

and the dome of the bladder are, therefore, not the controlling factors in this respect as claimed by Ferguson (1934 and 1937).

The importance of local urinary conditions in the localizations of aniline tumors is demonstrated further by observations of Sebening, Mueller (1936) and Gay. These investigators reported the occurrence of tumors in renal pelves in association with anatomic anomalies of the corresponding ureters which interfered with the free flow of urine through these conduits. A status of prolonged urinary retention and mucosal contact within the affected area thus was produced similar to that existing normally in the bladder. These factors may be considered on the bases of the urogenous theory as predisposing to the development of tumors in the region of the urinary tract situated above the obstruction.

The urogenous theory also receives support from the experimental histological observations recorded in regard to the sequence of cellular changes in the different layers of the bladder in dogs. The fact that the first cellular reactions developed in the epithelium strongly suggests action through urinary contact.

The hematogenous theory, sponsored by Ferguson and Gay, assumes that the carcinogenic agents circulating in the blood have a special affinity for the bladder tissue, causing there specific primary injury to the terminal capillaries of the submucosa of the bladder and other parts of the urinary tract. The validity of this hypothesis is supported, according to its authors, by the following evidence: 1. The majority of the aniline tumors occur in the lower half of the bladder, i.e., in the best vascularized part of the viscus, but do not involve most often its most dependent part, the trigonal area. 2. Aniline tumors develop not only in the bladder but also in the kidneys, renal pelves and ureters, indicating thereby a systemic and not merely a local organic affinity. 3. Histological examination of early lesions of the human bladder demonstrates that the vascular changes precede the epithelial reactions, which originate in the basal layer. 4. The mucosa in the vicinity of bladder tumors of occupational and nonoccupational origin does not show, on microscopic study, any sign of irritation, such as hyperplasia, which can be expected if action is through urinary contact. 5. Attempts to demonstrate a carcinogenic substance in the urine of persons with occupational and nonoccupational tumors have failed. 6. The urinary excretory metabolites of aromatic amines have been proved to be carcinogenically inert. 7. The assumption that there is an exclusive chemical tissue specificity in the causation of bladder tumors is not unique, as a similar hematogenous mechanism is claimed to be present in the causation of arsenical cancers, the occurrence of which is restricted to the skin.

The hematogenous theory is an interesting conception which deserves further investigation, especially with experimental methods. Ferguson proposed, to this end, transplanting the ureters of an animal into the rectum