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Chronological Aspects of Gene Action: A Twin Study*

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Monozygotic twins often have equal life spans and several other synchronous events in their physiology and pathology, thus proposing and permitting a study of the genetic conditioning of biological timing.

It was along these lines that we at the Mendel Institute decided to conduct a chronological investigation on dentition in twins, a subject we had already studied from other points of view.

Dentition in the human species, in fact, has several characteristics that can be applied to the study of the chronological aspects of hereditary mechanisms; such are:

- 1) the sequential character of this phenomenon (two different dentitions, one following the other);
- 2) the apparent onset of the phenomenon that can be observed in both phases even by untrained individuals;
- 3) the end of the phenomenon that may be easily verified, especially in the case of the first dentition.

Our study was conducted by means of a questionnaire and an analysis.

The questionnaire addressed to 1614 twin pairs aged 7 to 12 years; the form was to be filled by the parents.

The questions concerned the age of appearance of the first deciduous tooth, the age at the first loss of a deciduous tooth, the age of appearance of the first permanent tooth, as well as information relevant for verification of zygosity.

It was possible to obtain the required information for a twin material consisting of 408 pairs.

The material is selected only for age. Its representative quality was verified by analyzing the sex distribution within pairs and comparing it to the figures for the

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Italian population (Tab. 1). The value of our material as a representative sample of the general population could thus be established ($\chi^2 = .301$; $p > .05$).

In order to verify the reliability of the answers, as far as data on the first year of life were concerned, we made a separate survey of 186 twin pairs aged 8 to 15 months. No significant difference was found between the distributions of data in the two surveys.

Tab. 1

Sample	♂♂	♀♀	♂♀	Total
Observed	145	129	134	408
Expected	140	130	138	408
χ^2	.178	.007	.116	.301

2 d.f.; $p > .05$

The analysis considered six parameters:

1. Age of onset of first dentition (t_1);
2. Age of initial loss of first dentition (t_2);
3. Age of onset of second dentition (t_3);
4. Duration of first dentition ($\Delta t a$), expressed as the time lapse in months between onset and initial loss of first dentition;
5. Duration of "interdentition" ($\Delta t \beta$), expressed as the time lapse in months between initial loss of first dentition and onset of second dentition;
6. Duration of the time lapse between onset of first and onset of second dentition ($\Delta t a + \beta$).

For each parameter we calculated the Bravais-Pearson correlation index (\hat{r}) between the values for the first and second twin of each pair in both the MZ and the DZ series, as well as the sample variability of the same index (Sr). We also estimated the heredity component (\hat{H}) for each parameter by applying Holzinger's formula ($\hat{H} = \frac{r_{MZ} - r_{DZ}}{1 - r_{DZ}}$) and the estimate of the probable error thereof (Pe \hat{H}).

Such calculations resulted in the figures reported in Tab. 2, on which our observations and conclusions are based.

The following observations seemed to us to be relevant:

1. The figures for \hat{H} (heredity) in the values for t are very high and distributed in decreasing order with the succession of phenomena:

— onset of first dentition	$\hat{H} = .82$
— initial loss of first dentition	$\hat{H} = .80$
— onset of second dentition	$\hat{H} = .75$

2. The figures for \hat{H} (heredity) in the values for Δt are practically constant, irrespective of the time lapse considered ($\sim .82$).

Tab. 2

		$\hat{r}MZ$	$SrMZ$	$\hat{r}DZ$	$SrDZ$	\hat{H}	$Pe \hat{H}$
1	t_1	.9502	.0076	.7153	.0325	.8251	.0156
2	t_2	.9528	.0075	.7548	.0294	.8075	.0179
3	t_3	.9628	.0065	.8464	.0209	.7578	.0249
4	$\Delta t a$.9179	.0142	.5457	.0538	.8193	.0175
5	$\Delta t \beta$.9651	.0062	.8092	.0262	.8171	.0106
6	$\Delta t a + \beta$.9692	.0054	.8286	.0234	.8203	.0186

On the other hand, the values of intrapair variability in the monozygotic series V_w (MZ), representing environmental influences, also tend to decrease:

$$\text{for } t_1 \quad V_w \text{ (MZ)} = .05$$

$$\text{for } t_2 \quad V_w \text{ (MZ)} = .05$$

$$\text{for } t_3 \quad V_w \text{ (MZ)} = .04$$

This indicates that the decreasing value of \hat{H} in the values of $t_1 - t_2 - t_3$ is due to a real decrease of the genotypical component and not to an increase of environmental influences (Fig. 1).

