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Current Perspectives on Aerosol Toxicity

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Synopsis—The TOXICITY of cosmetic, household, or personal product AEROSOLS is primarily the result of either deliberate abuse or allergic reactions to one or more of the ingredients. Hair sprays, antiperspirants, deodorants, and feminine hygiene sprays, among others, have been reported to produce toxic reactions in some users. A review of the published experimental and clinical data does not substantiate the contention that, when used as directed, they are hazardous. It is true, for instance, that the fluorocarbon PROPELLANTS, in experimental situations, can sensitize the myocardium to catecholamine-induced arrhythmias and thus produce a situation detrimental to the user, but not in the amounts to which the consumer is ordinarily exposed. The differences between toxicity, the inherent ability to produce undesirable alterations in biological tissue, and HAZARD, the likelihood that toxicity will occur, may explain the case for aerosol products. The potential for toxicity of properly packaged cosmetic, household, and personal product aerosols is present; the hazard is small under conditions of normal use.

Introduction

As with any other type of packaging or delivery system for cosmetics, drugs, or household products, aerosols have characteristics that are uniquely their own. In general, they are safe, convenient, easy to manipulate, and, for the most part, economical to use. In addition to these advantages, however, this particular method of packaging and delivery is somewhat harder to control once the contents have been liberated from the container. Foams, paints, and cosmetic powders are easily seen and handled; but many drug and liquid cosmetic formulations, such as deodorants and hair sprays, are hard to see once released and often the respect that other aerosol products are given by the consumer is not accorded these items.

Individuals often have a difficult time relating to a substance that, because of its small particle size, is difficult to see; thus, the potential hazards, including warning labels, are often ignored. This can be illustrated in the case of a

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hypothetical man who sprays an entire can of an aerosol insecticide into a small room and then, without opening any windows, goes to sleep in the room; rising later he finds manifestations of a contact allergy. Yet he probably would not have treated a can of gasoline that way, despite the relatively innocuous nature of the chemicals in the can of gasoline.

Types of Aerosol Toxicity

Toxic reactions to aerosols have been reported in the literature for several categories of products: cosmetics, such as hair sprays (1–3) and deodorants (1, 4, 5); perfumes (6); personal products such as feminine hygiene deodorant sprays (7, 8); and household products, such as spray paints (9), insecticides (10), aerosolized vegetable oils (11), and room deodorizers (5, 9). Medicinal aerosols have also been reported to produce some of the same toxic effects, but they will not be discussed in this paper. The types of toxicity reported can be broken down into two main categories, those due to the propellants and those due to the active or inert ingredients in the formulations.

Propellant toxicity can result either from the refrigerant properties of the propellants (freezing of tissues or local anesthesia) or from the chemical nature of the propellants and the biological responses they elicit (12).

Many of the reported cases of aerosol toxicity are likely due to toxic reactions to the active or inert ingredients in the formulation, rather than to the propellants. Allergic reactions are among the more common forms of toxic responses to cosmetic aerosols. It has been estimated that approximately 10% of the population as a whole has some type of allergic disease (6) or has suffered an allergic response to some foreign substance during their lifetime; and it is a well-accepted medical fact that people who are allergic to one substance, or have an allergic disease such as asthma or hay fever, are prone to be allergic to other products as well—especially upon repeated exposure.

The incidence of persons allergic to cosmetic products, on the other hand, is probably between 2 and 3%, when verified by a patch test (6). In the data compiled by one cosmetic company who markets a broad range of products, only 448 reactions were reported in 114 million units sold (6). In an earlier reference, the incidence of allergic skin reactions to lanolin was 1.14% in an unscreened sample of users. (Lanolin is widely used in cosmetic formulations for its unique emollient and emulsification properties.) On the other hand, when a controlled sample with no history of allergic skin disease was tested, no allergic reactions to lanolin were reported (13). Recent refinements and improvements in the purification of the lanolin used in cosmetic products have eliminated lanolin allergy as a significant problem. Reactions to perfume oils, a ubiquitous ingredient in cosmetic aerosol products, are almost entirely due to an allergic or hypersensitive response, rather than due to primary irritation (6). There are more than 5000 odiferous substances in general use

today as perfumes. Most cosmetics contain approximately 0.5% perfume oil; colognes about 4%; and perfumes up to 20%. Each of these perfume substances may contain up to 50 different chemical ingredients, so the task of identifying the cause of an allergic response is, at best, a difficult one (6).

