of the ratio to the high side: (1) Ovule or embryo abortion occurred as a result of an effect of the cytoplasm of the "high" parent. (2) Selective fertilization occurred due to an incompatibility associated with the cytoplasm of the "high" parent. (3) Cytoplasmic inheritance of agglutinating activity was manifested in at least some of the homozygous recessive progeny.

The "low" lines, apparently homozygous recessives, were not completely devoid of activity, and the difference between "high" and "low" lines seems to be merely a difference in the concentration of agglutinin present, or alternatively, in the concentration of one or more agglutinin-inhibiting substances. We have not yet attempted to purify the agglutinin from plants of different activities.

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*THE HUMAN CHROMOSOMAL SATELLITES IN NORMAL PERSONS AND IN TWO PATIENTS WITH MARFAN'S SYNDROME**

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In 1958, quantitative characterizations of all the human chromosomes were published in which measurements of total length and centromere position of each member were presented.[1] These measurements were shown to be sufficiently reproducible to permit unequivocal identification of each chromosome (including the sex chromosomes), provided that a sufficiently large number of clearly defined and well separated mitotic figures is available for analysis, a feature characteristic of the methodology employed by us, since it permits indefinite cell multiplication *in vitro* without change in chromosome constitution.[2, 3] Two pairs of satellited chromosomes were described and characterized, listed as number 18 and 21 in Figure 1. Subsequently two other laboratories also published quantitative morphologic analyses of the entire human karyotype which agreed with ours

virtually completely, within the limits of the experimental uncertainty (which need be no more than a few per cent), and confirmed the group identity of the

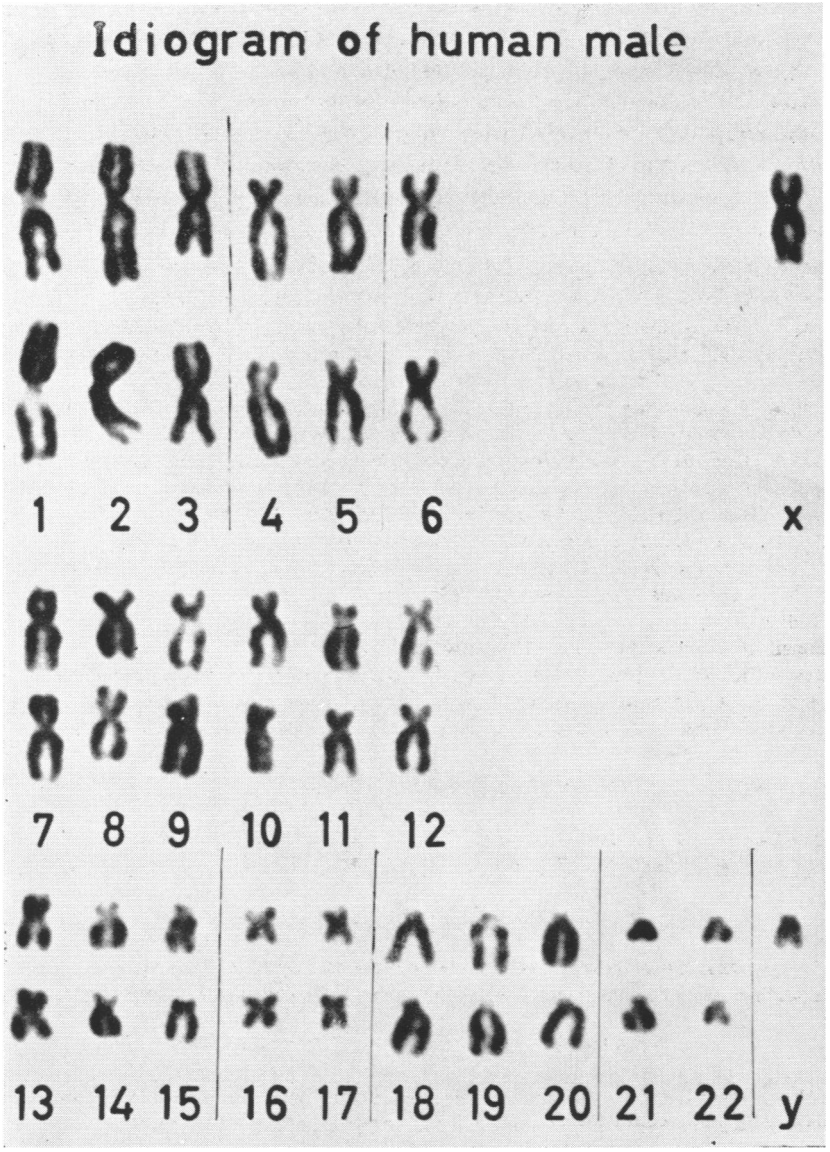

FIG. 1.—Idiogram of chromosomes from the normal human male.[1] The female is identical but with two X chromosomes and no Y. Chromosome pairs number 18 and 21 are satellited as previously described[1] although the structures are so lightly delineated in normal cells that they photograph only faintly and often fail to be reproduced in printing.

