

different routes to the various aromatic amines (Grandhomme; Jaffé; Schwerin; Posner and Huldshiner; Fischer; Askanazy; Oppenheimer, 1926-1927; Adler; Henkel and others). In these experiments various animals were used (mice, rats, rabbits). The mortality among the animals was high. Postmortem examinations showed inflammatory conditions in the lungs and fatty degeneration of the liver and kidneys. With the exception of the temporary acute and the chronic inflammatory and hyperemic conditions in the mucosa of the bladder, nothing was seen indicating a neoplastic response to the substances used. Burrows, Hieger and Kennaway were unsuccessful in their attempt to produce bladder tumors in mice subcutaneously injected with 1.2.5.6-dibenzanthracene.

The more recent attempts of Leitch, Kennaway and Fry to produce bladder tumors in mice and guinea pigs by the treatment with aniline, benzidine, fuchsin, scarlet red, alpha- and beta-naphthylamine were negative. Repeated applications of 1.2-hydronaphthoquinone to the skin of mice similarly were without neoplastic response. Berenblum and Bonser also failed to produce bladder tumors in rats maintained on a diet containing 85 per cent marmite, 5 per cent beta-naphthylamine, 5 per cent alpha-naphthylamine and 5 per cent aniline (spread on bread for one series and on meat for a second series). This management was continued in the first series for an average of 28 weeks (4 to 76 weeks), and in the second series for an average of 46 weeks (25 to 57 weeks). A third group of rats inhaled vapors of 5-chloro-o-toluidine for two hours daily, showing an average survival period of 25 weeks (3 to 45 weeks). Except for some congestion of the blood vessels, occasional ulcerations of the mucosa, leucocytic infiltrations, and hemorrhages in the submucosa, the bladders of these rats were normal.

Brief mention may be made of the experiments of Climenko on rabbits and dogs fed with o-toluene-azo-beta-naphthol and toluene-azo-beta-naphthylamine for periods up to three months. There were no pathological changes of any kind in the urogenous organs of these animals. In view of the insufficient time of exposure, a negative outcome could be anticipated.

More recent experiments of Schär (1930), and of Perlmann and Staehler (1932 and 1933), were somewhat more promising, but the results could not be confirmed by Berenblum and Bonser, or by Hueper, Briggs and Wolfe. In Schär's experiments, 16 young rabbits inhaled ethyl-beta-naphthylamine hydrochloride, phenyl-alpha-naphthylamine hydrochloride, alpha-naphthylamine and beta-naphthylamine, respectively, for periods of between six and twenty months. The concentration of the dust was low, so as to imitate plant conditions. At the end of the experimental period, one animal, which had been exposed to alpha-naphthylamine, showed a lesion in the bladder which was interpreted as a fibrous polyp; and a second rabbit revealed epithelial changes in the vesical mucosa which were considered as carcinomatous.

These diagnoses, however, have been doubted seriously on various grounds