Photosensitization is a type of allergic response and has been reported for a number of essential oils, such as neroli, pettigrain, cedarwood, lavender, and bergamot (6, 14). In addition, dermatitis has been reported following the use of oil of bergamot. Chlorophyll, traces of copper, and psoralens, all found in oil of bergamot, are suspected of being the cause of the allergies. Aging of the oil reduces its sensitizing propensity (6). Even once the allergy-causing ingredient has been found, the problem of cross-sensitivity may arise. Persons allergic to oil of citronella, for example, are also often allergic to lemon oil (15).

A partial solution to the problem of allergy to perfume oils may have been found with the marketing, by a number of companies, of a group of chemically-reproducible perfume substances which have been patch tested to prove a low incidence of allergic responses (16). Hypoallergenic cosmetics may be another solution. These are a group of cosmetic products, marketed by a few companies, which are specifically for the use of individuals hypersensitive to many cosmetics. The raw materials for these products are selected on the basis of a reported low incidence of allergic responses (6).

The pyrethrins, found in many insecticide aerosols, may also cause a variety of allergic manifestations in susceptible individuals; erythema, rash, loss of feeling in exposed parts of the skin, and diminished vision have all been reported (10).

Another type of toxicity, though less important, that may result from the active or inert ingredients in many cosmetic aerosols, is primary irritation of the skin (17). This is not an allergic response but rather is a result of the caustic nature of certain ingredients in the formulation. Calcium thioglycolate is a primary irritant found in many aerosol foam depilitories (6). Antiperspirants often contain salts of zinc, zirconium, or aluminum which can cause primary irritation (6). Ocular irritation from dandruff shampoos has been reported (18, 19), probably as a result of certain zinc salts.

Effect of Aerosols on Anatomy and Physiology of the Skin and Respiratory System

The underlying cause of many of the toxic reactions resulting from the use of cosmetic and household aerosols seems to be the result of an alteration in the basic anatomy and/or physiology of the skin and respiratory systems. The type of alteration produced depends, to a degree, on the product in question and the area of the body it comes in contact with. Alterations in skin pH are thought to be the basis for the primary irritation produced by the depilitories in foam aerosols. Preparations containing calcium thioglycolate, for example,

usually have a pH of about 12, while the normal pH of the skin is between 4 and 6 (6). The metallic salts of zinc, aluminum, and zirconium used in aerosol antiperspirants may cause superficial skin infections because they produce narrowing of the ducts of sweat glands which may give rise to apocrine sweat gland occlusion and a true hydradentitis (6, 18).

The refrigerant action of propellants in personal or household aerosols can produce cooling or freezing of the sensitive corneal (5) or vaginal (7) tissues if they are used improperly. Many facets of skin metabolism, including cellular respiration, can be altered by some cosmetic aerosols (20). The propellants have been reported to sensitize the myocardium to arrhythmias caused by anoxia and catecholamines (21), although there is no definitive evidence that this type of cardiac toxicity can result from normal use of any aerosol product (22, 23). The interruption of the normal bacterial flora of several body orifices was formerly a potential problem with vaginal deodorant sprays containing antibacterial agents (24). It is known that once the normal flora of the vagina or rectum is altered (as with tetracycline therapy), an abnormal overgrowth of yeasts and fungi (usual symbionts in these areas) may cause pruritis (25) and/or other bacterial infections. Since most vaginal sprays no longer contain antibacterial chemicals, this problem has essentially ceased to exist. Keratitis, due to a foreign body reaction of the skin, has been reported in response to the presence of materials from several household aerosols that have, in effect, been driven into the skin by the force of the spray (5). An increased formation of pulmonary edema fluid and lipid pneumonia has been reported following a foreign body response to the inhalation of oil droplets from an aerosol containing a vegetable oil (11). Edema fluid is an ideal medium for the growth of pathogens, resulting in aspiration pneumonia. A slight reduction in specific airway conductance, posing no clinical danger, has been reported following the inhalation of several bronchodilator aerosols. The bronchoconstriction reported, which was less than that caused by smoking a cigarette, was attributed to the aerosol propellant and/or the surfactant chemicals (sorbitol trioleate and soya lecithin) contained in the two bronchodilator aerosols evaluated (26).

Propellant Toxicity and Abuse

The controversy regarding the toxicity of aerosol products, in general, and the propellant chemicals they contain, in particular, began several years ago with the publication in the lay press of several deaths due to "sniffing," especially by teen-agers, of the vapors from a wide variety of aerosol products (27). The practice involved the deliberate, deep inhalation of the concentrated vapors, usually from a balloon or paper bag (28).