satellited chromosomes.[4, 5] However, question was raised whether the satellited chromosome pair of group VII is indeed the largest pair (i.e. number 18 in the Tjio and Puck classification system) or one of the smaller pairs.

In a preceding work, we had described characteristic variations in the satellite structures of two human subjects.[3] These exhibited heterozygously enlarged

satellites, in the one case on both numbers 18 and 21, and in the other only for the latter chromosome. While both of these subjects had been hospital patients, no feature of their records revealed any genetic defect that could be related to their unusual satellite conditions, nor were the patients' families available for study of the inheritance of this cytogenetic marker. While the poor response of the satellites to the conventional chromosome stains and the need to obtain chromosomes in early metaphase for clearest delineation of satellite morphology make such studies difficult, the problem is of an importance warranting careful study. This communication deals with two further findings concerning the human satellites.

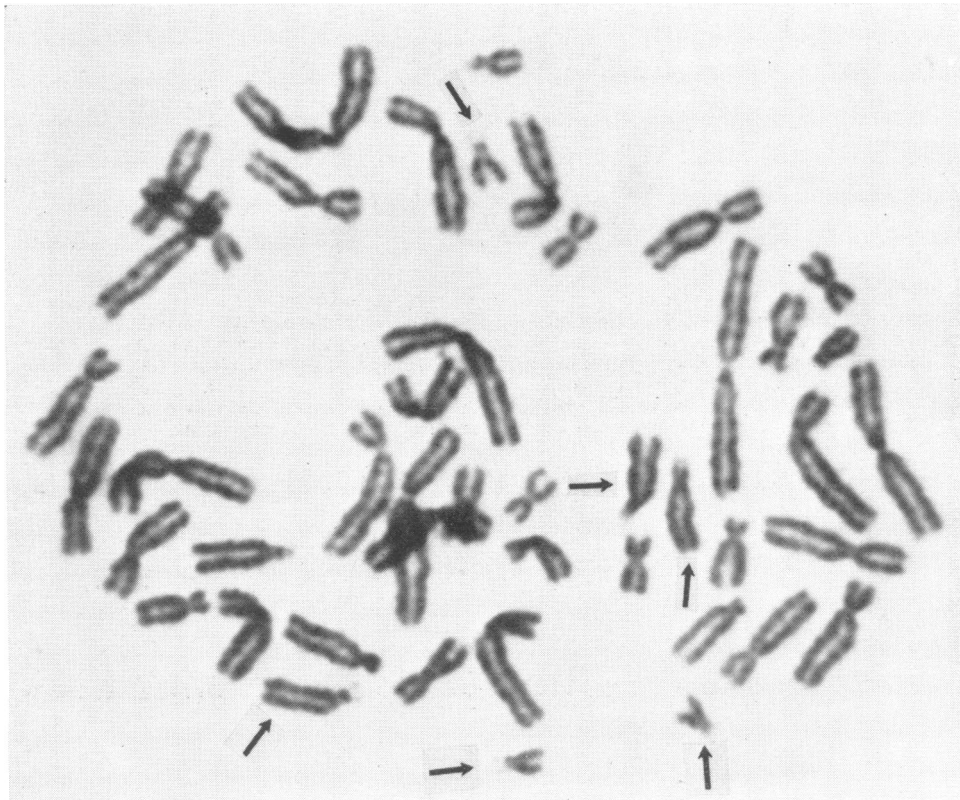

FIG. 2.—Typical human chromosome set showing six satellites (arrows). The satellites often are too faint to be well delineated, but this number has now been found in several human subjects, with unrelated genetic conditions.

