THEORETICAL ANALYSIS OF CARCINOGENESIS

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1. Introduction

Several comprehensive reviews of our total experimental knowledge of carcinogenesis have been published recently: J. Huxley [1], E. Boyland [2], L. C. Strong [3], G. E. W. Wolstenholme and M. O'Connor [4], A. Levan [5]. In another paper we plan to give a more detailed discussion of the experimental material on carcinogenesis and its interpretation (R. Eker and N. Arley [6]). We shall, therefore, here limit ourselves to giving a review of a stochastic theory of carcinogenesis worked out previously by S. Iversen and N. Arley [7] to [14].

From the total experimental knowledge now available, and especially from the results of the chromosome studies of the last few years [5], more and more evidence has been brought forward which tends to indicate that in all forms of neoplasia, whether spontaneous or induced by chemicals, irradiation, virus, or disturbance of cell environment as in tissue culture and in the Oppenheimer effect, *the key step*, a necessary although not necessarily a sufficient step, *is an irreversible change in the genetic apparatus of the somatic cells.* All alternative hypotheses, especially the virus hypothesis, seem to reduce on closer investigation to being special cases of a genetic interpretation of the neoplastic phenomenon (J. Schultz [15]). Although the basic mechanisms of the two fundamental biological phenomena of cell division and cell differentiation are still unknown, even in normal organisms (D. Mazia [16], J. Huxley [1]), great progress has in recent years taken place in our understanding of a third fundamental biological phenomenon, namely the structure, function, and replication of DNA (M. F. Perutz [17], M. B. Hoagland, [18], L. A. Bliumenfel'd [19], H. Gay [20]). Also, our knowledge of the structure of the chromosomes has progressed (A. E. Mirsky [21], J. H. Taylor [22]).

Thus, more specifically, the picture of the key step now emerging is one of somatic mutation by *cytogenetical loss engendered by interference with the synthesis and function of the DNA of the chromosomes and leading, presumably, to the deletion of growth-controlling and/or regulatory proteins* (A. Haddow [23]), as well as to the loss of some, or all, of the tissue-specific antigens (H. N. Green [24], [25]). Once this necessary, irreversible step has taken place, the population of these

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