These reports of aerosol abuse brought the toxic potential of the various propellants to the attention of the aerosol industry. The toxicity of the propellants can be divided into three major categories: toxicity due to the refrig-

erant action of the propellants (12), which may cause reflex airway obstruction, especially of the larynx, and tissue damage to the delicate mucous membranes of the vulva (7) and eye (29); decomposition into phosgene when the vapors come into contact with an open flame (30); and finally, systemic toxicity, chiefly referrable to the cardiovascular system (21, 22). It is this latter type of toxicity which has been accorded so much unwarranted publicity by the press.

The problem of teen-age abuse of aerosols is one over which the aerosol industry has little control, other than to update the warnings printed on the aerosol cans. The Inter-Industry Committee on Aerosol Use has established the Aerosol Education Bureau (31) to administer a safety campaign which is designed to warn teen-agers of the potential lethal consequences of abusing aerosolized products.

Soon after the controversy regarding the deaths from aerosol "sniffing" began, Taylor and Harris (21) reported that the exposure of mice to several propellants, followed by asphyxia in a plastic bag, produced sensitization of the myocardium to hypoxia, resulting in arrhythmias such as sinus bradycardia, atrioventricular block, and T wave depression. They used these experiments to postulate that the sudden deaths that followed aerosol abuse by teen-agers could be the result of a toxic action of the propellants used in almost all aerosol packages, as well as to provide a basis for warning against the possible hazards to frequent users of a variety of aerosol products. It is well known, and has been for some time, that high concentrations of many propellants frequently used by aerosol manufacturers can produce a wide variety of toxic effects. Ataxia, tremors, liver, and kidney damage are among some of the more common findings (32, 33). But these experimental results in animals, especially at the high concentrations studied, bear little or no relationship to the lower concentrations to which the consumer of aerosol products is exposed (28). Also, there is lack of general agreement as to the accuracy of the data on aerosol toxicity when it is extrapolated from animal studies to humans (22, 34).

Following several reports by Taylor and Harris on the cardiac toxicity of aerosol propellants, other investigators attempted to reproduce their findings, with little success. McClure, in 1972, failed to produce significant changes in the heart rate or electrocardiogram of anesthetized mice after the administration of several propellants in aerosol form, followed by asphyxia (35). In general, he found that the cardiovascular effects produced by propellant exposure were similar to the cardiovascular effects of asphyxia alone. McClure was also unable to confirm similar findings reported by Taylor and Harris in dogs (21). Egle *et al.* (23) also attempted to repeat the results of Taylor and Harris. They exposed mice to several propellants, either alone or with nitrogen-induced asphyxia, and reported no augmentation of the asphyxia-induced bradycardia or atrioventricular block by the several fluorocarbon propellants

studied. In all, four groups of investigators have failed to repeat the findings reported by Taylor and Harris (22).

On the other hand, many investigators have reported the safety of the fluorocarbon propellants in concentrations generally produced following normal use. McClure (35) reported no effect on heart rate, blood pressure, and electrocardiogram in dogs following the intratracheal administration of an epinephrine aerosol. Azar *et al.* (36) were unable to produce arrhythmias in anoxic and hypercapnic dogs following repeated exposure to several commercial aerosols. Others were unable to produce significant electrocardiographic changes in several patients, ill with a variety of bronchopulmonary disorders, following the repeated inhalation of Propellant 11 and Propellant 12 (27).

There is little question that the various propellants can, when administered in high concentrations over a prolonged exposure period, produce cardiac arrhythmias. Flowers and Horan (37) exposed anesthetized dogs to several commercial aerosols in high concentrations; their data showed bradycardia and ventricular arrhythmias in many of the dogs thus treated. Reinhardt *et al.*, in 1971, reported that the inhalation of high concentrations did, in fact, sensitize dogs to catecholamine-induced cardiac arrhythmias (28). In addition, the propellants also produced questionable sensitization to endogenously-released catecholamines resulting from audiogenic stimuli (28). The conditions described in these experiments, as well as many others, do postulate a mechanism for the sudden deaths resulting from aerosol abuse, but in no way pertain to the safety of the thousands of commercially available aerosol products currently in use today, assuming reasonable use of such products.

Toxicity of Cosmetic and Personal Product Aerosols

Antiperspirants and Deodorants

These have been reported to cause granulomas of the axilla (38), which are probably linked to a hypersensitivity to the zirconium, aluminum, or other heavy metal salts used in these preparations (12). While the few reported cases to date have resulted from using either lotion or stick deodorants, similar reactions may possibly occur in allergic individuals using aerosol deodorants or antiperspirants containing these chemicals.

Other toxic reactions reported to be associated with the use of antiperspirant/deodorant aerosols include: pulmonary granulomatosis (1), epithelial keratinization of the eye (9), and clogging of the sweat glands with subsequent infection (18). There have not been enough reported cases in any of these incidents to establish a definite cause-effect relationship.

