

Among the large number of compounds included in the group of aromatic amines and their derivatives, there are substances with more or less marked allergic properties, which are responsible for the frequent appearance of dermatitis, asthma, and rhinitis among persons coming in contact with them (phenylene diamines, para-amino-phenol, aurantia, and phenylhydrazines). Also, there are compounds which combine with allergic qualities those of cellular growth stimulation, sometimes leading to tumor formation (aniline, benzidine, naphthylamine, toluidine, chrysoidine, Bismarck brown, and amido-azo-toluol) (Koelsch; Mayer; Sulzberger; White; and Sachs). Teutschlaender; Mayer; Kimla; Bettazzi; and Beck called attention to the allergic nature of tar dermatoses and tar cancers, respectively. Similar combinations of allergic and carcinogenic qualities exist in certain, inorganic, blastogenic agents, such as nickel, arsenic, and chromates.

Definite proof of the allergic nature of carcinogenesis depends upon the demonstration of chemospecific, carcinogenic allergens by chemical and immunological methods, and of an effective prevention of carcinogenesis in a sensitized organism by means of a specific desensitization. Mayer; Hueper; Needham; and Oesterlin have advanced the conception that the carcinogenic action of various synthetic and occupational, carcinogenic chemicals depends upon their ability to couple either directly or as metabolites with protein molecules in the body, thus forming allergenic, hydrocarbon-protein complexes.

While the isolation of such chemospecific, carcinogenic hydrocarbon (hapten)-protein complexes from cancerous tissue has not been accomplished as yet, there exist a large number of observations in which such conjugations have been obtained in vitro with relatively simple chemical means. The resulting allergenic products (immune sera) showed a high degree of chemospecificity in the haptenic group in immunological reactions, and exerted, under proper experimental conditions, when tested in animals, an anticancerous effect.

There exist various methods by which aromatic substances, especially aromatic amines, may be coupled with proteins. The oldest and most often used technique is that leading to the production of the so-called azo-proteins. It was discovered by Pauly and later on elaborated and applied to the chem-immunological field by Landsteiner. The following procedure is used: aromatic amines are diazotized by the addition of sodium nitrite and hydrochloric acid, and the resulting diazo-compound is conjugated with certain aminoacids (histidine and tyrosine) of the protein molecule. If the diazo-compound is present in excess it may also combine with the indole group of tryptophane, the imino-group of proline and oxyproline, the imidazo-group of histidine, or with free amino-groups of any aminoacid present. The azoproteins obtained have the general structure $R-N=N-C_6H_5$. Such azoproteins have been formed with aniline, benzidine, beta-naphthylamine, alpha-naphthylamine, toluidine, beta-anthramine, amidoantipyrine, p-aminophenylazobenzene, p-aminobenzophenone, p-aminophenylmethane, and atoxyl (Landsteiner and