

Dublin listed the workers of the following occupations among whom bladder tumors of industrial origin may occur: aniline workers, artificial leather makers, calico-printers, coal-tar workers, compositors, compounders (rubber); dye makers, explosive workers, feather workers, lithographers, millinery workers, mixers (rubber), painters, paint makers, pencil (colored) makers, photographic workers, pressroom workers (rubber), printers, reclaimers (rubber), rubber workers, tannery workers, vulcanizers. Thus aniline, benzidine and naphthylamines are industrially important chemicals.

III. ETIOLOGICAL AGENTS

The question concerning the chemical character of the carcinogenic agents causing these vesical neoplasms is still controversial in spite of the fact that tumors of this type have been known for more than forty years. While Rehn attributed the development of such tumors only to fuchsin, which is made by melting aniline, toluidine, nitrobenzene and iron chloride, subsequent investigators have added a large number of substances to the list of suspected carcinogenic agents. The great difficulties which confront the investigator in this respect were pointed out by Hamilton: 1) Workmen handle usually more than one compound and are often shifted from one department to another. 2) Different degrees of danger exist with the same compound when different processes are used. 3) Certain impurities or by-products which occur in traces and are often unsuspected may be more harmful than the parent substance. 4) The nature of the dyes and the methods of producing them vary in different factories.

It was soon recognized, however, that the appearance of bladder tumors was often associated with prolonged occupational contact with the following aromatic bases: phenylamine (aniline), its isomers and homologues (toluidine and xylidine) and other amino derivatives; diphenylamine (benzidine), its isomers and derivatives (e.g., tolidine or dianisidine); naphthylamines and related compounds (e.g., naphthylene diamines). The contention of Nassauer, that aniline alone was the carcinogenic agent since it was presumptively contained as an impurity in all other substances incriminated, has no basis in fact.

In addition to these basic substances, various and numerous intermediary products (secondary and tertiary arylated and alkylated aromatic amines, such as dimethylaniline), formed during the production of dyestuffs, have been claimed repeatedly to be carcinogenic (Engel, 1937). In this connection attention may be called to the many impurities occurring in the commercial aromatic amines, such as beta-beta-dinaphthylamine, alpha-beta-naphthazine, 1,5-hydroxynaphthalene and various other related substances (benzcarbazoles) (Hueper, Briggs and Wolfe; Boyland and Brues; Cook and associates).

The various possibilities as to the formation of such impurities during the production of aromatic amines were investigated by Boyland and Brues. They