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New Frontiers of Gemellology

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The good result of this congress (the fifth of the series), in terms of quality of papers and number of participants, proves we were on the right track when in 1974 we founded the International Society for Twin Studies, and even more proves that the interest in gemellology is increasing.

I wish to thank our many colleagues who contributed to the promotion, construction and success of this field of biomedical research, and particularly Gordon Allen, Ian MacGillivray, Walter Nance, Paolo Parisi, and of course Aldur Eriksson.

For my part, I would like to emphasize that going from the title "Study of Twins" given to my book in 1951 to the word *gemellology* placed in the title of our quarterly *Acta Geneticae Medicae et Gemellologiae* in 1952, I wanted to affirm: first, that the study of twins is a branch of modern genetics; second, that the study of twins represents a "logos," that is, a subject composed of acquired concepts, of constant phenomena and specific methods of research on twins in normality, in pathology and in population. With this word, now also adopted by Professor Nance in his Presidential Address, "Introduction to Gemellology," twin research has become an identified field of science.

In order that the Amsterdam Congress may be as fruitful as the previous ones, I believe it useful to look out of the window of the future with you to see some roads which could be new frontiers of gemellology.

In a paper that Brenci and I presented at this congress, we reported on the mechanism of twinning and its hereditary control to the modulation of cell-adhesion molecules (CAM) both in the female gamete and in the first stages of embryogenesis: morula and blastocyst. I will not dwell on this hypothesis which we entrusted to the proceedings but about a possible subsequent objective fact, and that is, the teratomorphisms.

Here are some examples of obvious teratomorphisms: a single fetus with two noses and two mouths, or a "duplicitas" that is, twins with the same limbs and one shared liver, two hearts in specular position, dead at birth, or pygopagous twins, such as those frequently separated surgically, etc. Such cases all deal with obvious teratomorphisms.

A spontaneous but hidden teratomorphism exists to which I would like to call your attention. The first one we observed concerns a set of French female monozygotic triplets, one

of whom was found to have three kidneys and three urethras that lead to the same vessel, thus showing that these triplets could have been quadruplets.

The second case is Italian and concerns a mother of MZ twin girls. Mother and daughters enjoyed excellent health, but on X-ray examination, while the twins presented a normal urinary tract, the mother appeared to have three kidneys and three urethras. The significance of this case, it seems to me, is even more interesting than the preceding one: first, because it concerns a person considered a non-twin; second, because this person is the mother of MZ twins; third, because it is the genealogical tree which shows that teratomorphism and twinning are one phenomenon; and fourth, because the genetic component of gemellarity, that is, its hereditary character, is proved in an unusual way.

I believe that research on teratomorphisms in twins and their families, perhaps particularly at the level of the urinary tract, could become routine research.

The second frontier on which gemellology should place itself firmly in the future is that of the environment, that is, the influence environment can have on man. To use a name unfortunately famous and symbolic to signify each natural, artificial and working environmental exposure, I will say: the Chernobyl effect.

Recourse to twins for a similar problem goes back to 1937 when Newman, Freeman and Holzinger studied 19 pairs of MZ twins reared apart. However, the point of view is overturned because these authors looked for concordant hereditary traits which showed themselves in the MZ twins in spite of the differences in the different environments in which they grew up. Thomas Bouchard and others worked along the same lines on MZ twins reared apart and they reported on this already at our Jerusalem Congress six years ago. This research reached interesting results, having demonstrated that the identical genotype clearly shows itself in the normal, pathological and psychological traits in twins of various ages notwithstanding the diversity of the environment resulting from early separation.

On the other hand, the authors observe that the findings on MZ twins reared apart, the numbers being small, do not easily apply to research of broad and routine dimensions.

We at the Mendel Institute have thought of considering the problem from the opposite point of view, studying in what way and how much the diversity of the environment can change the phenotypic alikeness of MZ twins.

To this end, we studied twins living apart and not only MZ but also DZ twins. The methodological novelty consists in the choice of marriage as the time of separation.

This method offers many advantages: 1) the large size of the sample because the twins arriving at marriage are very numerous; 2) the definitive separateness of homes, food and often of locality and occupation, as well as the procreative event which characterize matrimonial living apart; 3) the possibility of a comparative statistical treatment of the data which concern MZ and DZ twins to verify the degree of a genetic nature of the single reported characters; 4) the possibility of establishing a qualitative and quantitative comparison among the characters considered before and after the separation, fixing, however, a temporal threshold for the comparison that we established of at least five years after marriage. The first results of the Twins Living Apart Test have already been published in our quarterly.

