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Possible Mechanism of the Heredity of Twinning

L. Gedda, G. Brenci
The Gregor Mendel Institute for Medical Genetics and Twin Research, Rome

It is a frequent observation that twinning runs in the families [5] and we have recently reported that such is also the case with Gregor Mendel's pedigree [4]. The problem we are concerned with, now, is the identification of the "gemellogenetic" factor postulated by Gedda already in 1951 [2].

We thought we should start by going back to experimental embryology. Clearly, as shown by the experimentally induced MZ twinning in Triton or the spontaneous multiple MZ twinning in Armadillo, there must exist a temporal threshold below which individual parts of a single conceptus can still show totipotence.

Interestingly, recent studies of molecular histology have stressed the role of cell membranes and of membrane receptors in the transmission of specific messages related to the position and function of the cell. This has led Edelman [1], in particular, to identify a specific kind of molecule that appears early in embryonic development and is responsible for cell adhesion, thus contributing to organogenesis and the shaping of the embryo by regulating cell movements and the topologic development of tissues.

These so-called cell-adhesion molecules (CAM) are proteins that can differentiate both in function and in expression. In terms of function, there are molecules responsible for the adhesion of nerve cells (N-CAM), of liver cells (L-CAM), etc. In terms of expression, there are embryonic forms (E-CAM) and adult forms (A-CAM), the former being characterized by larger quantities of sialic acid. This chemical difference accounts for a different aggregation effect on the cells, that is, for a different cell adhesion. Moreover, the E-CAM and A-CAM can be interconverted, at different times and with variable speed.

These findings have interesting implications for the mechanism of MZ twinning. In fact, one could easily assume that a reduced cell-adhesive action resulting from CAM modifications at a time when the early post-zygotic embryo cells are still totipotent, may result in a cleavage of the embryo and consequent MZ twinning, similarly

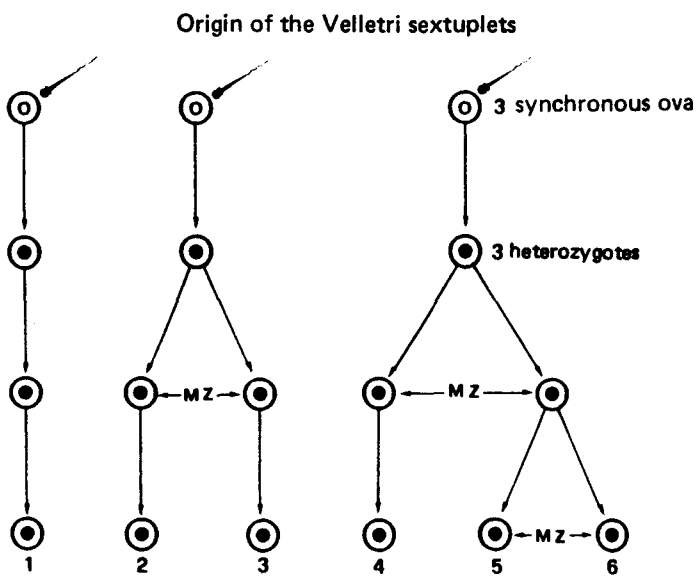
to what can be experimentally induced in Triton and as apparently occurs naturally in the Armadillo.

Edelman's considerations on the chemical modulation and reduced cell adhesion that occurs, for instance, at the time of the intense cell multiplication process characteristic of the early growth of the embryo, make the above hypothesis sufficiently realistic. Edelman considers the reduced adhesion to result from the enzymatic splitting of some of the sialic acid of the CAM on the cell surface. If enzymes are involved, then the phenomenon must have a genetic basis.

The gene(s) responsible for CAM might then be viewed in the light of our own chronogenetic theory [3], whereby the genetic information is assumed to also possess a time dimension, with a lifespan (chronon) that is a function of the gene's informatic potential (ergon). The influence of hereditary factors in MZ twinning might in fact be due to the inheritance of an earlier onset (anticipation) of the production of the enzymes responsible for the splitting of sialic acid and the resulting reduced cell adhesion.

Our hypothesis that the chemical modulation of CAM may account for the hereditary influences on MZ twinning could perhaps be extended to DZ twinning as well, by assuming CAM modulation at the level of graafian follicles and oogenesis, resulting in the simultaneous production of two haploid gametes rather than one. That would then contribute to explain the occasional finding of a simultaneous, repeated occurrence of both MZ and DZ twins in the same pedigree, as well as the related finding of the simultaneous occurrence of the two mechanisms among higher multiple births.

The latter situation is well illustrated by a case of sextuplets born in 1985 in Velletri, near Rome. Based on blood groups and on embryonic membrane analysis, the six cotwins have been subdivided into three groups: 1) a single twin, with own chorion and amnion; 2) two MZ cotwins, with identical blood groups, single chorion and two amnions; and 3) three MZ cotwins, with identical blood groups, single chorion and



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three amnions. The probable mechanism is illustrated in the Figure. Clearly, in this case as in similar ones, the two mechanisms of twinning coexist, the twins being MZ within groups and DZ accross groups.

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Correspondence: Prof. L. Gedda, The Mendel Institute, Piazza Galeno 5, 00161 Rome, Italy.