Infertility: a proposed scheme of action in the light of cytogenetic investigations

by
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Infertility may be based upon a number of factors – endocrine, metabolic, nutritional, mechanical, immunological, toxic, infectious, psychological or genetic –. We shall emphasize the latter, and will consider cases in which a couple's inability to produce children is due to lack of vitality in the foetus, which in turn is affected by factors of genetic nature which may be recognized on the basis of a chromosomal aberration (chromosomal infertility), or the constitution of lethal genotypes, which were not evident in the parents because they were in the heterozygotic stage, but which became operative in the foetus due to recombination of genes (genic infertility). It is now considered that chromosomal anomalies in the foetus are present in about 60% of cases of spontaneous abortion. Such a high frequency of chromosomal anomalies cannot be considered accidental; on the contrary, the relevance of the statistical findings leads to the conclusion that abortion, in such cases, is only a biological defence mechanism intended for the elimination of genetic errors, thus limiting the birth of malformed individuals. Though they vary in their relative frequency, chromosomal anomalies can mostly be included in three principal groups: autosomal trisomia, especially affecting groups D, E (Fig. 1) and G, monosomia X and polyploid. To these may be added, though much less frequently, cases of autosomal monosomia, mosaicism and structural alterations. The pathogenic mechanisms whereby these chromosomal anomalies arise, find their phase of action at the level of gametogenesis, fertilization and the first division of the zygote. Factors that have an influence upon these phases of the development of the gametes and ovum, may be listed as follows: (a) *maternal age*; ([2]) *delayed fertilization*, in relation to the three groups of causes that may bring it about, producing intrafollicular or intratubal hypermaturation of the oocyte or ageing of the spermatozoon within the female genital tract ([3,4,5]) (c) *chromosomal aberrations in the parents*, especially translocations (Fig. 2) ([6,7]); (d) *radiation* ([8]).

As regards the supporting role of the viral diseases, oral contraceptives, inductors of ovulation and psychopharmaceutical drugs, there is still much uncertainty.

Genetic infertility may also be caused by the constitution of lethal genotypes which had not appeared in the parents because they were at the heterozygotic stage, or for other reasons. Genetic recombination may thus bring this potentially lethal character into the open, or it may even appear at the pre-implantation stage or after the first implantation, in subclinical form; it is expressed most frequently in the form of abortion, stillbirth or death of the newborn infant, and in the birth of malformed individuals.

At this point we need to consider what line of action should be followed when faced with a case of infertility (Fig. 3). The couple concerned should not only be given a clinical examination and be questioned about their family history, with

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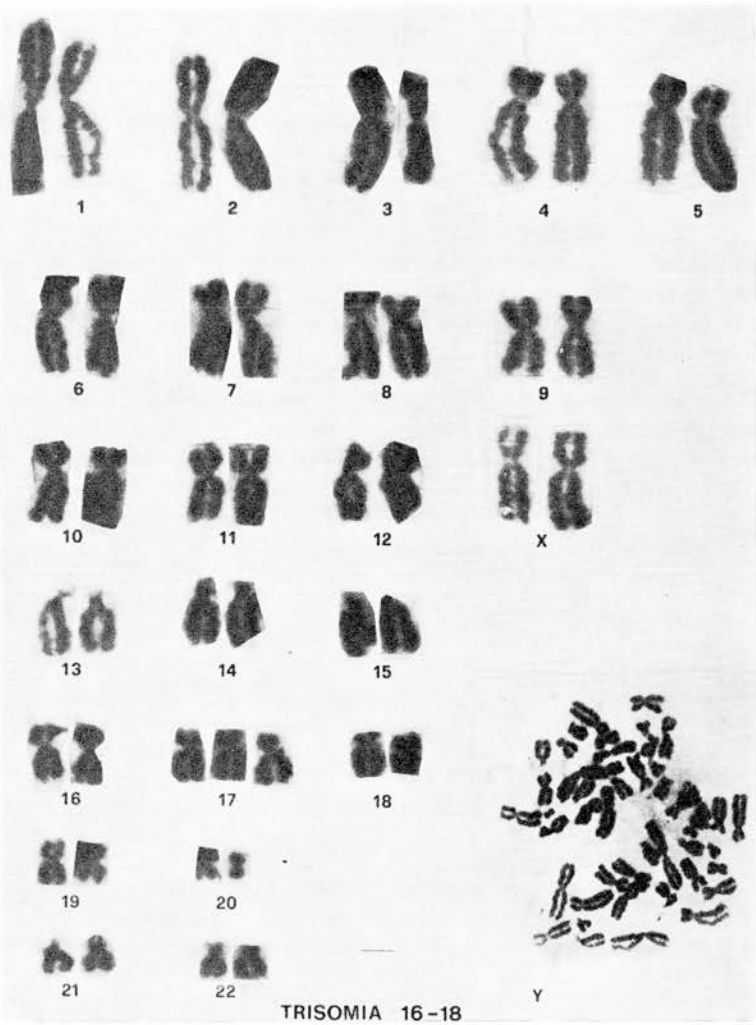

