TWIN RESEARCH 4

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Chronogenetics: A Meeting Point for Medicine and Twin Research

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Abstract. The program of any individual's vital cycle encoded in the genetic information is executed according to a time schedule that is the object of study of Chronogenetics. MZ twins provide the best evidence of the existence of this hereditary biological time and they represent, therefore, the natural test of Chronogenetics. Twin research can thus serve medicine in developing its most modern perspective, individual preventive medicine. Moreover, through approaches such as the Twins-Living-Apart Test, twin research can help to identify the influences of the environment on the health of man.

Key words: Chronogenetics, Preventive medicine, Twins living apart

In 1951 I published a book entitled "Study of Twins", and in 1952 I started the publication of the journal, "Acta Geneticae Medicae et Gemellologiae". Moving from the expression, *Study of Twins*, to the neologism, *Gemellology*, has been like crossing a border. The border between a "Catalog" of about 6,000 works disseminated in the literature of widely differing areas, and a "Logos", that is, a systematic treatment with its own methods and observations. This Logos is a science that refers to twins but leads very far away into the nature of life and of the cosmos.

Chronogenetics is a typical example of the wealth of knowledge and of applications that Gemellology can originate.

First of all, in a historical perspective, MZ twins have been the starting point of Chronogenetics, of which they still represent the natural test and an essential point of reference. The existence of a heriditary, biological time was first suggested to me by the observation of some developmental synchronies in MZ twins, such as in the primary and secondary dentition, in the development of pubic hair, in menarche, as well as in hair loss or white hair. Similarly, the simultaneous occurrence in MZ cotwins of diseases such as diabetes, epilepsy, glaucoma, appendicitis, etc., has convinced me that a hereditary timing exists, not only with respect to ontogenetic processes, but to the errors of genetic programming as well.

As one among many examples of pathological synchrony, let me simply refer to some striking concordances in two MZ twin sisters, Alessandra and Roberta (Fig. 1a). At the age of 7 years, while playing tennis in Rome, Alessandra broke her left radius. Ten days later, in a mountain resort, Roberta fell down, having been pushed by her brother, and she also broke her left radius (Fig. 1b). At the age of 11, Roberta underwent appendectomy on January 12. The following night Alessandra had a colic and subsequently underwent appendectomy on January 15.

I have now come to realize that it is not strictly needed to refer to the synchrony with which MZ twins reach specific ontogenetic stages or show the onset of a disease. The existence of a hereditary time is clearly shown by the identicalness of MZ twins at different times and by the simple observation that "identical" twins would not even exist if their genomes were not identical also from a chronogenetic point of view. Following the neonatal period and catch up, MZ twins usually look alike throughout their development, sometimes to such an extent that their parents cannot easily tell them apart. If that happens, it is because in all organs and functions, structural and functional genotypes continously scan the same times. In other words, synchrony is an institutive law of the MZ twinning phenomenon. MZ twins *are* Chronogenetics, evident and alive.

One should realize, of course, that with their synchronous timings, MZ twins shed light on aspects that are not restricted to them, but involve singletons as well, and more generally all living systems.

It should be noted, so as to avoid confusion, that another research area, Chronobiology, deals with operational times and circadian rhythms. However, the "chronos" of Chronogenetics is different from the "chronos" of Chronobiology: the former concerns the genic information, and therefore is endogenous, inherited and continous, while the chronos of Chronobioly concerns the rhythms of activation and inactivation of the informatic activity, and is therefore induced and discontinous. Even better, Chronobiology is a branch of Chronogenetics, since there would be no reaction of living systems to cosmic influences, and more generally no operational times of the genic information, if the information itself were not characterized by a fundamental, intrinsic timing. And the twins show that the endogenous time of the living matter is inherited and heritable.

Life thus appears as a gigantic complex of chronometric units, of genes that operate simultaneously and in sequence, according to the temporal program estabilished at the time of amphimixis.

The hereditary time, lived explicitly by MZ cotwins, but also implicitly by any singleborn, becomes apparent within the family and within the species.

Within the family, this is particularly evident in the case of the time of onset of hereditary disease that appears to be very similar in family members at risk. For instance in a family I studied with Martini, constisting of the two parents and their six children, four of these were affected by facial hemiparesis, which is transient at rest but persistent under strain (Fig. 2 a, b, c). All of them were affected between 8 and 11 years of age. Pedigree study shows that a maternal uncle presented the same pathology at 14 years of age.

The chronogenetic pattern concerns and characterizes every living species. As examples for the plant world, and the animal world, respectively, Table 1 refers to the

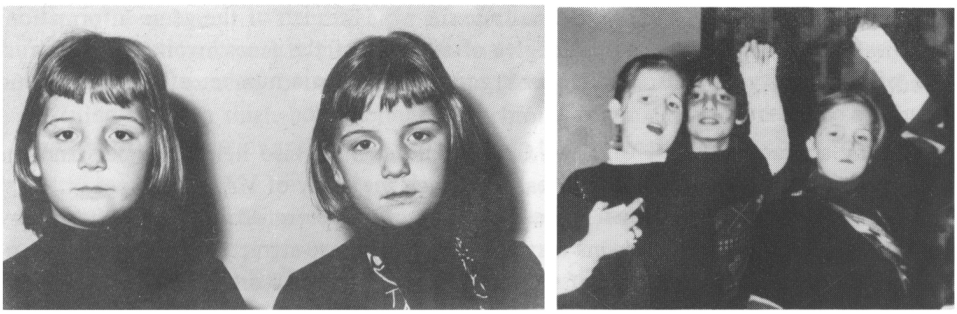

Fig. 1a and b

Fig. 2a, b and c

Table 1 - Lifespan Diversity in the Plant World

Plant lifespan		Pollen lifespan	
Sequoia	2000 yrs	Persea americana	153 days
Cupressus arizonica	300 yrs	Onion	191 days
Magnolia	120 yrs	Rhododendron	1095 days

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diversity of individual lifespan in plants of different species and in different pollens, while Table 2 refers to the diversity of the timings of developmental stages following fertilization in different animal species.