With this method applied to 1500 Italian twins between 30 and 50 years of age, we are presently, in collaboration with the Cardiology Department of the University College of London, sending out questionnaires concerning clinical aspects, sports practiced, family and personal anamnesis, referred to heart ischemia and infarction.

Furthermore, we proposed to the Italian Ministry of Health to apply the Twins Living Apart Test to the twins living in a radius of 20 km from the Italian atomic energy centers

as compared to their cotwins living not less than 100 km from these centers. There being about one twin every forty inhabitants, it would be useful if the municipality could be convinced to computerize the vital statistics of the twins who live in the area.

A third frontier should be known by whoever studies twins, because it concerns a fruit ripened on our tree and because it could lead gemellology to objectives which relate to the entire human family. This deals with knowledge and utilization of the fourth dimension of the gene. The passage from the spatial dimension of DNA to its time dimension occurred in the Second International Congress of Human Genetics we organized in Rome in 1961.

In my paper, "Clinical Genetics", I found a useful comparison. Just as on birthday cakes, human life can be represented by a number of candles which are all alight at the time of birth. These candles represent the genes, which, however, make their entrance at different times and have a different duration of information. "One aspect of the gene," I said then, "to which I call your attention is the time dimension, that is, the period of the gene. In fact, each gene has a qualitative and quantitative function determined in time. If we accept the comparison of the candles, it must be said that each candle has its length and that the variability of this length is inherited."

Broadening of the research took place in the following years, when we realized that also in the family ambit there exists a temporal covariance. With Brenci, I gave the name *chronon* to the duration of genetic information, the name *ergon* to the energy of stability which determines the duration of the information, and the name *chronogenetics* to the study of hereditary time.

I should like to stress that chronogenetics is distinct and different from chronobiology, which concerns the operative time of cyclic activities of living organisms. On the other hand, chronogenetics concerns the lifespans of genes and genomes of living organisms transmitted by the hereditary structure itself.

We recently had the satisfaction of learning that scientists of Rutgers University and of the University of Rochester stated that their studies of biopolymers converge with our conclusions on DNA. At this moment I cannot dwell longer on this subject, that I indicated to show that it was the twins that led us to this knowledge. But I do not want to deprive you of an intuitive image created by our American colleague Sunchul Ji to explain the fourth dimension of the DNA and of other biopolymers, that is, the simultaneous presence in the DNA molecule of the information and energy parameters. Sunchul Ji states that "in macroscopic machines, the energy and the information parameters can be separated (for instance, gasoline and the structural design of an automobile), but in microscopic or molecular machines, the energy and information parameters are packaged into one entity."

To this new way that the twins taught us (MZ twins being identical also because of identical timing and lifespan of their genes), we are happy to add that chronogenetics is fundamental for all those who deal with predictive medicine, which establishes the times of risk of hereditary diseases and for those who deal with preventive medicine, to avoid this happening through appropriate treatment. All this will go beyond the frontiers of gemellology for the health and life of *homo sapiens*.

I am very grateful to Professor Eriksson for remembering 1974 in Rome when I, together with Professor Parisi and others of The Mendel Institute, promoted the foundation of the International Society for Twin Studies. It was perhaps the most satisfactory scientific step of my life.

This road led us to Washington, to Jerusalem, to London, and now to Amsterdam, where Professor Eriksson is our esteemed host. As Founding President, I would like to express my

appreciation over the local arrangements and the entire organization of our Fifth Congress. And I should like to express our warm gratitude to the outgoing President of our Society, Professor Walter Nance, whose leadership over the past three years we have all greatly appreciated.

Permit me to recall, from the medical history of Amsterdam, the Danish anatomist, Niels Stensen, who here in 1660 discovered the *ductus stenonianus*, which leads saliva to the mouth. I remembered Steno not only because each of us keeps his name in the mouth, but also because Niels Stensen from the Netherlands went to Italy, where he made important studies of geology and cristallography. Thus Stensen, who loved Florence as a second native city, established a bridge between The Netherlands and Italy.

The present issue of the journal – the first of a number of 1987 and 1988 issues in which Congress proceedings are to appear – assembles papers dealing with twin research methodology. This is an area of vital importance, in which fundamental advances have been made over the past few years, with the development of entirely new approaches and designs. A very large number of papers stemming from congress presentation, amounting so far to some 800 pages and organized into various sections (twin research in development, twin biology, multiple pregnancy, chemical studies) will appear regularly in the following issues.