FIG. 1.

a view to the definite exclusion of any anatomico-functional causes, but should be investigated in order to demonstrate all the factors already referred to (maternal age, characteristics of the menstrual cycle, radiation, etc.) which may be responsible for the occurrence of hereditary anomalies in their ancestry. In this connection particular stress should be laid on the drafting of a family tree and the cario-

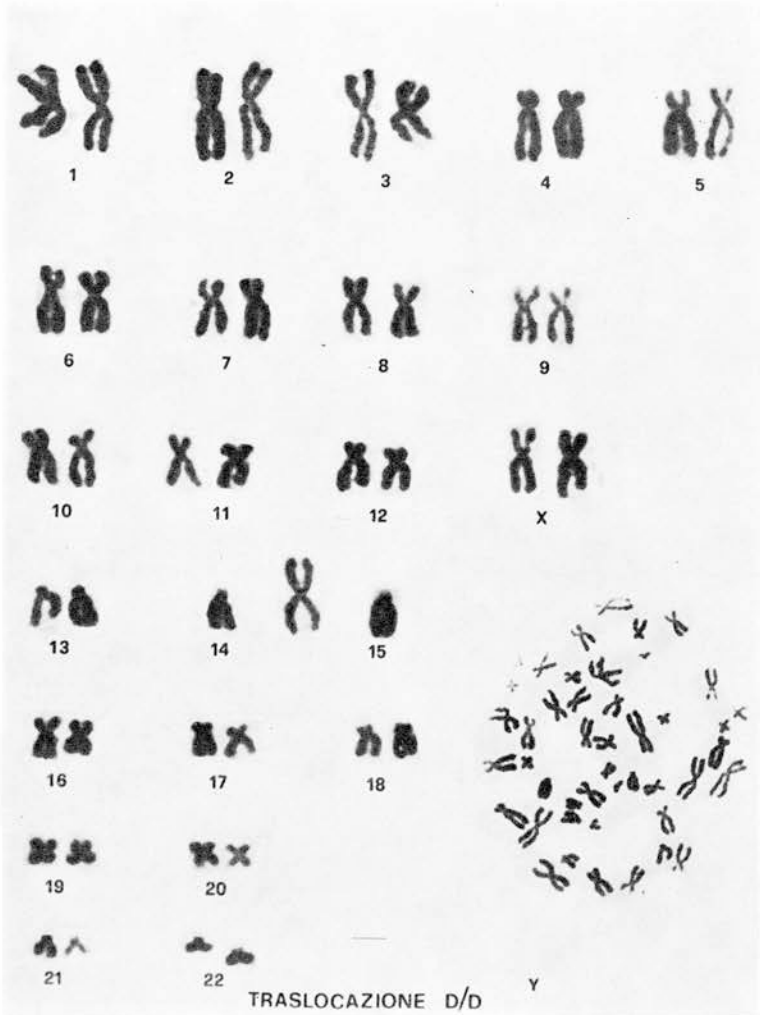

FIG. 2.