In analysis of the chromosomes of a variety of human subjects, several instances have been found in which additional satellites are observed. In every case these have been present on another chromosome pair of group VII, probably number 20, in addition to the ones previously described on pairs 18 and 21. The uncertainties of visualization of these structures makes it impossible yet to ascertain whether 6 satellited chromosomes always appear in human cells, but the fact that these are visualized at times in cells from a variety of different human subjects makes it probable that these will turn out to be a frequent, if not universal, characteristic of Man's karyotype. This finding also resolves the apparent discrepancy about the

identity of the satellited pair of group VII, since two pairs can carry these structures. A photograph of a chromosome set with six clear satellites is presented in Figure 2. It is obvious that means must be found to delineate the satellites with greater reliability.

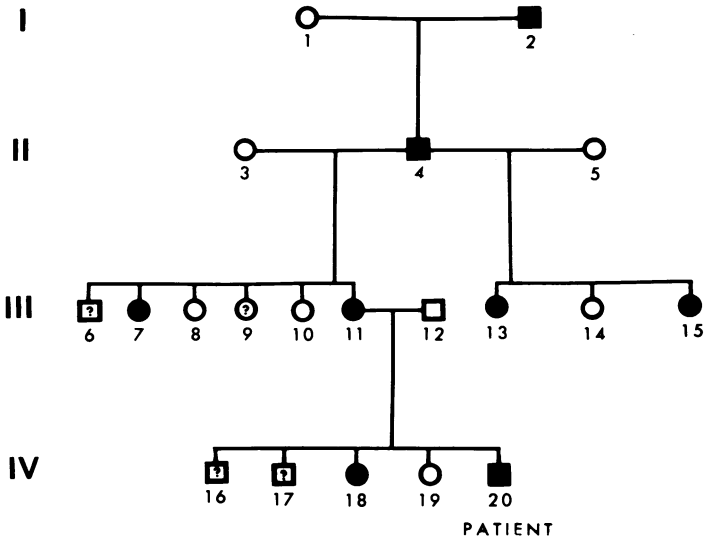

FIG. 3*a*.—Inheritance of Marfan's Syndrome (Patient of Fig. 4). The genealogy was established from the patient's hospital record. Circles indicate females and squares males. Presumptive evidence of the presence of the condition as indicated by heart disease, with or without arachnodactyly and eye defects, has been indicated by a solid figure. Possible presence of the syndrome as indicated by reported death in infancy or other suggestive symptoms is shown by a question mark.

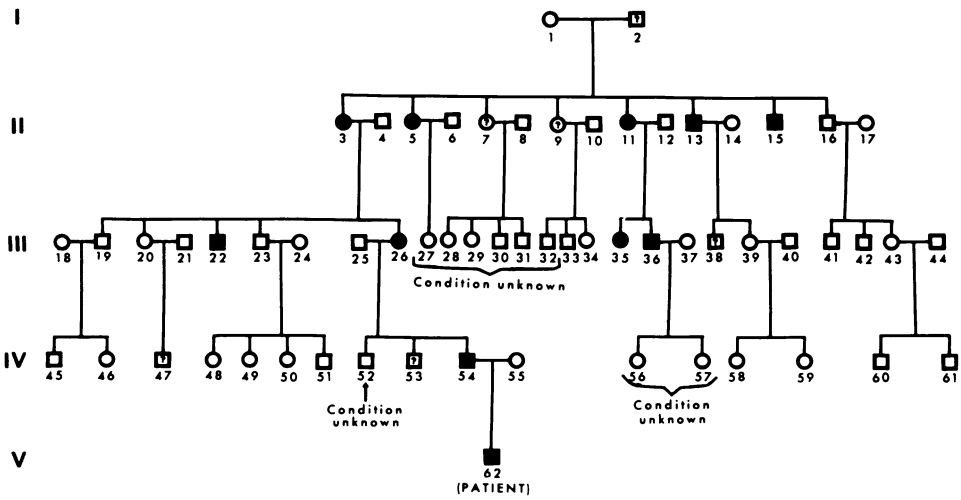

FIG. 3*b*.—Inheritance of Marfan Syndrome in patient corresponding to Figure 5. The genealogy was established from questioning of members of the patient's family, who have been very cooperative. The system followed is the same as in 3*a*. The pattern indicates the typical autosomal, dominant transmission.

