Induction of Aryl Hydrocarbon Hydroxylase in the Lungs of Mice in Response to Cigarette Smoke

The mechanism by which cigarette smoke enhances pulmonary tumorogenesis has recently been the subject of intensive research. A number of machines have been developed which duplicate the human smoking habit with experimental animals[1–3] and have been employed successfully in long-term studies of the effect of smoke inhalation on the respiratory tract. We now report on the induction of an enzyme which metabolizes polycyclic aromatic hydrocarbons (aryl hydrocarbon hydroxylase) in the respiratory tract of mice exposed to cigarette smoke for up to 40 weeks. The enzyme has previously been shown to be elevated in the placenta of smoking human mothers[4].

Materials and methods. C57 Black inbred mice were exposed daily to the smoke of 30 cigarettes over a period of 8 min in the Hamburg II small animal smoking machine (Heinrich Borgwaldt, West Germany). Aryl hydrocarbon hydroxylase activity in homogenates of lung, liver, spleen and intenstine was determined by the method of NERBERT and GELBOIN[5]. Cigarettes were supplied by the Australian Tobacco Research Foundation.

Results and discussion. The activity of aryl hydrocarbon hydroxylase in the lungs and livers of control mice and those exposed for varying periods to tobacco smoke are shown in the Figure. Enzyme activity in the lung show as rapid increase within 24 h of the first exposure, followed by a slower decline. From the 5th week of exposure onwards, the activity remained 3–4 times that seen in control lungs. In the liver, the activity of aryl hydrocarbon hydroxylase increased at a much slower rate than in the lungs. After 40 weeks exposure, the activity in the livers from smoked animals was increased by approximately 50% over that in controls. The activity in both organs from smoked animals showed much greater inter-animal variation than was seen in the control group. The activity of aryl hydrocarbon hydroxylase in the spleen and intestine showed no consistent alteration following exposure to cigarette smoke. Previous work[6] has shown that the exposure of rats to cigarette smoke for 5 h on 3 consecutive days produces a 12-fold increase in lung aryl hydrocarbon hydroxylase, with smaller increases in other organs. The study was not continued after this period. The data presented here indicated that in the mouse the very high levels of enzyme activity observed in the lung after short-term exposure to tobacco smoke do not persist, but instead fall back to a relatively constant level (3–4 times controls) within a short time. A recent report[7] has also shown that the activity of aryl hydrocarbon hydroxylase in the lungs of hamsters following the repeated intratracheal administration of tobacco extract was significantly lower than that produced by a single dose.

Aryl hydrocarbon hydroxylase may play a dual role in tumorogenesis in the smoker's lung a) protection from chemical carcinogenesis by detoxification of tobacco tars, b) promotion of carcinogenesis by the production of highly carcinogenic intermediates during detoxification. The elucidation of its true role in this situation awaits further investigation.

Résumé. L'absorption, par inhalation, de la fumée de cigarette, produit une accélération rapide de l'activité de l'aryl hydrocarbure hydroxylase dans les poumons de la souris. Après une exposition de 4 semaines, ces niveaux sont 3–4 fois plus élevés que ceux du contrôle. Dans le foie, ces actions se manifestent d'une facon beaucoup plus faible et lente.

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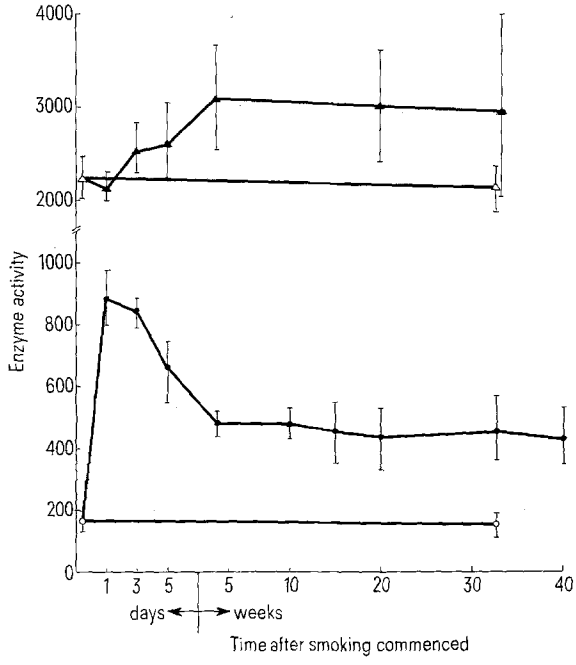

The effect of cigarette smoke inhalation on the activity of aryl hydrocarbon hydroxylase in the lungs and livers of mice. Enzyme activity is expressed as ng 8-hydroxy-benzpyrene formed/g wet wt. lung/h. Each point represents the mean ± S.E. of at least 6 separate determinations. Lung: ○, control; ●, smoked; Liver: △, control; ▲, smoked.

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