

mice with lowered vitality, and suffering from severe, general poisoning by tar were less apt to develop skin tumors than animals vitally unimpaired.

A great deal of effort and speculation has been expended in attempts to shed some light upon the causative mechanism which is responsible for the remarkable differences noted in the susceptibility of various species to carcinogenic action of tar. Production of tar cancers was accomplished rather readily in mice and rabbits; however, great difficulties were encountered when attempts were made to obtain similar results in the closely related species of rats. An appreciable number of investigators (Buschke and Langer; Borrel; Itchikawa; Boez and de Coulon; Itchikawa and Baum; Yamagiwa; Calvanico; Halberstaedter; Deelman; Teutschlaender; Möller; Joannovič; Bonne; and Neumann) failed to elicit any neoplastic reactions in rats subjected to prolonged, cutaneous applications of tar. Consequently, for some time the opinion prevailed that rats were entirely refractory to tar.

In recent years, several investigators succeeded in obtaining cancerous responses in the skin of rats after very extended applications of tar. Dentici (1923) found one papilloma in one out of 30 rats, after 176 days of cutaneous treatment with tar. Herlez (1926) reported one carcinoma among 100 rats, painted for 511 days with a mixture of coal tar, glycerol, and arsenious acid. Cholewa (1929) succeeded in developing one cancrroid in 10 rats subjected for seven months to repeated scarifications of the skin by burns, on which tar was applied the following 5 months. Guilera, Roca, and Corachán (1930) found one cancer among 40 rats painted with tar. Watson reported that of 11 rats treated cutaneously with ether extracts of rat tissue, followed by paintings with gas-house tar, four developed squamous cell carcinomas with extensive metastases. Papillomata appeared in these animals after 415 days of treatment; malignant tumors were present after 630 days. Giuffrida (1930) also, obtained positive results in rats after paintings with tar. It appears that the difference in reactivity to carcinogenic tar existing between mice and rabbits, on one side, and rats, on the other side, is not of a fundamental nature, but merely a matter of degree.

Attempts to produce tar cancer in the skin of guinea pigs have failed, according to reports of Leitch; and Neumann. Similar, negative results were obtained in regard to dogs by Itchikawa; Itchikawa and Baum; Dentici; Borrel; Boez and de Coulon; Bloch; Teutschlaender; and Halberstaedter. Recently, however, Passey recorded the successful production of malignant melanomas of the skin in three dogs which had received tar applications for more than 6 years. This result is the more remarkable, as the development of melanotic tumors by cutaneous treatment with tar appears to be highly exceptional and somewhat controversial in regard to the actual, neoplastic nature of the melanotic accumulations obtained. Only Lipschütz made a similar claim in connection with neoplastic responses seen after tarring the skin of grey mice.