Chronogenetics is itself in a developmental stage with respect to the molecular understanding of its underlying mechanisms, since the lifespan of the genic information, or *chronon,* is clearly linked to the degree of stability of the genes involved in the structure of the genotype. This stability, *or ergon,* depends on a number of parameters and especially on redundancy.

From a practical point of view, Chronogenetics may also help to understand the influence of environment on human health through the study of MZ twins.

At our Jerusalem Congress, three years ago, we were informed of the studies by Bouchard and others on MZ twins reared apart, which have attracted the interest even of the general press. We deemed it useful to apply a somewhat similar method using MZ twins that are considerably more common. I refer to those MZ cotwins who, following marriage, have been living apart for a number of years. Marriage determines a differentiation of housing, of nutritional and other habits, sometimes even of place of residence and of work; in a short period of time, marriage differentiates the environment which had previously been very similar for the two cotwins. This particular twin population becomes separated, on the average, at the age of 28: it therefore has the perspective of a long period of second and third age, it corresponds to about one half of all MZ twins, and it is continously renewed.

Brenci and I have developed a method for the utilization of this material and called it "Twins Living Apart Test". The data of interest are collected both in a sample of MZ twins who have lived apart for at least five years and in a control sample of MZ twins living together, and the two samples are compared with an appropriate formula. Some of the data we have collected so far – concerning height, weight, onset of presbyopia and of presbyacusia, systolic and diastolic blood pressure, use of alcohol and tobacco, duration of sleep – are summarized in Fig. 3. The preliminary results indicate that environment has a strong effect on the use of alcohol and tobacco, as well as on the onset of presbyopia and presbyacusia, whereas its influence on the other traits is much lower, as was to be expected. These results are promising in that they point to the possibility of a more reliable quantification of environmental factors.

Finally, the application of chronogenetic criteria may prove fruitful in the context of individual preventive medicine. So far, prevention in medicine has essentially implied general measures of disinfection, disinfestation, hygiene, and vaccination against infectious diseases and pollution. Chronogenetics offers the doctor the possibility to apply preventive medicine at an individual level, shifting from the evaluation of diseases that are possible to the evaluation of diseases that are probable. This is important, since genetic factors play a role, though to a variable extent, in all diseases, including allergic or tumoral disorders.

If a clinically healthy person wants to have an idea of his specific risk of disease, the chronogeneticist can calculate that risk based on the probabilities stemming from the analysis of the paternal and maternal genotypes, wiht the indication of the age of highest risk also in relation to the characteristics of the environment. The chronogeneticist can finally advise that person with reference to those pharmacological, nutritional, and behavioral factors that can help him overcome or push further the time of risk.

And it is clear that twin research is a fundamental tool for the scientific development of such and individualized preventive medicine. The relation between twins and Chronogenetics is stressed even further in the following considerations recently made by Jean-Pierre Nénon, of the University of Rennes, France, that I should like to report by way of conclusion: "The development of Chronogenetics sheds new light on the concept of 'false' (or fraternal) twins, showing that their degree of biological similarity, which is half of that existing between 'true' (or identical) twins, is actually higher than that existing between single-born siblings. The chronogenetic criterion tends to eliminate the notion of 'false' twins and to substitute it with that of 'real' twins".

Table 2 - Diversity in Timings of Developmental Stages in Different Animal Species

Developmental stage	Hamster	Opossum	Rabbit	Man
2 cells (hrs)	16	40	8	38
Implantation (days)	4.5	6	7	8
End of embryonic period (days)	9	10	10	36
Birth (days)	16	12.5	32	267

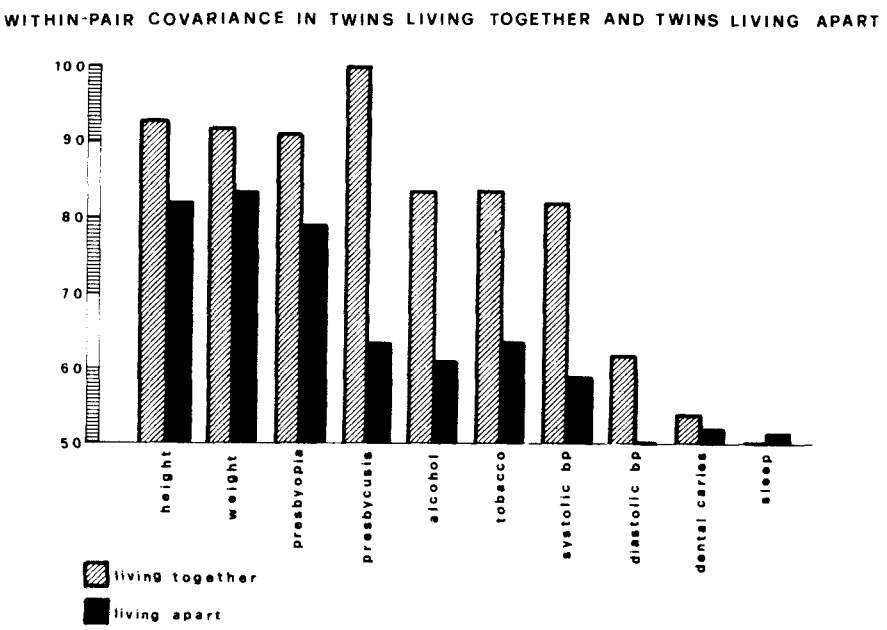

Fig. 3

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