Chromosome Structure and Function in Man, III. Pachytene Analysis and Identification of the Supernumerary Chromosome in a Case of Down’s Syndrome (Mongolism)

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Abstract. Recently developed pachytene maps of the two small acrocentric autosomes (numbers 21 and 22) of man have been applied to a case of Down's syndrome mosaic for normal and trisomic cells (46,XY/47,XY,21+). Trivalents in trisomic spermatocytes, and thus the supernumerary chromosome, were recognized as compatible in length and chromomere pattern with the shorter of these two chromosomes at the pachytene stage. With the exception of the region of the centromere and the short arm, association among constituents of the trivalent appeared complete.

We report here the results of our first studies of pachytene chromomere patterns in a patient with Down's syndrome (mongolism).

The chromosome present in extra dose in Down's syndrome is by definition1 number 21; however, some controversy has existed concerning its identity in terms of relative size at somatic metaphase. (The two small acrocentric autosomes, numbers 21 and 22, are closely similar in size and morphology at that stage.) Chromosome 21 has been thought by some investigators to be somewhat longer than 22, although quantitative data suitable for such discrimination are lacking. A minority opinion has held that the shorter of the two is trisomic in Down's syndrome.

In the preceding paper in this series2 we have presented provisional pachytene maps of the two small acrocentric autosomes. The maps are markedly different from one another both in length and in chromomere pattern, and these two distinct segments of the genome were closely similar among the eight males studied.

Results. We have been fortunate to obtain testicular biopsy material from a 23-yr-old patient [RM071047 (745H)]3 who had been recognized, from earlier studies of somatic metaphase chromosomes, 4 as a mosaic case of Down's syndrome (46,XY/47,XY,21+).5 Part of the tissue was fixed in Bouin's solution for histological study. Normal testicular architecture was present, but there was marked oligospermia as evidenced by the rarity of spermatozoa in the tubular lumina. Other portions of the tissue were prepared for cytogenetic study by methods described elsewhere.5

Primary spermatocytes of two types were present: those with an apparently normal chromosome complement and others in which trivalents were clearly
apparent. Pachytene figures were studied with respect to the two small acrocentric autosomes. Several classes were recovered, namely 10 cells with the longer and shorter small acrocentrics present as bivalents (Fig. 1A); nine cells with the longer as a bivalent and the shorter as a trivalent (Fig. 1B); 16 cells with only the longer recognizable (as a bivalent); and those with only the shorter recognizable [either as a bivalent (in 10 cells) or as a trivalent (in 23 cells)]. No other classes were observed, for example figures with a univalent, or figures with both a trivalent and the shorter of the two normal bivalents. The chromomere patterns of the trivalents were in agreement with the map of the shorter of the two normal bivalents, which would thus appear to be chromosome 21. Small acrocentrics from a number of primary spermatocytes are shown in Fig. 2.

**Discussion.** It is fortunate that the mosaic condition of this patient, already known from studies of somatic cells, is reflected in the germ cells. We were thus able to compare the two classes of spermatocyte, one in which both small acrocentrics are bivalent and the other in which one is bivalent and the other trivalent.

The short arms of the trivalent usually appear entirely unassociated or with two of the three constituent elements paired (Fig. 2A and B); the unpaired short arms often show chromatids. In contrast, the long arms of all three chromosomes are closely associated and show few of the asynaptic regions frequent in trisomics of other organisms. The parallel array of the long arms and the relative flatness of the configuration suggest that two separate synaptinemal complexes.
FIG. 2. Representative small acrocentric autosomes at the pachytene stage. Scale indicates 10 microns. Sizes of the classes of primary spermatocyte recovered in this study are given in the text.

(A) The shorter acrocentric as a trivalent.
(B) The shorter acrocentric as a bivalent.
(C) The longer as a bivalent and the shorter as a trivalent in five different nuclei. Rightmost two are from nucleus shown in Fig. 1B.
(D) Both small acrocentrics as bivalents in four different nuclei. Leftmost two are from nucleus shown in Fig. 1A.
(E) The longer acrocentric as a bivalent.
may be present. This apparent difference in pairing between long and short arms of the trivalent remains to be explained.

The analysis presented here indicates the potential of pachytene maps in man. While further studies will be necessary to rule out the possibility that the other small acrocentric can be likewise involved, the acrocentric involved in this case of Down's syndrome has been precisely identified.

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