Further interesting features of the human satellited chromosomes have appeared in an analysis of the cells of patients in whom the disease, Marfan's syn-

drome, had been diagnosed. This condition is a relatively poorly characterized clinical situation, usually inherited as a simple, Mendelian, autosomal, dominant character.[6] However, the first patient available to us had occurred in a family with no history of this disease, or, indeed, any indication of previous metabolic abnormality. The patient was not available for examination by us, and while the diagnosis of Marfan's syndrome was made on the basis of arachnodactyly, congenital heart disease, with probable ventricular septal defect, dislocated lens, a high, arched palate, and arthrogryposis, the absence of any other familial history of this disease renders it uncertain whether this case is identical to those in which a clear, hereditary pattern exists. The chromosomes of this patient were found to be normal, as indicated in a previous publication.[7]

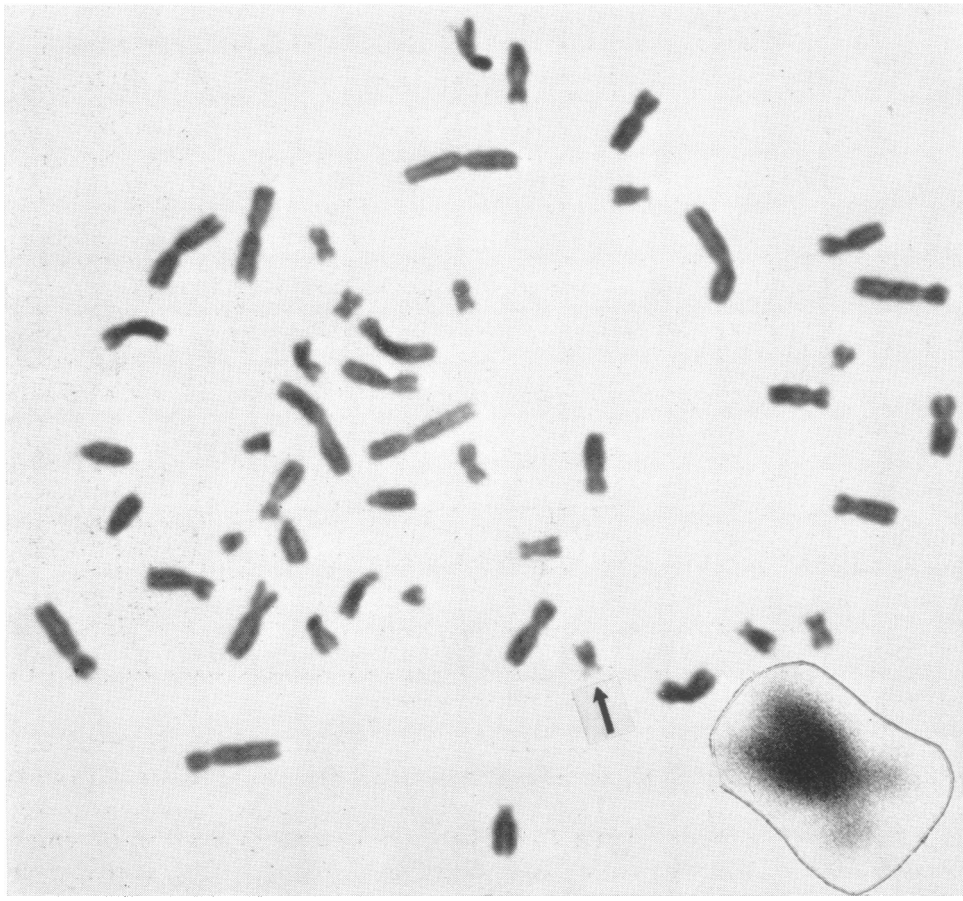

FIG. 4.—Metaphase chromosome set of patient with inherited Marfan syndrome. The arrow indicates the enlarged satellite on one member of chromosome pair 21, which is also shown enlarged in the lower right-hand corner of the picture.

In a second patient in whom the diagnosis of Marfan's syndrome was made, a clear familial history was evident. The pertinent clinical findings were: hypotonia, arachnodactyly, inguinal hernia, pigeon breast, high, arched palate, and cyanotic, congenital heart disease (tricuspid atresia, atrial and ventricular septal defects). The genealogy, indicating transmission by a single, dominant, genetic

determinant is shown in Figure 3*a*. Chromosomal analysis carried out on cells originating from a tiny biopsy of the skin and cultivated *in vitro* in accordance with the methodologies previously described[2, 3, 8] revealed a normal 46/XY complement, with the individual members all essentially normal in total size and arm length. However, an outstanding characteristic of this patient's karyotype is the possession of a tremendously enlarged satellite on one member of pair number 21. This structure, as shown in Figure 4, was consistent in all the cells examined, and was clearly greater than that of any other satellite previously seen, not excluding those which we had already described as enlarged.[3] Unfortunately, no other members of this patient's family are available for study.

