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**Significant Trends in Cancer Research**

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Medicine is applied biology. Medical problems, therefore, are fundamentally biologic problems. This includes cancer, which was recognized as belonging in this sphere many years ago by a few pathologists but, curiously enough, remained with little attention on the part of biologists themselves until quite recently.

Until comparatively recently, cancer was studied mostly in its gross pathologic-anatomic aspects. Better microscopes made possible enunciation of the cell doctrine, whereupon cancer was placed in its true category of being a cellular growth and maldevelopment. Even so, few biologists, in whose fields the problems of cellular growth and development are paramount, recognized the relationship to a sufficient degree to work on it. Virchow’s dictum that all cells come from preexisting cells led to a persistent search for cellular beginnings, and the literature teems with demonstrations which often were anything but conclusive as to the exact cellular origin of the various types of cancer.

A serious difficulty faced by pathologists in this type of work is lack of sufficient knowledge of the growth and development of normal cells for comparison. The pathologist studies a tumor as of the instant when it is removed and fixed and from this point tries to figure out what happened when the tumor arose and how it progressed while it was still in the patient. The hazards need no emphasis. To prophesy the future of a given tumor on the basis of what it looks like at one fleeting instant of its life is to assume wishfully that all the variables but one are controlled. Most pathologists now realize this. In the last analysis, prognosis as to the fate of a patient with cancer depends not on the type of cancer, its cellular details, behavior of the cancer cells or the name given to it but on whether or not, in its treatment, every last cancer cell has been removed or destroyed. Some surgeons and/or radiologists still refuse to be radical in the presence of a small cancer or of one said to be of low malignancy. A good maxim is “faint heart never cured cancer patient.” Of what use otherwise is the propaganda “come early”?

The need and value of comparing malignant growth with the corresponding normal has been generally admitted only since the end of the first world war. In fact, it is now emphasized that the use of biologic technics offers a most fruitful approach to cancer....

The crucial problems in the biologic approach are the differentiation and organization phases of cellular growth. Cancer cells, while differentiating even to high degrees at times, nevertheless show qualitative anatomic differences from corresponding normal cells. Translate this fact from static to dynamic terms. How does the cancer cell get that way? And translate again from this language to chemical and physical terms. Devise methods of quantitative estimation of degrees of differentiation. How far can a cell normal or cancerous differentiate until it can no longer divide? What potencies remain in cells after some of their original complement has been expressed? What environmental chemical factors govern potencies and with what intracellular substances do they react to form what new substances? What are the qualitative changes when a cancer cell or cells originate? What are the enzyme patterns catalyzing these reactions both in the normal and in that “new” cell that is cancerous; in that cell which has undergone “somatic mutation”; in that cell which is no longer quantitatively different but qualitatively?

A similar set of questions is constructed for the organization problem. Cancer cells do not organize into organs and parts as do normal cells. Here the separated problems of blood supply, nerve supply, organizer substances (Spermann), hormones, function (Wilhelm Roux) enter the picture.

The applications of these problems are not only in such general questions as causation but also in details such as origin, cellular patterns, diagnosis and even nomenclature, which should be changed from the weird and confusing words now used to a more logical and accurate language. For example, instead of saying that a squamous cell carcinoma arises from squamous cells, it should be stated that a squamous cell carcinoma arises from but partially differentiated cells and they differentiate out into squamous-like cells.

Another part of the biologic approach which has helped stimulate biologists but also has medical interest is the recognition that cancer is not confined to human beings but has been found in most multicellular organisms. In addition to the spontaneous tumors studied in horses, dogs, fish, turtles, frogs and mice, botanists have shown that much can be learned from plant tumors. As one clinician said, “At least I can tell patients and their relatives that the fundamental cause of their cancer is not too much worry, or eating food cooked in certain pots, or sleeping with their beds east and west, because fish do not eat tinned food, nor do geraniums worry, and yet they too get cancer.”

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**Editor’s Note:** JAMA Revisited is transcribed verbatim from articles published previously, unless otherwise noted.

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