

Initiation of Enzyme Formation by Birth

An earlier study of glycogen metabolism in mammalian liver unexpectedly revealed that glucose-6-phosphatase is absent in the fetus. Further examination of the liver showed that this enzyme appears first at term, increasing rapidly to adult levels immediately after birth. It seemed possible that all enzymes unique to liver and subserving special liver functions would have this same pattern of development in the mammal. Subsequent work in our laboratory and elsewhere has supported this idea.

We are now attempting to determine the factors initiating the formation of the unique liver enzymes after birth. Tryptophan pyrrolase was chosen as the subject of study. First, compounds known to increase enzyme activity in the adult liver such as substrate and adrenal cortical hormones were tested in the fetus. None of these compounds were able to stimulate enzyme formation in fetal liver and one would suppose they do not limit enzyme formation during fetal life. Secondly, the effect of birth and maturity on enzyme formation was studied by varying the gestation period. Tryptophan pyrrolase was studied in the rabbit, a species in which the gestation time can be shortened or lengthened by several days without interfering with growth or morphological development. Premature delivery resulted in an immediate and rapid increase in enzyme activity. Prolongation of the gestation time prevented enzyme formation until after delivery. Therefore, it would seem that some factor in the uterine environment represses formation of the unique liver enzymes.

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A Minute Chromosome in Human Chronic Granulocytic Leukemia

In seven cases thus far investigated (five males, two females), a minute chromosome has been observed replacing one of the four smallest autosomes in the chromosome complement of cells of chronic granulocytic leukemia cultured from peripheral blood. No abnormality was observed in the cells of four cases of acute granulocytic leukemia in adults or of six cases of acute leukemia in children. There have been several recent reports of chromosome abnormalities in a number of cases of human leukemia [including two of the seven cases reported here: Nowell and Hungerford, *J. Natl. Cancer Inst.* 25, 85 (1960)], but no series has appeared in which there was a consistent change typical of a particular type of leukemia.

Cells of the five new cases were obtained from peripheral blood (and bone marrow in one instance), grown in culture for 24-72 hours, and processed for cytological examination by a recently developed air-drying technique (Moorhead, *et al.*, *Exptl. Cell Research*, in press). The patients varied from asymptomatic untreated cases to extensively treated

cases of several years' duration in terminal myeloblastic crisis. All seven individuals showed a similar minute chromosome, and none showed any other frequent or regular chromosome change. In most of the cases, cells with normal chromosomes were also observed. Thus, the minute is not a part of the normal chromosome constitution of such individuals.

The findings suggest a causal relationship between the chromosome abnormality observed and chronic granulocytic leukemia.

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Cytoplasmic Ribonucleic Acid Which Is Nucleolar and Nuclear Dependent and Its Relation to Amino Acid Incorporation

A comparative study has been made of the kinetics of nucleoside incorporation into ribonucleic acid of the nucleolus, extranucleolar portions of the nucleus, and cytoplasm of normal HeLa cells and cells in which the nucleolus is inactivated by means of localized ultraviolet micro-irradiation. Based on these studies, a model for RNA synthesis in actively growing cells is proposed in which (i) approximately two-thirds of the cytoplasmic RNA is synthesized in the nucleolus and the other one-third in the nucleus, and (ii) the nucleolar and nuclear RNA's are independent in their synthesis and movement to the cytoplasm.

A parallel study has been made of amino acid incorporation into normal and nucleolus-inactivated cells, and, in contrast to the above, no evidence of a significant nucleolar or nuclear dependence is found when the incorporation is followed for periods which are short compared to a cell generation time. These results support the belief that nucleoside and amino acid incorporation need not necessarily be simultaneous.

These experiments were carried out together with Prof. Maurice Errera while I was an American Cancer Society fellow in the Laboratory of Prof. J. Brachet, Brussels.

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Chemically Induced Life-Shortening and Its Probable Genetic Basis

Exposure of animals, including man, to ionizing radiation results in acute effects and in such delayed effects as cancer appearing long afterwards, and life-shortening in general. The acute effects seem based in chromosomal damage. More recently, experiments with *Drosophila* have shown that life-shortening has a similar basis (Oster 1959, Ostertag and Muller, 1959). For such studies, appropriate stocks have been synthesized. Exposure of preimaginal stages that are soon followed, normally, by a period of in-

tensive cell proliferation, growth, and differentiation leads to a relatively early onset of damage. Thus, death resulting shortly before or after eclosion, following treatment, probably represents a life-shortening comparable in principle to that observed in higher forms.

Since many carcinogenic chemicals possess other radiomimetic properties (for example, produce chromosomal breaks), it is essential to know whether they can also shorten the life-span otherwise than by causing cancer.

Stocks were made up containing chromosomes (ring-chromosomes) which allowed for normal functioning of the cells but which were more easily lost following breakage than normally structured chromosomes (rod-chromosomes). Untreated controls containing either type of chromosome had good survival rates (794/800) for the period studied, from larva to adult, while feeding nitrogen mustard to larvae resulted in lower survival (595/900) amongst the individuals containing the chromosomes which were more susceptible to induced damage than amongst those containing normal chromosomes (735/900). These results indicate that chemical carcinogens may cause premature "ageing" via the formation of chromosomal breaks and point to an especially insidious effect following contact with such chemicals.

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Mechanical Properties of Blood Vessels and the Regulation of the Cardiovascular System

The mechanical properties of blood vessels determine their biological functions, that is, the dissipation and distribution of the mechanical energy produced by the heart and, therefore, the distribution of blood and blood flow.

These properties have historically been referred to by the entirely descriptive term "tone." We have recently been able, for the first time, to define analytically and evaluate quantitatively the parameters of tone, therefore making it possible to quantitatively analyze the biological effects upon the blood vessels of such things as the nervous and endocrine systems, aging, and disease. These mechanical properties are defined by the relationships between the force tending to cause vessel wall motion (stress) and the resulting motion (strain). Instantaneous radial stress (blood pressure) and strain (vessel diameter) from multiple sites in the vascular system have been recorded on magnetic tape and the data have been analyzed using digital or analog computers, or both. The properties of arteries which describe their "tone" can now be stated as a discrete equation whose terms can be evaluated. Moreover, since the so-called "pressure receptors" lying within blood vessel walls are really strain receptors, we have studied the interrelationship of blood pressure, vessel wall strain,