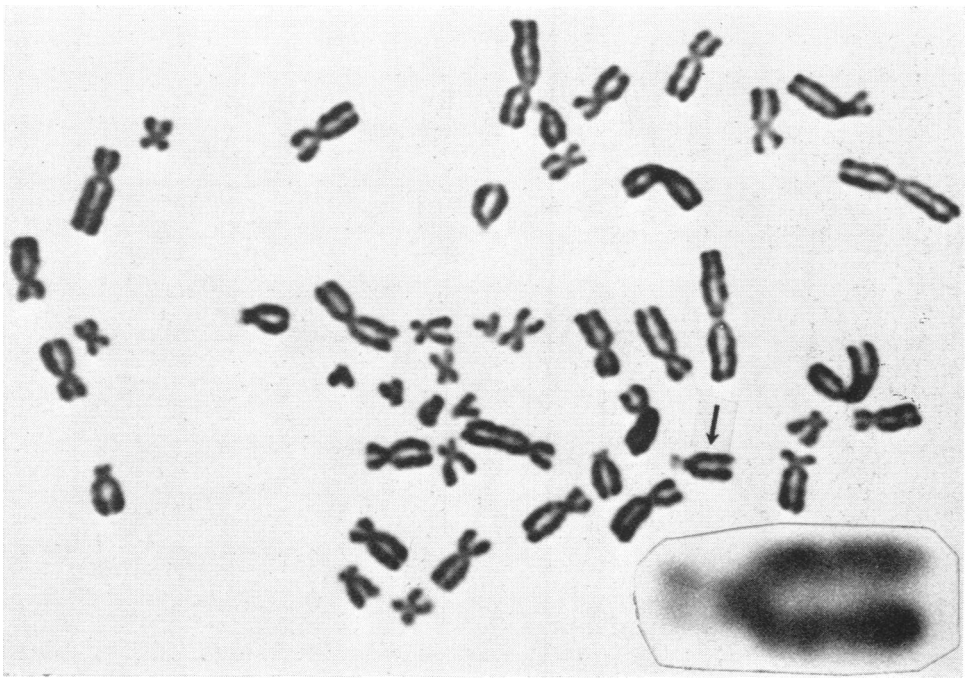

FIG. 5*a*.—Chromosomes of second patient with Marfan syndrome, showing the enlarged satellite on one member of pair 18 (arrow and enlargement in corner).

A third patient with the same diagnosis of Marfan syndrome has also been analyzed chromosomally. The diagnosis was established on the basis of a typical habitus including arachnodactyly, dolichomorphism, marked pectus excavatum and brachycephaly in an 18-month-old boy, and a genealogy indicating a simple, dominant mode of inheritance of Marfan syndrome (Fig. 3*b*). This patient again exhibited a set of chromosomes completely normal except for the satellites (Fig. 5). In this case, however, the abnormality was on a chromosome of pair number 18, instead of 21. Again, it was consistent in all cells, and involved an enlargement clearly beyond the range of those seen in any other human subjects.

Discussion.—The satellite enlargements here described conceivably may arise through any of several mechanisms, such as duplication of the material of which the satellite is composed; interchange or reciprocal translocation between the satellite and part of some other chromosome; or an intrachange within the satellited chro-

mosome itself, such as an inversion containing the satellited region, or a reciprocal interchange between the 2 arms of the chromosome. Hence it is possible that satellite enlargement of itself might be accompanied by a variety of different kinds of phenotypic behavior.

While the present data do not prove the given abnormalities to be the underlying cause of Marfan's syndrome, a relationship is definitely suggested, since

