lead levels and criminality does not appear in our cases, at least for the group of prisoners studied here.

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Release of histamine from lung tissue *in vitro* by dimethylhydantoin-formaldehyde resin and polyvinylpyrrolidone

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A small but definite proportion of hairdressers suffer from symptoms such as dry throat, cough, and mild breathlessness usually towards the end of a busy day (C. S. Darke, personal communication, 1965). The symp-

toms appear to be associated with the use of aerosol hair lacquers. It is unlikely that concentrations of the lacquer are high enough to allow sufficient deposition of resin in the respiratory tract to produce mechanical

obstruction leading to diffusional problems. Two possible hypotheses, however, suggest themselves to account for these effects. First, that the symptoms are due to upper respiratory tract irritation thus causing the dry cough and throat irritation. Secondly, that the symptoms are the result of a localized bronchial or bronchiolar constriction caused by a pharmacologically active agent in the inhaled lacquers acting by direct or indirect mechanisms.

As the decrease in maximum expiratory flow rate observed in human volunteers inhaling hair sprays is prevented by an antihistamine drug (Zuskin and Bouhuys, 1974), it was decided to examine the second hypothesis by investigating the histamine-releasing activity of two non-volatile film-forming agents, dimethylhydantoin-formaldehyde resin (DMHF) and polyvinylpyrrolidone (PVP, Draize *et al.*, 1959). Although these compounds are no longer commonly employed in hair sprays, they were very popular at the time the observations on hairdressers were made by Darke.

Material and methods

The synthetic histamine releaser, compound 48/80 was purchased from Burroughs Wellcome, England. Samples of DMHF and PVP were obtained from Dr C. S. Darke (Northern General Hospital, Sheffield). For the investigation DMHF and PVP were dissolved in Tyrode's solution

Guinea-pigs of the Hartley strain and Rhesus monkeys, both of either sex, were killed by stunning and exsanguination. The lungs were removed immediately into Tyrode's solution at a temperature of 4°C. Specimens of human lung tissue that appeared macroscopically normal were obtained from surgical lung resections in patients with

bronchial carcinoma. These were also kept in Tyrode's solution at a temperature of 4°C until used for incubation. The animal lung was prepared for incubation without delay, but in the case of the human lung, there was an interval of approximately 2 hours between removal of the specimen and the beginning of incubation.

The histamine-releasing activity of the film-forming compounds was determined according to the procedure of Nicholls, Nicholls, and Bouhuys (1966). Chopped lung (1 g) was incubated for 25 minutes at 37°C in Tyrode's solution (3 ml) containing these agents or compound 48/80. At the end of incubation histamine released into the medium was determined spectrophotofluorimetrically (Shore, Burkhalter, and Cohn, 1959). None of the substances included in the incubation interfered with the assay of histamine. For each lung specimen used, the histamine content was also determined by this method.

Results and discussion

The synthetic histamine releaser compound 48/80 produced a substantial release of histamine from the lung of all the species (Table). DMHF also released histamine from all three species (Table). Although only a limited number of experiments was carried out, it was evident that this effect was dose-related. PVP was a less effective histamine releaser than DMHF on lung tissue; a concentration of 5 mg/ml did not release histamine from guinea-pig lung and was effective in only one out of three specimens of human lung.

Although DMHF is a more potent histamine liberator than PVP, it was less potent than compound 48/80 in all three species studied. However,

TABLE
HISTAMINE RELEASE FROM LUNG TISSUE *IN VITRO*

Material	Concentration* (mg/ml)	Histamine release (%)†								
		Guinea-pig		Monkey				Human		
		1	2	1	2	3	4	1	2	3
DMHF§ ..	5	2.4	—	—	—	—	5.4	7.9	8.8	—
	3	—	—	—	4.1	2.7	—	—	—	8.7
	1	—	0.9	2.24	—	—	0.9	1.8	2.9	4.1
PVP§	5	0	0	—	1.2	—	1.5	0	0	2.0
	1	—	—	0.56	—	0.11	—	—	—	—
Compound 48/80	1	4.2	7.9	4.5	4.3	2.5	7.6	6.0	9.2	14.0
Histamine content (µg/g of lung)		30.0	17.0	51.0	62.1	39.5	24.5	17.0	29.4	23.1

For each species, chopped lung (1 g) was incubated in a final volume of 3 ml Tyrode's solution for 25 min at 37°C. Histamine liberated into the incubation medium was assayed fluorimetrically. Blank spaces indicate that no determination was made

*Final concentration in incubating medium

†Histamine released expressed as percentage of the total histamine in the lung sample (1 g); results are the means of duplicate determinations from one lung sample in each experiment

§DMHF = dimethylhydantoin-formaldehyde resin; PVP = polyvinylpyrrolidone

these findings demonstrate the potential of these agents, and thus of hair lacquer containing them, to produce changes in lung function by an indirectly acting mechanism. It is interesting to note that the activity of these hair spray constituents is apparently not species-dependent in contrast to the histamine-releasing activity of cotton dust (Evans and Nicholls, 1974). Inhalation of histamine releasers by human subjects has been shown to produce changes in pulmonary function related, in part, to bronchoconstriction. Thus inhalation of cotton dust causes a rise of airway resistance and a decrease in the forced expiratory volume during 1 s (Bouhuys and Nicholls, 1966) and inhalation of 48/80 by asthmatic subjects gives rise to mild bronchoconstriction (Vukobratović, 1966). It is possible, therefore, that the histamine-releasing activity of DMHF and PVP is sufficient to cause changes in pulmonary function when these compounds are inhaled as part of hair lacquer aerosols. The release of histamine could account for the slow disappearance of the airway constrictor effect of inhaled hair sprays in man (Zuskin and Bouhuys, 1974) and DMHF would appear to be the more likely to precipitate such functional changes. Further studies are needed to establish the importance of the histamine-releasing activity of these hair spray constituents and if the components of the currently widely used sprays share this activity.

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