

In contrast to these either negative or doubtful results obtained by the experimental inhalation or insufflation of tar, the cutaneous application of this substance had a definite and evidently undeniable effect upon the development and incidence of pulmonary neoplasia of mice and rats in the hands of several investigators (Murphy and Sturm; Möller; Bonne; Schabad; Lynch; Puccinelli; Koose). When a tar solution in benzene was painted on alternating sites of the skin of mice, three to four months old, Murphy and Sturm observed that after 36 of these applications, given within 83 days, twelve out of twenty surviving mice showed one to six months after the arrest of the treatment single or multiple tumors of the lung, while no pulmonary neoplasms were found in twenty-two control mice of the same stock and age. In a second experiment on forty mice similarly treated Murphy and Sturm found a lung tumor incidence of 78.3 per cent among 23 surviving mice (being 9 to 10 months old), while control animals, which were even one to six months older than the test animals, did not show any tumors. Similar observations were made by Schabad after painting the skin of mice with tar (control series with normal incidence of spontaneous pulmonary tumors: 3.5 per cent; experimental tarred group: 20.56 per cent). There was also an increase in the primary neoplastic multiplicity of the lung tumors in the tarred series (63.6 per cent in comparison to that present in the control series 37.5 per cent), thereby corroborating observations made by Lynch. The results obtained by Puccinelli on mice and rats following the repeated application of tar to alternative sites of the skin in order to prevent the development of skin tumors, confirmed those of the previously mentioned investigators. Rats painted cutaneously by Möller, at first three times weekly and later twice weekly, did not develop tumors of the skin, while hyperkeratoses, hypertrichoses and epithelial cysts were formed. Six of the 24 rats surviving the treatment for 56 to 435 days, however, showed malignant cornifying bronchiogenic squamous cell proliferations. These cancers were found in rats painted for more than 300 days. The first evidence of a carcinomatous transformation of the bronchial mucosa was represented by the development of folds and papillary excrescences, sometimes associated with metaplasia, in the bronchial mucosa. The effect of cutaneous tarring upon the incidence of pulmonary tumors is illustrated by the following compilation of Bonne:

Age in Months	Tarred Mice		Non-Tarred Mice	
	Number	Lung Tumors	Number	Lung Tumors
5-6	11	0	5	0
7-12	216	14	54	0
13-18	63	19	66	7
19-23	10	7	21	5