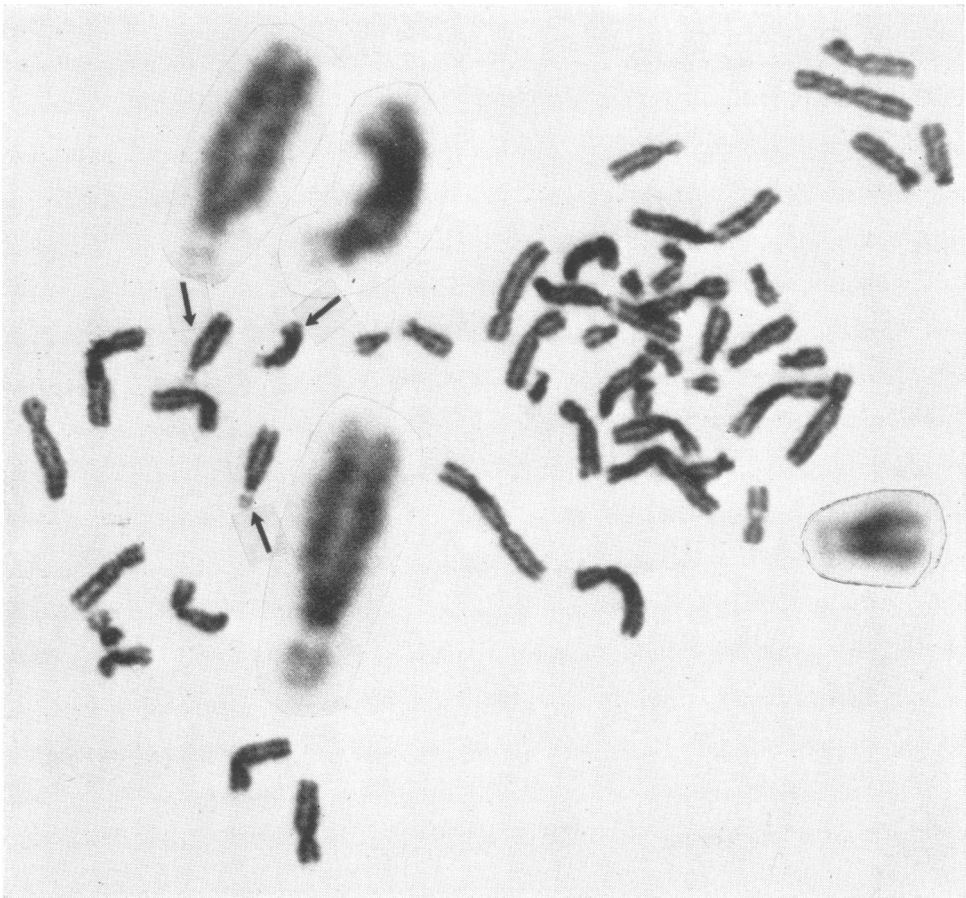

FIG. 5*b*.—An early metaphase chromosome set from the same patient as in 5*a*, demonstrating the enlarged satellite on one member of pair number 18 (lower arrow). Two of the other satellited chromosomes of Group VII are also clearly shown in this picture. Enlargements of each of these chromosomes have been attached close to the corresponding arrows. At the right side an enlargement of one of the satellited chromosomes of pair number 21 has been included for comparison.

in the analysis of chromosomes from more than 30 human subjects, satellites enlarged to the degree here described have been found only in those two patients who exhibit this particular disease, and in the form which displays a dominant genetic pattern. The heterozygosity of the defect in each case is in accord with the mode of inheritance. It is unexpected, however, that the structural defect obtained in these two cases should involve different chromosomes, and a causal connection between this aberration and the given clinical condition can only be maintained on the assumption that damage to either satellite can cause similar

cellular derangement. While the role of satellites in the economy of the cell is still far from clear, evidence shows that the satellited chromosomes involve function of the nucleolus.[9] Therefore, the suggestion is tenable that at least some forms of Marfan's syndrome are due to a dominant genetic defect involving satellite formation which affects a cell function requiring normal interaction of satellites from more than one chromosome. Work is continuing on this problem, investigating satellite cytology and nucleolar behavior in families with this disease. In a forthcoming report, additional pictures will be presented of normal and abnormal human satellited chromosomes, demonstrating their characteristic changes from prophase through late metaphase.

Summary.—Human chromosomal complements have been found with six instead of four satellites. These observations reconcile one of the contradictions in the literature dealing with the human karyotype, and raise the possibility that the higher figure may be a common or possibly universal satellite number in man.

Chromosomes of three patients with a diagnosis of Marfan syndrome have been described. One patient with no familial history of the disease, revealed a normal chromosomal constitution. The other two patients' genealogies exhibited the typical pattern of a simple dominant, autosomal defect. Both patients' chromosomes demonstrated a single, abnormally enlarged satellite, in the one case on a chromosome of pair number 18, and in the other on number 21.

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