients who were at least 6 feet (183 cm.) tall, and showed criminal tendencies.

There were 5 men who came into this category; they were studied by means of blood and buccal smears and chromosome analysis. No chromosome abnormality was found in 2, and the other 3 revealed the abnormalities already described.

**Clinical Features.** The 3 patients in this investigation were all tall, mentally retarded, and had histories of antisocial and delinquent conduct such as have previously been associated with the YY syndrome (Jacobs *et al.*, 1965; Casey *et al.*, 1966a, b). The two patients with 47,XY/48,XXYY mosaicism showed the physical features of Klinefelter's syndrome in addition. We have been unable to find an account of this mosaic in the literature, and the only comparable case we have been able to discover is one of 47,XXY/47,XY mosaicism, reported by Gilgenkrantz, Hartemann, and Arnould (1964) in a patient with the physical stigmata of Klinefelter's syndrome but only 171 cm. tall. The Klinefelter phenotype appears to be associated with the presence of the additional X chromosome in these cases.

Our three patients all had an acromegalic skull configuration, with bulky mandibles and prominent supra-orbital ridges. This particular feature was recorded in a case of an XXYY man described by Ellis *et al.*, (1961), and in a case of an XXXXY man reported by Bray and Josephine (1963). In Case 1 the 17-ketosteroid and 17-hydroxycorticosterone excretions were below normal, as may be found in

![Fig. 4. Metaphase spread of the karyotype shown in Fig. 3.](image)
Klinefelter's syndrome. In Cases 2 and 3 the values were just within the normal range. Dermatoglyphs in Cases 1 and 3 showed proximally situated axial triradii with small and angles such as are found in the YY and Klinefelter's syndromes. Case 2 had more distally placed axial triradii with larger and angles, and on the right hand a carpal loop in the hypothenar area, a characteristic found in cases with the 48,XXYY chromosome complement (Uchida, Miller, and Soltan, 1964). The fingerprint patterns were less typical.

As the two patients with 47,XYY/48,XXYY mosaicism showed certain features of both Klinefelter's and the YY syndrome, their classification poses a problem. Because they exhibit characteristics of Klinefelter's syndrome they could be called YY mosaic variants of this syndrome or, alternatively, XXXY Klinefelter mosaic variants of the YY syndrome.

**Cytogenetic Findings.** There are several ways in which the cell-lines in the two mosaics could have originated. The production of a normal XY zygote, followed immediately by double non-disjunction of the sex chromosomes, would give the 48,XXYY cell-line (Fig. 8); further non-disjunction of one pair of X's would then give the 47,XYY and 49,XXXYY cell-lines. This mechanism seems the most probable because it involves mitotic non-disjunction only. It explains Case 1, assuming the 49 cell is not artefact, and it can also explain Case 2 though no cells with 49 chromosomes were found.

There are other possible explanations postulating the formation of abnormal zygotes, either 47,XYY or 48,XXYY, followed by further non-disjunction. As these mechanisms would involve both meiotic and mitotic non-disjunction and the production of unwanted cell-lines, they are considered less likely.

**Summary**

This paper reports two cases of 47,XYY/48,XXYY mosaicism and a case of the 47,XYY syndrome found in a hospital for the mentally subnormal in which
there are no special security facilities. 47,XY/48, XXYY mosaicism has not been previously reported. All the cases showed mental subnormality, tallness, and antisocial and delinquent behaviour, together with some acromegalic features. The two patients with mosaicism also had many of the features of Klinefelter's syndrome. Hypotheses concerning the origin of the mosaicism are presented and the question of the classification of these mosaics is considered.

We are grateful to Mr. D. N. Howard and the Medical Photographic Department, St. James's Hospital, for the photographs.

REFERENCES

**Fig. 7.** Karyotype of Case 3, showing 47,XYY chromosomes.

**Fig. 8.** Suggested mechanism for the production of the mosaicism.
XYY syndrome, and XYY-XXYY mosaicism also showing features of Klinefelter's syndrome.
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