tomas observed in these animals were larger than those elicited by the treatment with injected urethane only. The same amount of methylcholanthrene administered to rats in an analogous way produced tumors (sarcomas and squamous epitheliomas) in 30 per cent of the treated animals (3), while in the present series only 9 per cent of the rats had these tumors. The question, whether the production of methylcholanthrene-elicited tumors is reduced by the simultaneous application of urethane, as these results seem to indicate, will be studied in further experiments.

The observation that urethane, injected or given by the oral route, is capable of producing pulmonary adenomas and hepatic tumors in rats should be taken as a warning against prolonged therapeutic use of this substance in human beings.

**SUMMARY**

One series of 57 rats was fed 0.15 per cent of ethyl urethane in the diet for 15 months. Fifty-nine per cent of the animals surviving more than 9 months developed pulmonary adenomas. Moreover, 1 case of an incipient hepatoma was found.

Twenty-eight rats were injected 30 times with 100 mgm. of urethane and 7 per cent of the animals surviving more than 9 months after the first injection developed pulmonary adenomas; 25 per cent developed hepatomas within 15 months.

Twenty-five rats received 1 intravenous injection of 2 mgm. of methylcholanthrene in olive oil and 30 injections of 100 mgm. in an aqueous solution of urethane intraperitoneally; 9 per cent of these animals had pulmonary adenomas and 27 per cent had hepatomas after 15 months.

**Appendix**

**Histological Findings in Lungs and Livers of Rats Treated with Ethyl Urethane**

Rudolf Jaffé, M.D.

A short description of the histological observations made in the lungs and livers of rats treated with urethane, as described in the foregoing paper, will be given.

The lung tumors found were mostly adenomas of the same type that occur in mice spontaneously or after treatment with carcinogenic hydrocarbons or urethane. They are well limited and consist of high epithelial cells, often glandular in arrangement. The cells are pale with large, well-formed and colored nuclei. Often transitions to other cell layers may be observed, which are more solid and consist of shorter cells. The cells are situated clearly intra-alveolars, but a connection with the branches of the bronchus has never been found. They are apparently derived from metaplastic alveolar epithelial cells.

A metaplasia of the alveolar cells without tumor formation can be observed frequently. These areas of metaplasia may be found in the neighborhood of atelectatic foci of various sizes or of vegetations of the connective tissue. As the metaplastic areas can be more or less of glandular-like aspect, it is sometimes difficult to decide whether the neoformation is a tumor or not.

Vegetations of bronchial epithelium are frequently observed; they may be situated either within or exterior to the bronchi. Vegetations with glandular appearance may be found surrounding larger bronchial branches. These formations probably do not deserve to be designated as tumors, although they may be quite tumor-like in their histological aspect. They are mostly found in combination with purulent bronchitis.

Infarcts were found frequently in the border zone of the lungs. They were always typical infarcts without the epithelial vegetations found in lungs of rabbits or rats injected intravenously with methylcholanthrene (3). The artery corresponding to the infarcted area showed an endoarteritic process, which was sometimes combined with a thrombus, but never with complete occlusion. The same kind of lesion of blood vessels without infarctation could be observed also, and infarcts without these lesions have been found. The blood vessels appeared dilated only in these cases.

The hepatomas found in the livers of the rats treated with urethane showed the same histological aspect as described by Opie (7) in rats fed p-dimethylaminoazo-
benzene. All the hepatomas observed in the present series were derived from hepatic cells and showed various aspects of solid and glandular forms. No tumors of the bile-duct epithelium similar to those in hepatomas induced by p-dimethylaminooxobenzene have been observed in these cases, although a few small bile-cell cysts have been found.

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Histological Findings in Lungs and Livers of Rats Treated with Ethyl Urethane

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