

of this fact. As histological data show that a well-vascularized, hyperemic tissue and not an ischemic, avascular tissue furnishes the basis of malignancy, occupational conditions characterized by anoxic, nutritive disturbances of a general or restricted type cannot be regarded as representing a suitable medium for an industrial malignancy.

Disturbances of the cellular or systemic sulfur metabolism were claimed by Hammett; Reimann; Grumme; Tanaka; and Sullivan to possess causal relations to the development of cancers. The most far-reaching contentions in this respect were made by Hammett. Elaborating upon his thesis that sulfhydryl, a natural constituent of all cells, is the essential and universal stimulus to growth by increase in the number of cells, and that the countless other auxenic factors exert their influence only indirectly through their effect on the sulfhydryl groups, Hammett proposed the following theory of cancerigenesis: The biological basis of malignant tumors is the distortion of the sulfhydryl equilibrium in the presence of genetically determined lines of cells, in which the heightened nuclear reactivity of hypersensitivity to stimulation to proliferation by sulfhydryl, characteristic of young cells, is retained without resulting secondarily in increased differentiation. In support of this dogma, Hammett referred among others to the statement of Voegtlin and Thompson that tumor tissue contains glutathione in amounts comparable with those present in the liver, the organ having one of the greatest quantities of glutathione present in the various tissues. In a detailed review on the significance of sulfhydryl as a growth factor, Hueper showed conclusively that this theory was in direct disagreement with a number of well-established biological facts, was based on evidence of doubtful reliability, and was contradicted by data of numerous other investigators.

The available evidence scarcely sustains the fundamental claim made by Hammett and endorsed by Reimann, concerning the role of sulfhydryl as a universal and sole mitotic catalyst. This statement shall not distract from the significance which sulfhydryl compounds (methionine, cysteine, and glutathione) have as activators of certain enzymes, as oxidation-reduction regulators, as aminoacids essential for synthesis of protein and therefore for a sustained proliferation of cells, and as agents important in the detoxication processes of the body (Lightbody and Lewis; Mitchell and Hamilton; Hueper; Baker; Womack, Kemmerer and Rose; and White and Beach). Voegtlin, Johnson, and Thompson showed that a deficiency of sulfhydryl containing aminoacids in the diet resulted in a demonstrable impairment of the proliferative activity of normal as well as malignant cells, and that an identical result ensued from a dietary deficiency of other aminoacids, such as lysine. However, Hueper showed on explants of normal cells and Carr, Connor, and Ginzton on tumor-bearing animals, that the availability of excessive amounts of sulfhydryl in the nutritive medium has no effect upon the proliferative rate of cells after a certain optimum has been reached.