While the carcinogenic chemicals so far studied exert, for the most part, a strictly local action in rats, certain nitrogen compounds are an exception to this rule—namely 3:4:5:6-dibenzcarbazol, studied by Boyland and Brues (1) and o-amidoazotoluene, studied by Sasaki and Yoshida (2), Shear (3), Nishiyama (4), and others. These substances, introduced subcutaneously, may produce both local tumors and hyperplastic changes in the liver or even true hepatoma. Kidney tumors induced by substances injected at a distance have not hitherto been described. The present report deals with renal changes following the subcutaneous injection of beta-anthraquinoline dissolved in lard.

The compound was prepared according to the method of Graebe (5), by distilling with zinc dust 3:4-dioxo-1:2-pyridinanthraquinone. The crude product of the distillation was at first sublimed at reduced pressure. The product was extracted with hydrochloric acid by heat and filtered hot from the anthracene, which is not separated by sublimation. Neutralization of the chloride with ammonia yields beta-anthraquinoline, which was twice crystallized from alcohol.

The structural resemblance between beta-anthraquinoline and 1:2-benzanthracene is evident: a CH-group in the 4 position is replaced by an atom of nitrogen (N).

In order to ascertain whether the nitrogen compound possessed a real carcinogenic activity as compared with the purely potential activity of 1:2-benzanthracene, 11 rats were given two subcutaneous injections of 4 mg. each with an interval of about a month between. Four rats received a third injection of 2 mg. after about five months. After seven to ten months there was observed at the point of injection a soft fluctuating swelling from which an opalescent liquid could be obtained. Microscopic examination revealed only edema of the connective tissue and lymphocytic infiltration.

Eleven months after the injection 8 animals had died. Of these, one showed cystic nephritis affecting both kidneys and two tumor nodules (Fig. 1) in the right kidney, one of microscopic dimensions and the other the size of a pea; another had a tumor the size of a millet-seed in the left kidney; while four other animals showed cystic nephritis in a more or less advanced stage but no tumors. In only 2 were there no changes affecting the kidneys.
Fig. 1. Kidney of rat containing two tumor nodules

Fig. 2. Adenocarcinoma of rat kidney
The structure of the affected kidneys was very characteristic. The epithelium of the convoluted tubules was swollen and the glomeruli were degenerated. Hyaline casts and hemorrhages were frequent: the interstitial connective tissue was irregularly increased. The more or less numerous cysts, of variable size, contained a clear transparent fluid. The smallest cysts were lined with a thick cylindrical epithelium in one or two layers; in the larger cysts the lining was atrophic.

The structure of the kidney tumors is that of adenocarcinoma (Figs. 2–4). The neoplastic cells are frequently closely grouped about the blood vessels, as commonly occurs in kidney tumors in man.

Ophüls and McCoy (6) have observed cystic nephritis resembling that recorded here in 2 per cent of wild rats. In our animals, however, it seems possible to exclude a spontaneous occurrence of both the nephritis and of the tumors, inasmuch as the animals belonged to a strain \(^1\) in which similar alterations were never observed by us and since spontaneous tumors of the kidneys in rats are only rarely mentioned in the literature (7).

Beta-anthraquinoline would therefore appear to be a substance of weak carcinogenic activity, but having the particular property of acting upon kidney tissues. It is the first chemical found to be capable of producing kidney tumors at a distance, and may thus explain certain occupational neoplasms in man. The only other quinoline for which carcinogenic activity had been ascertained is 2 (p-amino styryl)-6-(p-acetylamino benzoylamino)-quinoline methoacetate, or styryl 430 (8), but this acts only at the site of application.

\(^1\) The Wistar strain supplied by the Glaxo laboratories to the Cancer Institute of Rome has for two years been kept under observation by one of us.
REFERENCES