logical examination of both partners. If analysis of the findings from all these investigations indicates causative factors of a genetic kind, the problem of the prevention of birth of genetically affected individuals can be dealt with in subsequent pregnancies. Therefore it will be necessary first of all to calculate the risk and to offer genetic advice. In the case of pregnancy, pre-natal checks must

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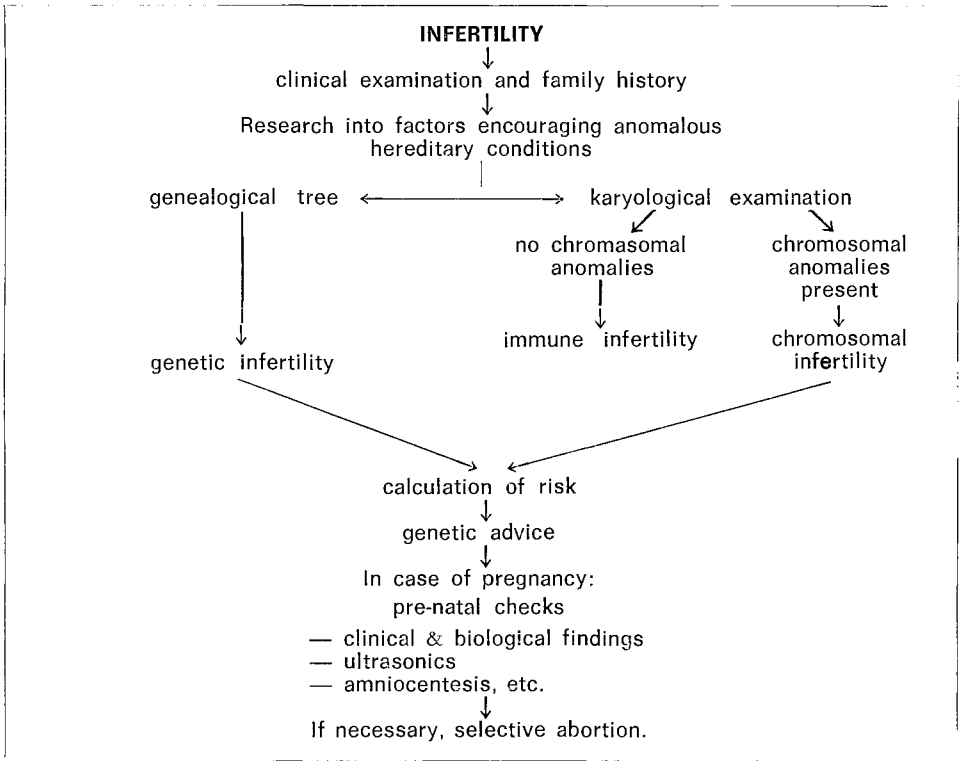

FIG. 3.

be made, with the help of ultrasonics and amniocentesis, in order to diagnose hereditary and chromosomal diseases. In such cases the problem of carrying out selective abortion will also arise.

BIBLIOGRAPHY

1. Bouè J.G., Bouè A.: *Rev. Franç. Ginéc.*: *68*, 11, 625, 1973. - 2. Penrose L.S., Smith G.F.: *Down's anomaly*, Churchill, London, 1966. - 3. Iffy L.: *Proc. Roy. Soc. Med.*, *56*, 1098, 1963. - 4. German L.: *Nature*, *217*, 516, 1968. - 5. Mikamo K.: *Am. J. Obst. Gyn.*, *106*, 243, 1970. - 6. Carr D.H.: *Advanc. Hum. Genet.*, *2*, 201, 1971. - 7. Sinet P.H., Dutrillaux B., Prieur M., Lejeune J.: *Rev. Franç. Gynec.*, *68*, 11, 655, 1973. - 8. Albermann E., Polani P.E., Fraser-Roberts J.A., Spicer C.C., Elliott M., Armstrong E.: *Ann. Hum. Genet.*, *36*, 185, 1972.