THE SIZE AND GROWTH OF TISSUE CELLS

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By

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INTRODUCTION

THE CELLS OF PLANT AND ANIMAL TISSUES HAVE BEEN seen from varying theoretical viewpoints for over a century and a half. The changes in cell morphology which accompany the processes of histologic differentiation have been described. These descriptions account for the general fate of a cell. Within a single stage of differentiation, however, there always appears a variety of sizes of otherwise identical cells. Thus, while the broad outlines of tissue cell lives are discernible, the manifold sizes of a single individual cell type as seen under the microscope are not yet accounted for.

It is the purpose of this book to indicate the basic aspects of the problem of tissue cell sizes. There are three distinct aspects which are discussed separately. They are: first, the physical problem of measuring the parts of a tissue cell; second, the time parameters in the life of a cell; and, third, the interpretation of cell size distribution as a problem in population dynamics. There is also given a brief outline sketch of the history of cell sizes as related to the study of human cancer. For it was in the diagnosis of cancer that the subject of tissue cell sizes received its first major impetus.

Although the sizes of tissue cells, or of their nuclei, have been interpreted as indicating malignancy of growth in one way or another, it is safe to say that current knowledge about how animal cell nuclei in general attain their various sizes is far too meager to permit any inference about the special properties of human neoplastic growth. While the diagnosis of human cancer is referred to repeatedly throughout this book, there is no attempt to justify the use of cell or nuclear sizes for that purpose. The treatment is aimed at indicating possible lines of thought which might lead to a basis for comparing normal and cancer cells. The actual comparison, however, is beyond the scope of this book which deals with the fundamental questions of the how and why of cell sizes.

In most respects the rationale of cell size measurements is in a neglected condition; the lack of good data has relegated it to the limbo of controversy. There are no adequate data on tissue cell sizes reported in the literature. The best data are of measurements on nuclei of tissue cells. The purpose of this book is to formulate the need and the requirements for suitable data, and also to sketch the lines of speculation which cell size would merit as a subject for scientific analysis.

This purpose has been undertaken in the belief that the proper measurements and analysis of the sizes of cell parts can ultimately yield information about the growth of cells. Of necessity this must be a speculative belief since factual laboratory data are scarce. The speculation, however, is sound in that it follows the lines of general population dynamics which have been applied to human populations or, to take an inanimate extreme, the population of neutrons in a moderator.

The point of view taken in this approach to cell growth may be said to be phenomenological in that it deals only with an enumeration of cells and a measurement of their visible dimensions. The myriad biochemical processes underlying growth and which eventually lead to the synthesis of a fundamental substance such as, say, desoxyribosenucleoprotein, are ignored for the moment.

Attention is focused solely on the entire cell as an observable and denumerable unit. The statistics of such units along with a knowledge of the time parameters of their lives can provide a quantitative measure of their growth. And, although the available data on sizes are in terms of nuclear data, the analysis applies with equal validity to any other cell part or to the cell as a whole.

The sizes and the time intervals in the lives of cells are analyzed in the so-called steady state of growth. The steady state is one in which no accelerations or decelerations (degeneration) occur which could give rise to transient states of the cell population. Such a steady state may be as ephemeral as the so-called normal tissue cell. But it must be postulated to indicate a reference state, if only to rule out the complications accompanying transient growth phenomena such as occur, for example, in endocrine stimulation.

It is probable that the steady state of growth is attained in the transplantable mouse (and rat) tumors, where the evidence points to an uninhibited cell multiplication in the early stages. For this reason, the analysis is illustrated in terms of mouse tumor cell data. The material, on the whole, deals primarily with the tissues of the standard laboratory animals such as mice, rats, dogs, as well as with data on human tissue as they are available. The vast and interesting material on lower biological forms is of necessity left out of consideration.

Since this is a biophysical evaluation of cell sizes, it is necessary to give figures on the orders of magnitude of the rate at which tissue cell sizes presumably change. In Chapter V is given an outline of the methods and type of data obtained in the measure of proliferation rates.

The range of values of nuclear sizes takes on added meaning when the time interval in which the range can be traversed is indicated in order of magnitude. A mouse tumor cell that doubles its volume in 23 hours is remarkable for speed of growth. Equally remarkable for its slowness is, say, a human epidermal nucleus which doubles its volume in 2,000 hours. Therefore, from the physical point of view there is a discussion of cells not only of "How big?" but also of "How fast do they become big?"

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J.G.H.

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THE QUESTION OF THE SIGNIFICANCE OF SIZES OF CELLS and their parts has been controversial from the earliest days of cell theory. The extension of the question to the cancer problem was natural, but here led to the sharpest divergence of opinion. The problem was formulated in the query: "Is size a distinctive feature of the cancer cell or any of its parts?" From a perusal of the technical literature one might be led to believe that every slice of tissue seen under a microscope was distinctly different from every other slice. At least the cells in each slice seemed to present a different appearance to each observer. Flurries of statement and contradiction have persisted across the century to the present times.