

solid epithelial papillary formations without any participation by, or simultaneous changes in, the submucosal connective tissue during the early stages (Watanabe, 1934; Löwenstein, 1910 and 1911; Hueckel). These papillary changes remain benign. It would be, however, of interest to know whether they may be transformed into malignant ones on coming in contact with the urinary metabolites of the compounds used by the Japanese workers, in analogy with the malignant changes produced by Rous in the Shope rabbit papilloma after local treatment with scarlet red. These considerations also must be applied to the report of Brancati, who found a broad-based papilloma at the posterior vault of the bladder in a rat fed for one year with aniline blue (arylrosaniline dye).

Attempts to produce such a transformation in the bladder of rats, infected with *Trichosomoides crassicauda* and showing a vesical papillomatous hyperplasia, by the administration of oestron given over a period of 47 to 465 days (total amounts ranged from 2,085 gamma to 25,920 gamma) were unsuccessful.

It may finally be mentioned, that Beck reported the production of a marked papillomatosis of the urinary bladder of rabbits which had been treated for a period of 10.5 months by repeated intravenous injections of an emulsion of a detoxicated tar. Beck attributed these lesions to the presence of tar excreted in the urine. This observation is of a certain significance, as claims have been advanced concerning the occupational genesis of bladder cancer in tar workers.

In addition to these attempts to produce bladder neoplasms by systemic exposure of animals to aromatic chemicals, numerous experiments have been made to elicit tumorous responses by placing foreign bodies of widely differing chemical composition directly into the bladders of animals. T. Bauer, making a separate pouch in the bladder of the rabbit and painting the mucosa of the pouch for several months with a mixture of tar, scarlet red, aniline and soot, observed the development of papillomas with epithelial metaplasia but without malignant changes. Maisin and Picard introduced into the bladders of rats by cystostomy small plugs consisting of equal parts of tar, paraffin and scarlet red. In 66 per cent of these animals, diffuse papillomatosis was seen after the lapse of one month and a half. The tumors were considered, in part, "histologically malignant", as they showed infiltrative growth. Similarly, the introduction of pellets, consisting of tricresol and aniline oil, into the bladder of rabbits by Roffo resulted in the development of a vesical papillomatosis. Leone placed in the bladders of guinea pigs and mice pellets of tar, cement, asphalt and licorice. These implantations were followed by metaplastic and keratinizing epithelial changes, with development of papillary processes and infiltrative epithelial growth into the muscular layer under a formation of epithelial cysts. The processes were interpreted as precancerous. By laparotomy, Watanabe (1934) inserted into the bladders of white rats pellets composed of a mixture of tar, scarlet red and paraffin. In 9 of 55 rats thus treated