Now let us remember again that the figures for \hat{H} (heredity) for the values for durations Δt are practically constant, irrespective of the time lapse considered ($\sim .82$).

As shown in Fig. 2, since the time lapse between onset of the first and onset of the second dentition ($\Delta t a + \beta$) represents the sum of $\Delta t a$ and $\Delta t \beta$, the value of \hat{H} (based on the variances) in the total time lapse, should be significantly different from the values for \hat{H} in the component-time-lapses if the latter were independent of each other. Yet, the equal values of \hat{H} for duration of first dentition ($\Delta t a$), of \hat{H} for duration of "interdentition" ($\Delta t \beta$) and of time lapse between onset of first and onset of second dentition ($\Delta t a + \beta$) indicate that the said events are inter-related in each individual, i.e. that there is one single timing system.

3. The observed events take place as if one genotype be responsible for the first and the second dentition, the genotype being expressed through a gradual release of energy, i.e. through the degradation of a "quantum" of energy.

We believe that the following conclusions be justified:

1. The effect of a gene corresponds to the gradual release in the time of a genetically determined *quantum* of information (Fig. 3). *Chronon* stands for total time, or period, of gene action.

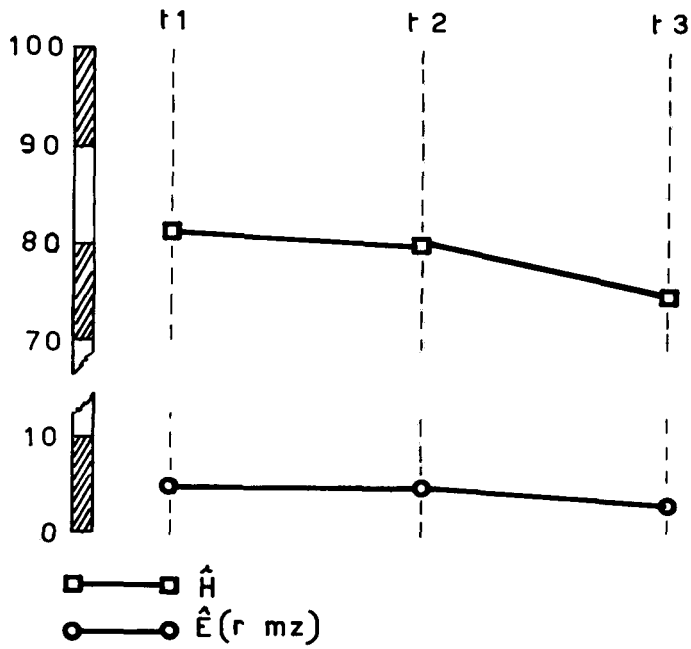


Fig. 1

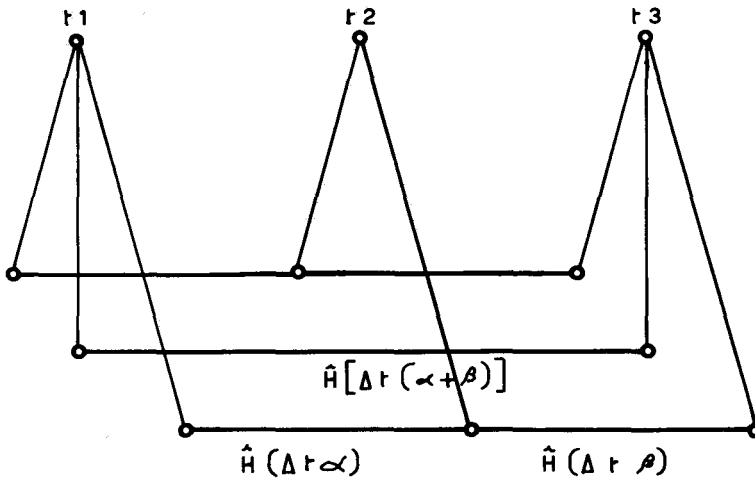


Fig. 2

I = quantum of gene information

A = gene action

t = time

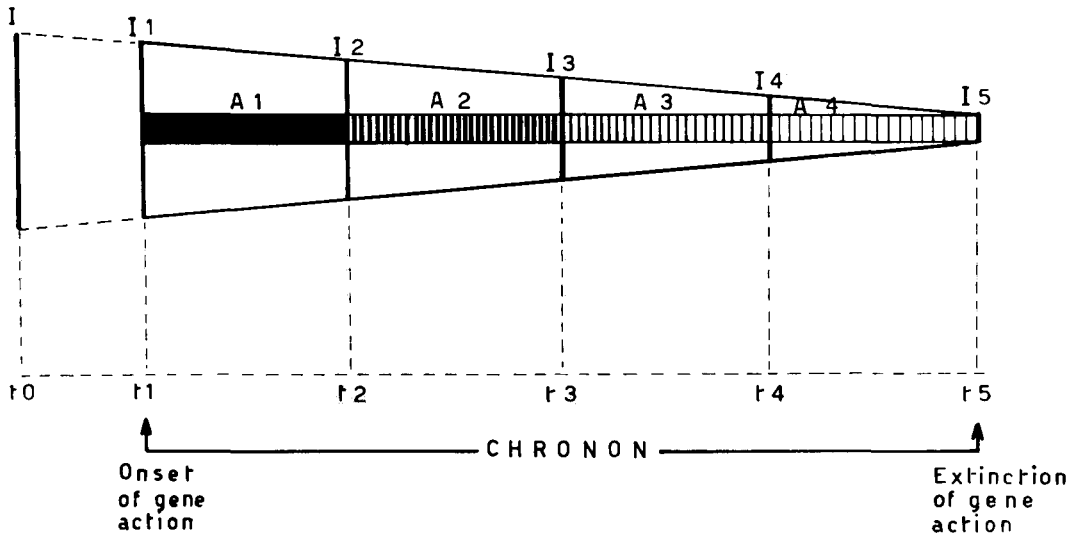


Fig. 3

2. The release involves a corresponding reduction, in the time, of the gene power of information, which may lead to the extinction of the gene after a time lapse representing an individual trait.

3. The measure of the period of action of a gene permits an estimate of the information potential of the gene.

4. The duration, or *period*, of gene action represents a measurable trait of the gene, that may be identified as its *Chronon*.

Summary

