

off the acetyl group. This urinary metabolite is obtained entirely in the alkaline fraction during extraction of the urine, while the acid fraction does not contain any part of it. On the other hand, when acetanilid is introduced into carnivores, only traces of p-aminophenol are isolated from the basic extract. The main part of the metabolized chemical appears in the acid fraction as o-oxycarbanil paired with the two acids above mentioned. The oxidation in this case takes place in the ortho-position without elimination of the acetyl group forming first the unstable o-oxyphenylcarbaminoic acid, which spontaneously changes into o-oxycarbanil. It appears not unlikely that differences of this kind may determine variations in the susceptibility of different animals to the same carcinogenic chemical.

Hueper, Wiley and Wolfe produced papillomatosis and carcinomatosis of the bladder in female dogs by daily subcutaneous and oral administration of beta-naphthylamine (from 300 to 450 mg. daily in capsules) for from twenty to thirty-two months. The lesions observed in cystoscopic and histologic examinations of the bladders of 12 of the 16 dogs thus treated were identical with those seen by these authors in cystoscopic and histologic examinations of dye workers. The tumors continued to grow and become more numerous in some of the dogs after discontinuation of the treatment during the last six months of observation, while in one dog the first neoplasms in the bladder were noted several months after cessation of exposure. The termination of contact with the carcinogenic agents thus was followed by progression in the appearance and development of the neoplastic manifestations. While none of the 5 dogs which have been killed so far has shown any metastatic deposits at autopsy, one dog presented, on histologic examination, neoplastic penetration into the subserosa of the vesical wall. The recent statement of Ferguson in regard to previous experimental production of bladder tumors in dogs is incorrect and apparently based on faulty translation and interpretation of cystoscopic observations made by Engel (1924) during acute experiments with naphthylamine poisoning.

Berenblum and Bonser, as well as Hueper, did not succeed in producing skin tumors in white mice painted for nine months with an ether extract of urine obtained from dye workers with bladder tumors and from dogs treated with beta-naphthylamine. This failure may be ascribed to several possibilities. The amounts of carcinogenic substances in the urine might have been too small to be effective even after concentration. The chemical manipulation of the urine necessary for extraction might have produced a fundamental change in the chemical and biologic properties of these metabolites. The skin of the mouse might possibly be a less sensitive tissue than the mucosa of the bladder of man or of the dog.

Boyland and Brues tested the following substances which they suspected as normal impurities in the various carcinogenic aromatic amines: alpha-alpha-dinaphthylamine, beta-beta-dinaphthylamine, 1.2.5.6-dibenzcarbazole, 1.2.7.8-