

Book Reviews

Conceptualizing Cancer

Neoplastic Development. Vol. 1. LESLIE FOULDS. Academic Press, New York, 1969. xii + 440 pp., illus. \$16.50.

CANCER *n*: a mass of tissue cells possessed of potentially unlimited growth that serves no useful function in the body, robs the host of nutrients necessary for survival, expands locally by invasion and systemically by transmission of cells along lymphatic and blood pathways, and unless recognized early and removed kills the host . . . [*Webster's Third New International Dictionary*, 1967].

Most of the advances in the control of cancer during the last half century have resulted not from research oriented toward elucidating mechanisms of tumor induction and progression but from preventive efforts and the application of research findings only peripherally concerned with neoplastic disease. Exceptions are the control of acute lymphatic leukemia in children by means of combination chemotherapy, of choriocarcinoma by methotrexate, and perhaps of Hodgkin's disease by super-voltage radiation. But the major credit for progress in the treatment of solid tumors must go to improvements in general medical care, advances in surgical management, the use of antibiotics, and especially the technology of transfusing large quantities of blood.

Yet the commitment of resources and effort to research on cancer has been vast; and without questioning the indispensable role of fundamental research, one may legitimately inquire why the great majority of cancer patients has benefited so little. By far the largest share of the research investment has been in molecular approaches to the study of neoplastic transformation; and despite the excitement of work in viral oncology, immunological aspects of cancer, and chemotherapy of leukemia, this reviewer is unaware of any remarkable new benefits to the cancer patient that may be expected in the near future from molecular studies.

These remarks will anger many workers in the field and will evoke denials from some. A few may be found who will agree, and those will recognize the book here reviewed—the first of a two-volume set by Leslie Foulds—as a statement of some of the reasons why the contribution of cancer research to the control of cancer has been so limited.

Foulds is a British pathologist who during more than 25 years of research in cancer has acquired impressive credentials as a profound student of the disease. The “unifying principle” of the book, he says in the preface, is “the concept of neoplasia as a *developmental process* [italics his] akin to normal development in some respects but differing from it in important particulars that are not yet well-defined. . . . This concept is not advanced as a revealed truth but as a working hypothesis, which has proved useful to myself in picking my way through a substantial proportion of the accumulated wisdom and folly of ‘cancer research.’” The “folly” merits special comment. Essentially it is embodied, I would say, in the unwarranted generalization all too easily inferred from the phrase “the cancer cell,” the generalization inferred by Smithers when he assailed the term in his “attack on cytologism” in *Lancet* in 1962. As of the present, we have been unable to identify a crucial biochemical lesion as characterizing cancer cells, to distinguish abnormalities that are incidental to or a consequence of neoplasia from relevant changes, and finally to establish a consistent correlation between the malignant transformation of a cell or cells and the subsequent development and natural history of a cancer. In short, a cancer cell as we define it is not the only prerequisite for cancer.

Foulds's volume begins with an admirable though sketchy history in which the great and near-great of the past and present are identified, with brief com-

ments on their areas of interest and the substance of their contributions to cancer research. A review follows of the general and experimental pathology of neoplastic development; its theme, though perhaps not intended as such, is found in the introduction where Foulds observes that “the multitudinous ways of inducing neoplasia in experimental animals have become something of an embarrassment.” This truth is documented repeatedly in the chapters devoted to etiological factors, neoplastic development, and the biological characteristics of neoplasia. The documentation emphasizes what one would have surely hoped would be obvious to all cancer researchers—that in the induction and progression of cancer most of the recognizable features are not consonant and cellular mechanisms are extremely variable. In the third section of the book, devoted to biological organization and developmental biology, Foulds examines the two complementary aspects of biological order, “structure-static order” and “functional dynamic order,” and analyzes their interplay ever mindful of the need to retain the concept and dimensions of life in the current analytical and reductionist approach to biology.

In discussing neoplastic development, Foulds draws heavily on his research over the past decades, during which he has formulated a concept of tumor progression. He emphasizes that progression occurs in a discontinuous, stepwise fashion in response to modulating influences mediated by the host. It is unnecessary to accept all the details of the “progression” concept, but experience provides strong support for the belief that malignant transformation, though an indispensable first step, is hardly the crucial determinant in the ultimate development and behavior of a cancer. The phrases “latent carcinoma,” “indolent natural history,” and “exuberant growth” are observational descriptors that reflect influences at work after the malignant transformation.

Cancers in the main are composed of a heterogeneous population of cells, with diverse characteristics, which act and progress as a population of cells, not as single ones. Foulds presents a schema of neoplastic development from initiation to the appearance of the overt neoplasm. He discusses diverse pathways of progression, by direct or indirect routes, and shows the resulting emergent lesions to fall into three main

groups: group A includes high-risk though nonneoplastic lesions or conditions, group B lesions that are benign or "imperfect neoplasms," and group C growths having the cardinal features of malignant tumors. Emphasizing that the principles on which the schema is based are most clearly applicable to skin, Foulds proceeds to examine them in relation to cancer of several visceral sites. It is here that the similarities between normal developmental growth and neoplastic development are presented.

