

isolate the true genetic ground of the phenomenon.

An account is given of basic techniques in time-series analysis, and results obtained in the field of infant mortality in Italy are discussed.

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## CHRONOGENETICS OF MUSCULAR DYSTROPHY

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A genealogical study has been carried out in the families of subjects affected by progressive muscular dystrophy.

The following parameters have been taken into account: (1) the age of onset, (2) the clinical characteristics, and (3) the age of the possible exitus.

Consanguineous series, with their genetic correlation, are drawn from this sample of families, and  $r$  correlation coefficients are calculated with respect to the above experimental parameters. The  $r$  values thus obtained are then compared with those that one would expect on the hypothesis that the temporal traits considered be genetically determined.

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## A CHRONOGENETIC APPROACH TO PSORIASIS

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Psoriasis is a genetically conditioned dermatological disease characterized by significantly different sex and age distributions. It could thus be the object of a chronoge-

netic analysis, using the age of onset as a genetically determined and quantitative phenotypic parameter.

A total of 2000 index cases has been considered and their families analyzed with respect to the segregation ratios in the sibships of the subjects and in those of their parents. The observed values of segregation are found to be not significantly different from those expected under the hypothesis of a diallelic monomeric autosomic trait.

It is concluded that the temporal trait, age of onset, must be genetically conditioned and that its chronogenetic variability — determined by the genetic variability of the starting ergons — may be assessed by means of standard techniques for quantitative analysis.

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## WILSON'S DISEASE AND MENKES' DISEASE—A CONTRAST IN CHRONOGENETICS

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In discussing the "timing" of hereditary diseases in their book *Cronogenetica: l'Eredità del Tempo Biologico*, Gedda and Brenci point out the limitations of the traditional classification of abnormal genes into lethal and sublethal categories.

The diseases with which this paper is concerned provide a striking confirmation of such limitation, in their clinical and metabolic aspects. Both diseases can be characterized by the disorders of the physiology of copper, an essential trace-element, which they display.

In Wilson's disease the patho-physiology is one of copper-toxicity associated with failure of biliary excretion of copper and its accumulation in various organs.

In Menkes' disease the problem is related to defective gastro-intestinal absorption of copper and the pathologic lesions are for the

most part secondary to copper deficiency. Yet internal kinetics of an intravenous tracer dose of radioactive copper are remarkably similar in each disease: in both there is prolonged whole-body and hepatic retention of the tracer and decreased gastrointestinal excretion.

Presumably, the genetic abnormality that determines the disordered physiology of copper in these diseases is present from the time of conception. The chronogenetics, however, of each condition is vastly different. Both genes are "lethal", clinically speaking; In Menkes' disease the condition is manifest at or soon after birth and runs its course to death in a few months to a year or so. In Wilson's disease, however, the phenotypical manifestations are frequently delayed for years. The contrast in chronogenetics of these two diseases emphasises the necessity of considering factors other than the demonstrable disorder of copper physiology in each condition.

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## TIME-DEPENDENT ELECTROLYTIC RATE IN TWINS

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The levels of Na<sup>+</sup> and Cl<sup>-</sup> electrolytes in the human sweat having already been shown, by a previous twin study, to undergo genetic conditioning, the age modifications of the electrolytic rate have now been examined in a sample of 4-20-year-old MZ male twins.

A separate analysis has been carried out for the two age groups, 4-10 and 11-20, so as to account for possible effects of puberal processes.

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## TWIN CHRONOGENETICS: EVIDENCE FOR TRENDS IN EARLY MENTAL DEVELOPMENT AND PHYSICAL GROWTH

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When DZ twins were evaluated for the degree of concordance in mental development during the preschool years, they exhibited relatively high within-pair correlations up to 3 years of age, then dropped significantly at subsequent ages. It was notable that as the measures of intelligence stabilized, the degree of concordance for DZ twins gradually regressed towards the value expected from within-family gene segregation plus assortative mating. It appeared that there was a time-linked differential gene action operating for DZ twins which gradually reached full expression by school age.

The evidence for timed gene action was further reinforced by the data for MZ twins, who maintained high concordance at each age, and who displayed coordinated patterns of spurt and lag between ages. Evidently, the course of mental development in the preschool years was heavily dependent upon the genetic blueprint of each twin. The data on physical growth confirmed results, and showed further that disparities in birth size for MZ twins were rapidly equalized as each twin got on his genetic growth curve.

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## TWINS: CONCORDANCE FOR CHANGES IN HAIR COLOR AND EYE COLOR DURING EARLY CHILDHOOD

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Hair color and eye color were assessed routinely from 3 months to 6 years for twins participating in a longitudinal study of