

series of Evans, 71 per cent of the tumors appeared within from one to fifteen years after exposure, while in the European series of Hueper only 47 per cent developed within the same time of contact. Whether or not this indicates differences in degree of exposure remains at present a problem for research. Attention may be called, however, to the fact that in the majority of the American cases the exposure was to beta-naphthylamine, which, according to Engel (1937), is apt to cause a neoplastic response more quickly than the other aromatic amines.

A characteristic feature of aniline tumors which is of great medical, medico-legal and social importance is that they may develop many years after exposure to the carcinogenic agents has ceased. Nassauer reported that in some of his cases tumors appeared from one to seventeen years (average eight years) after the termination of the hazardous work. This phenomenon is not unique, as similar observations have been made regarding the time of manifestation of carcinoma due to arsenic, tar, soot and roentgen-rays. A reliable explanation of this peculiar behavior is, however, still missing. It may be assumed that the exposure produces at the time a conditioning of certain cells or cell complexes in the wall of the bladder which may make them especially sensitive to normal or abnormal stimuli of growth. Whenever this cell-fixed quality can exert itself, owing to lack of normal growth-restraining influences or to an excess of agents promoting proliferation, tumor formation will result, similar to the sudden manifestation of a chemical hypersensitivity following many years of apparently harmless contact.

The length of exposure has been related to the biologic characteristics of the ensuing tumors (Henschen). It was assumed that the neoplasms were primarily benign and were transformed subsequently into malignant growths as contact continued with the carcinogenic substances. This was soon recognized as incorrect, for it was observed that malignant tumors may develop as early as benign ones (Oppenheimer, 1926, Curschmann). This conception is confirmed by Hueper's (1934) compilation of 93 instances recorded in the literature:

Years	1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40
Benign tumors	2	0	2	4	4	2	0	0
Malignant tumors	8	13	16	24	8	5	2	3

Furthermore, histological observations in sections from the bladders of dogs with aniline tumors furnished definite proof that many of these neoplasms are malignant from the start and do not pass through a benign stage (Hueper, Wiley and Wolfe).

VII. CHEMICAL CHARACTER OF COMPOUNDS AND NEOPLASTIC RESPONSE

Engel (1937) stated that of the three aromatic amines (aniline, benzidine, beta-naphthylamine) beta-naphthylamine appeared to be the most carcinogenic,