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From Gregor Mendel to Medical Genetics*

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While I receive, with great joy and pride, the honorary degree of this University, commemorative celebrations to honor the Bohemian scientist Gregor Mendel are being held in the Czechoslovakian town of Brno.

One hundred years ago, Gregor Mendel announced his discoveries concerning the hybridization of " pisum sativum ", and opened to science the way to understand the principles underlying modern Genetics. I feel it my duty to recall with admiring devotion this great man, whose name is just as much connected with Biology, as Galileo Galilei's name is linked to Physics. All the more so, because the honorary degree conferred on me by the President and the Professors of Villanova University is a doctorate in Natural Sciences.

Two other reasons prompt me to recall the work of Mendel. One is that Gregor Mendel was an Augustinian monk, and such an exemplary one indeed, that he directed the Brno Monastery as Abbot from the forty-sixth year of his life to his death. In a personal letter addressed to the Augustinian General, Father Luciano Rubio, on the twentieth February of this year, Pope Paul the Sixth stressed the significance of the fact that the Augustinian Order had given to the Church and to Science such an eminent man. Now, there is no better place to recall the religious gifts and the scientific genius of Gregor Mendel than your University, founded and directed by Augustinian Fathers.

Moreover, allow me to recall that, twelve years ago, God granted me the grace to be the founder of the Institute of Medical Genetics in Rome, which I have the honor of directing, and which, in the capital of Catholicism, bears the glorious name of Gregor Mendel; so that, every day, all of us working there, feel the incentive of his great example. The characteristic feature of the Mendel Institute is that the University of Rome has established in it the chair of Medical Genetics of its Faculty of Medicine. This chair is the first of its kind in Italy. Consequently, the Genetics we are developing is principally the one dealing with human disease. We endeavor to introduce into Medicine the discoveries made during the last hundred years in the branches of Plant Genetics, Animal Genetics and Human Genetics. This task is important from the scientific viewpoint, because a genetic vision of Medicine leads to a better knowledge of the nature of diseases.

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As a matter of fact, today we know the hereditary nature of diseases which, up to a recent past, were not considered from this angle, such as Cooley's disease, galactosemia, Marfan's and Ehlers-Danlos syndromes, Gaucher's disease, muco-viscidosis, congenital hip-joint malformation, a number of lethal malformations, and so forth. Moreover, all other diseases show the presence of a hereditary *quantum*, that is to say, in such cases where the cause of the disease is external, being due, for instance, to a microbe or a virus, there exists an inherited disposition to contract that disease. Such a disposition is a very important causal factor. This has been demonstrated by our research concerning brothers affected by pulmonary tuberculosis, concerning families with trachoma, concerning infective children diseases in twins. The same applies to diseases due to other external causes, such as allergic and professional diseases. In this connection, I wish to recall our research concerning silicosis in Sardinian miners. Although silicosis is due to inhalation of quartz particles, we demonstrated the existence of a family predisposition to contract this serious and irreversible disease.

In the course of our genetics studies concerning, on one hand, hereditary diseases and, on the other, hereditary dispositions, we have been able to ascertain the importance of the time-factor in the genetics of man. The human body develops according to a chronologic programming of gene effects, from the period of organogenesis on to old age and to death.

The function of certain organs, of the endocrine glands, for instance, shows very clearly such programming, which makes the hormones start functioning at the right moment. Hormones are usually activated by enzymes, and enzymes often represent the primary effect of a gene. Therefore, we think that the gene does not only represent a unit of function (*cistron*), of recombination (*rekon*) and of mutation (*muton*), but also a unit of specific energy released in due time. To this parameter of the gene we have given the name *chronon*.

The concept of *chronon* was suggested to us by the study of human twins, which we have been carrying out for a long time. It is known that twins are divided in two types, i. e.: identical, or monozygotic, and nonidentical, or dizygotic. The former are especially useful for the study of Human Genetics, because the hereditary characteristics, both normal and pathological, must be the same in monozygotic twins. Naturally, this also applies to animal and plant twins, but it is of greater methodological importance in Human Genetics, human experimental crossbreeding being unconceivable, both for ethical and practical reasons.

Hence, the material preferred in our studies of Human, Medical and Clinical Genetics is represented by twins. The special archives collecting this material at the Mendel Institute are called " Gemelloteca ", and contain data concerning about ten thousand twin pairs, with whom we are in regular contact.

Now, every day, monozygotic twins grant us the possibility of controlling that the hereditary characteristics they have in common show an identical *chronon*. As a matter of fact, physiological phenomena, such as dentition, puberty, menopause and so forth; as well as pathological ones, such as dental caries, pernicious anemia,

mammary cancer and so forth, happen to appear simultaneously in both partners of monozygotic twin pairs. Under this aspect, monozygotic twins are comparable with two identical clocks which, having both been wound at the same moment, keep on showing exactly the same time.

The *chronon* principle is very useful when applied to human life and disease. In fact, everyone may note the existence of a chronologic variability between families in the onset of diseases and the manifestation of hereditary dispositions. A cataract, for example, is often a hereditary disease of the lens, which may begin at very different ages. Usually, the age is constant for the members of one family. Analogously, this is also the case for adult diabetes and for many other diseases.

This means that the mutation of a normal to a pathological gene leaves its mark on this particular parameter of the gene.

The concept of *chronon* includes the starting-time of gene activity, as well as of its extinction. The starting-time is fundamental for the study of human growth. On the other hand, the study of the time of extinction is fundamental for the study of old age. Old age, in fact, consists in the progressive extinction of gene-actions, which gradually diminish the efficiency of homeostasis up to the point of making it impossible. This is when life stops. During this long process of gradual gene extinction, the sequence of the old age phenomena follows a strict family pattern. In this case, the term " family " means heredity, and the repetition of the pattern in the same family, by which the genotype progressively spends its genes, is another demonstration of the fact that every gene has its time of function.

Undoubtedly, individuals of the same families grow old in a similar way. Relatives resemble one another more in old age than in any other period of their lives.

This concept of pathological heredity, being due to a limitation of the activity of every gene during its *chronon*, also gives rise to a great hope. This concept, in fact, makes it possible to consider hereditary diseases, and even old age, as being due to an extinction of the normal function of single genes. Thus, hereditary diseases and old age assume the significance of defective diseases. Consequently, when Medicine is able to ascertain the nature of the various deficiencies, physicians could be able to substitute from the outside what is missing in the organism, thus allowing a re-establishment of the homeostasis.

These still distant hopes and the great recent progress of Genetics in all its branches represent the development of the clear and unshakable, not hypothetical but true principles which Mendel, the Augustinian monk, established one hundred years ago.

For this reason, it is my whish to conclude, just as I began, by paying to Gregor Mendel the tribute of my grateful admiration.