The AA. have studied the characteristic steps of the first and permanent denaturation on 408 twin pairs (156 MZ and 252 DZ). These phenomena appear to be significantly genetically controlled. According to the AA., the hereditary units might possess a characteristic potential time span, which is a function of an energetic genetically conditioned charge. This parameter of the hereditary unit is called *Chronon*.

Literature

- GEDDA L. (1965). Application de la génétique à la pratique médicale. (La constitution au point de vue de la génétique - Le "chronon": concept et application au service de la médecine). *A.Ge.Me.Ge.*, **XIV**: 1.
- (1965). From Gregor Mendel to medical genetics. *A.Ge.Me.Ge.*, **XIV**: 3.
- (1965). Da Mendel alla genetica clinica. In L. Gedda: Centenario delle Leggi Mendeliane. Ed. Istituto Mendel, Roma, 1966 (in corso di stampa).
- *et al.* (1966). La predisposizione genetica nella malattia tubercolare. (Studio su 447 coppie di fratelli ammalati). *A.Ge.Me.Ge.*, **XV**: 1.
- *et al.* (1966). Malattie, malformazioni e malposizioni dentarie studiate con il test clinico-gemellare. *A.Ge.Me.Ge.*, **XV**: 2.

RIASSUNTO

Gli AA. hanno studiato i tempi caratteristici della prima e seconda dentizione sopra 408 coppie di gemelli (156 MZ e 252 DZ). Questi fenomeni risultano essere controllati dall'eredità in modo significativo. Gli AA. pensano che le unità ereditarie posseggano una caratteristica durata potenziale nel tempo, che è funzione di una carica energetica geneticamente condizionata. Questo parametro dell'unità ereditaria viene chiamato *chronon*.

RÉSUMÉ

Les AA. ont étudié le temps caractéristique de la première dentition et de la dentition permanente chez 408 couples de jumeaux (156 MZ et 252 DZ). Ces phénomènes paraissent être significativement contrôlés par le génotype. D'après les AA., les unités héréditaires possèdent une caractéristique durée potentielle dans le temps, qui est une fonction d'une charge énergétique génétiquement conditionnée. Ce paramètre de l'unité héréditaire est appelé *chronon*.

ZUSAMMENFASSUNG

Bei 408 Zwillingspaaren (156 EZ und 252 ZZ) untersuchten Verf. die charakteristischen Etappen der ersten und zweiten Zahnung. Es zeigte sich dabei eine wesentliche Erbbedingtheit. Verf. nehmen an, dass die Erbinheit eine charakteristische, potentielle Zeitspanne besitzt, die von einer erbbedingten Energieladung abhängt. Dieser Parameter der Erbinheit wird als « Chronon » bezeichnet.