The large number of agents that can induce cancer, the extreme variability in their chemical and physical properties, the dissimilarity in properties of cancers arising from different anatomic sites, the extreme variability of cancers from a single tissue source, the variable behavior of any one cancer during its long natural history, and the unpredictable effect of therapy appear incompatible with the notion that a single molecular event or a series of unique molecular events has initiated irreversible changes in a cell or population of cells. The relationship between transformed cells and the ultimate cancer and its properties is obscure. Dulbecco, in discussing transformation and neoplasms, has observed that "a precise relationship between transformed and neoplastic cells . . . cannot be established because the definition of a neoplastic cell is too vague. In fact, the cells of different neoplasms can differ greatly." The corollary of this would appear to be that the transformed cells initially present are further modified by as yet ill-defined internal environmental stimuli, but it is of prime importance to recognize that these ill-defined influences are crucial in relation to cancer. Foulds, in approaching neoplastic development as a problem in development, emphasizes the need to consider modifying influences and their relationship to and possible control of progression. The very nature of this approach denies the likelihood of a unifying concept for cancer induction and progression, and as of the present unifying concepts have little experimental or clinical basis and their contribution to cancer control has been negligible. Each neoplasm is indeed as individual as the host bearing it. Recent evidence suggesting the increasing incidence of patients with multiple primary neoplasms or new primaries subsequent to the treatment of earlier ones further em-

phasizes the systemic nature of the controlling factors.

In omnibus fashion Foulds reviews the various dogmas, such as somatic mutation and viral activation, all within the framework of biological organization. His argument from studies on malignant transformation is emphatically supported by data from studies on cancer induction, which show that there is no consistent relationship between etiological agent and natural history.

The experienced and mature *cancer* researcher will find the book of less use than those probing the "molecular mysteries" of the transformed cell. This should not dismay the author. The comprehensiveness of his approach provides a perspective unavailable in any other text of which this reviewer is aware. To the young or innocent cancer researcher, the volume is a mini-encyclopedia with a comprehensive and pleasingly current list of references. Discussion of the exciting area of viral oncology is limited to 16 pages, but this is an apparent rather than a real deficiency; studies in viral oncology are referred to throughout the text, particularly in the discussion of nucleic acids and of certain dynamic aspects of normal tissue and neoplasm organization. Readers will carry away a strong and responsible series of impressions which may be summarized provocatively as follows:

Cancer is a generic term for a group of diseases rather than a simple problem in growth. Malignant transformation and cancer are not synonymous terms. Exploitable biochemical differences between neoplastic and nonneoplastic tissue, when identified in the future, will, as in the past, be almost certainly specific to individual cancers only. As research subjects, homogeneous cell populations whether in tissue cultures or transplantable tumors are best characterized by the poverty of similarity to autochthonous tumors.

Foulds remarks in his preface that "cancer has always been a Problem . . . [and now] it is a Biological Problem." In reality, it is a constellation of biological problems, each for the most part an independent microcosm. Or in another view of reality, as Foulds also notes, "cancer is still a disease that kills people."

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Anthropology before Its Time

The Observation of Savage Peoples. JOSEPH-MARIE DEGÉRANDO. Translated from the French and edited by F. C. T. MOORE. University of California Press, Berkeley, 1969. xii + 124 pp. + plates. \$4.

Historians of anthropology generally agree that scientific approaches to the study of primitive peoples, as opposed to unsupported speculations, are the product of the last half of the 19th century and that the development of systematic field methods is the result of the trend toward empiricism at the turn of the 20th century and later. Hence it comes as a distinct surprise to read this short book authored by a not-too-well-known French philosopher in 1800 in which he produces a "complete framework comprising any point of view from which these [savage] societies can be envisioned," an essay which proposes ethnographic field techniques of a high degree of sophistication as well as introduces ideas which embody the essentials of several key concepts of modern cultural anthropology. Written as a guide to a French exploring expedition to Australia and adjacent areas, Degérando's work was forgotten until it was discovered and edited by F. C. T. Moore, who introduces the paper by discussing in detail the historical and intellectual context of its creation.

Degérando, who probably never saw a "savage," would study primitives in much the same manner as would a skilled 20th-century field observer. Discarding as useless the superficial and erroneous accounts of most travelers, he points out the distinction between the overt and covert in a culture and urges a thorough examination of each of the facets of savage society, supplying detailed suggestions for securing data on the economic, material, linguistic, social, and psychological aspects of life. Like Boas 110 years later, he cautions against the unconscious biases of the investigator and he demands a wide sampling of informants in any group studied. And unlike the first recognized anthropologists of more than a half century later, Degérando takes an approach to the study of man that is primarily inductive. Some of his ideas foreshadow anthropological functionalism in that he brings out the interplay of the different features of a society. His recommendation that the observer try to understand the native's