

INHALATION INDUCTION OF EXPERIMENTAL LUNG CANCER

- A CRITICAL REVIEW -

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The lung appears to be an organ of average sensitivity to the action of carcinogens. It is not surprising that the development of a number of techniques by which pulmonary tissues can be exposed to significant levels of carcinogenic materials, has resulted in the induction of pulmonary neoplasms. These techniques have proved particularly valuable in the study of the morphogenesis of lung cancer. They have made possible the examination of materials suspected of being human lung carcinogens and have yielded insights into the mechanism of action of carcinogens in the lung. Nevertheless, they represent highly artificial situations. The lung is normally exposed to noxious agents by inhalation. Determinants of inhalation dose involve an additional set of mechanisms to those involved in instillation or implantation techniques. These are comprised of the factors that determine respirability, sites of deposition, rates of mechanical and metabolic clearance, focal retention, etc.

Induction of experimental lung cancer by inhalation has been achieved with a number of agents or combinations of agents. These include ionizing radiation, hydrocarbons and viruses, hydrocarbons and irritants, and inorganic materials such as asbestos and compounds of nickel and beryllium. These experiments are to be reviewed in a pth.

A review of successful attempts at inducing lung cancer reveals that a variety of tumors have been produced. Some are quite comparable to human tumors; others differ considerably from human tumors. The differences must be carefully interpreted if the relevance of the experiment to human experience is to be evaluated.

Negative inhalation experiments, particularly with agents and with species that have yielded tumors with other technique, must be examined for dosage deficiency and for the absence of the probable necessary action of multiple factors.

Careful study of inhalation induced tumors leads to the strong suggestion that a single agent or a combination of agents must be capable of superimposing specific carcinogenic action and non-specific regenerative, proliferative, and metastatic alterations. This hypothesis will be examined in the light of the effects produced by each of the successful exposures.

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