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Early Cancer

GUEST EDITORIAL

It is often said that early cancer is curable. Yet almost everyone sees exceptions to the statement. Some friend discovered a tiny mass, had prompt treatment, but died of disseminated tumor. It is obvious that "early" needs clarification. It is used in a number of ways, some of which are often not in harmony with the statement.

"Early" has been used variously: in the clinical sense of having recently first produced signs and symptoms; in the histological sense of being preinvasive; in the anatomical sense of being small; in the topographical sense of being localized and having a low stage number; in the therapeutic sense of being still accessible to treatment; in the prognostic sense of having a high probability of cure; in the biological sense of being early in its life course; and in other ways. These attributes may coincide in some instances, but frequently they do not. They are not synonymous. "Early" has meant different things to different people.

Curability of cancer is today dependent on its being diagnosable, accessible, localized (i.e., not disseminated—with rare exceptions), and on not involving essential structures. Regardless of which definition is used for early cancer, some are incurable in one organ or another on one or more of these four counts. Tumors that have just begun to produce symptoms, that are still small, that have a low clinical stage number, that appear to be localized, that seem to have a good prognosis, or that are still accessible may have metastasized. Cancers that are early by all criteria may involve parts that are inaccessible to diagnosis and treatment. Even a localized small tumor may be clinically late because it involves structures essential for life. Many early cancers cannot be recognized because of internal location, silent nature, and inaccessibility. Preinvasive cancers in some sites are undiagnosable and inaccessible, as are some biologically early tumors. As used here, these two terms are nearly synonymous, but the biological concept is both broader and more precise. It concerns the tumors which are early in their course but not necessarily preinvasive, thus including sarcomas and other varieties as well as carcinomas, and it excludes those preinvasive lesions presently sometimes called carcinoma which are not neoplastic. Biologically, early cancer is both truly "cancer" and "early."

Three facts in the biological nature of cancer account for most of the exceptions to the slogan that early cancer is curable. They are its origin in every tissue and organ, its microscopic size in the beginning, and its ability to disseminate and to do this at any stage including the small.

Although cells of every type can give rise to cancer, most tumors fortunately arise at sites that are expendable. By metastasis, however, the number of tumors involving vital parts is greatly increased. The surgeon is constantly reducing the number of anatomical structures that are essential to life, but at this time there appears to be a limit beyond which he cannot hope to go. The brain, heart, some lung tissue, and other organs will probably be indispensable for some time. The neoplasms involving these parts are threats to life from the time of their origin.

The biological life history of an untreated cancer from the time of the first irreversible, progressive, neoplastic change may be divided into the following phases: (1) local cell multiplication to a visible level; (2) visible local growth of the colony; (3) dissemination, followed by growth of each focus to visibility; (4) growth of visible metastases; (5) tumor death because of death of the host. Dissemination of cancer cells may take place during the latter part of the first or in the second phases. The third stage and sometimes the fourth may be concurrent with the first and second. Early-disseminating tumors, in many sites in the body, are incurable almost from the start and before they are diagnosable. In the biological sense, they are already late in their youth.

After the essential change from normal to tumor

cell (i.e., carcinogenesis) has taken place, the second phenomenon, that of self-unregulatable cell reduplication to form a new tissue mass, begins. This is growth of tumor. Regardless of whether the initial neoplastic transformation takes place in one or many cells or whether there is progressive cancerization of the normal cells about a tumor and incorporation of them into the neoplasm, it is obvious that these phenomena alone would not produce a new mass. For this, cell growth and repeated division are necessary. This usually implies increased local tissue turgor, supplantation of other tissues, and abnormal juxtapositions of cells including, sooner or later, access to preformed spaces such as serous cavities and lymph and blood vessels, providing opportunity for metastasis. The most important characteristic of a cancer to the bearer is its ability to disseminate.

Although the ultimate extinction of each cancer is inevitable from its nature, it takes its host along. Dissemination of the growth to new foci does not save the tumor but hastens its end by reducing the life span of the bearer. Only the hand of man, by artificially metastasizing a tumor to a new host or a culture tube, saves it. Even though neoplasms begin in somatic cells, there are those who maintain that they henceforth influence the germ plasm. If this is true, a cancer partakes of biological immortality, threatening the stream of life. This characteristic, however, does not modify the threat to its bearers, which is purely a somatic-cell phenomenon.

In theory, there is a period in the life of each malignant tumor, after cell division has begun but before extensive infiltration and metastasis have occurred, during which it is early and curable, again provided it does not involve a vital site. The duration of this period is not known for specific growths but there is reason to believe it sometimes ends in the subvisible stage. In such tumors, the relative numbers of which are not yet known, the outlook is bad. For some tumors in visible sites, as for example, in basal-cell carcinomas of the skin, the premetastic period is known to be long. In others, such as malignant melanoma, it has a great range and variability. It is probably different for every tumor. Internal cancers, usually being silent, are not found and diagnosed in this stage except occasionally by chance and in those examples of low malignancy in which slow bulky growth precedes dissemination.

The principal biological characteristics of each tumor are probably determined at the moment of its inception. Its capacity for doing little or much evil, its rate of cell reduplication, and its ability to metastasize soon, late, or never may be determined at this time. Although these characteristics may later be modified, and generally in the direction of greater malignancy, in many human tumors they seem to be fairly constant if considered on the basis of dividing cells. Many of the apparent vagaries in tumor behavior are explained by the mathematics of cell multiplication. This inherent behavior is now sometimes further modifiable by therapy.

The biological behavior of tumors is not yet fully understood or predictable, and, until it is, it constitutes an important subject for research. Some of the concepts here expressed may have to be revised. In the meantime, they cannot be ignored. No usage or definition for "early" comes to mind which would invariably fit the slogan. It would seem, therefore, that thought should be given to its qualification. In medical and scientific writing, the usage of the term "early" should be defined. In our thinking we should recognize the concept and its consequences.

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