Aerosol deodorants have been reported to produce "flashback" reactions in users of hallucinogenic drugs, such as mescaline and LSD. Two such

cases have been reported in teen-agers (4); and either Propellant 12 or a mixture of Propellant 11 and Propellant 12 has been implicated, although not conclusively.

Feminine Hygiene Deodorant Sprays

Such products have been reported to be no better than frequent bathing to keep the vaginal area free from unpleasant odors (24, 39). Despite this, they have caught on in popularity and are sold widely, probably because many women believe they need them, despite the opinion of some gynecologists to the contrary (40). There are certain formulation differences between vaginal and underarm deodorants, i.e., vaginal deodorants commonly have less alcohol and less perfume—in order to reduce the possibility of irritating the tender vaginal mucous membranes (41). Irritation is more likely to occur with vaginal than underarm deodorants because the user is more likely to spray the can longer, in that the spray is quite dry and there is little apparent residue. Also, the delivery rates of vaginal deodorants are likely to be higher than underarm deodorants because they are often packaged under substantially higher pressure. Propellant 12 is often used to reduce chilling (41).

The Food and Drug Administration has reported that reactions to the vaginal spray deodorants are usually due to one or more of the following: injuries resulting from the high pressure of the propellants; primary irritation from the alcohol, antibacterial chemical, or perfume; the rapid chilling effects of the propellants on the delicate mucous membranes or skin in this area; allergies to the antibacterial chemicals or perfumes (40). Women users have reported irritation of the skin or mucous membranes, vulvitis, weeping dermatitis, chemical burns, and various hypersensitivity reactions, such as pruritis, burning, and edema (7, 40). Some of the special anatomical features of the vaginal area that make it more susceptible to deodorant sprays include the apocrine sweat glands, the thin horny stratum, and the special bacterial flora of the vaginal mucous membranes (24).

Hair Sprays

Hair sprays have been implicated, in a cause-effect relationship, with the development of pulmonary granulomatosis (3) and blood dyscrasias (2) in chronic users of such products, possibly due to a hypersensitivity reaction. The resinous ingredients contained in these products have been reported to be the noxious agents. In several reported cases, radiographic examination of the chest showed infiltration of the lung field in users of hair sprays which cleared when the usage of these products was discontinued (3). However, several attempts to duplicate these human findings in rats (42), guinea pigs (43), and dogs (44), exposed to commercial hair spray preparations for as long as two years, failed to demonstrate any pulmonary pathology that could be attributed

to exposure to these products. The PAS-staining biopsy material, reported by Bergmann *et al.* (3) to indicate the presence of hair spray resins, was also found in the control animals (44). Furthermore, hematologic studies of dogs exposed to commercial hair sprays for up to 2 years (44) failed to demonstrate the blood dyscrasias (aplastic anemia, thrombocytopenia, and leukopenia) reported as being compiled from the AMA Department of Drugs Registry on Adverse Drug Reactions by DeNosaquo (2).

Further evidence of the safety of commercial hair sprays has been reported in two separate studies of hairdressers in Great Britain. In the first, John (45) studied 146 hairdressers, both men and women, who used hair sprays for between 3 and 5 years. Radiographic examination of these hairdressers, from 14 different salons, failed to demonstrate any pulmonary abnormalities. In a similar study by McLaughlin *et al.* (46), an X-ray survey of 505 hairdressers in Great Britain was reported. The hair sprays included both shellac-based sprays and sprays containing polyvinylpyrrolidone (PVP). In all groups a significant number of hairdressers had used the sprays for more than 6 years. No abnormal X-ray appearances, suggesting the presence of pulmonary granulomatosis (thesaurosis), were reported, despite the fact that the majority of particles in both types of hair sprays had a diameter of less than 1 μ and were thus capable of being inhaled. In a study of the particle sizes of hair sprays manufactured in the United States, at least 50% of the hair spray particles had a diameter of 35 μ or greater (47), which is larger than the size that is capable of penetrating the lungs to a significant extent. Further studies by Larson (47) also attest to the safety of commercial hair sprays. In this study, no differences in midexpiratory flow rate, measured spirometrically, were found between users of hair sprays and nonusers, in a controlled population of female college students. While the controversy over the safety of hair sprays continues, the bulk of scientific evidence at present indicates that earlier concerns over their safety is unfounded.

Toxicity of Household Aerosols

Because of the diverse nature of the products in this category, and the large number of users in all age groups, the toxicity of these products is of major interest to both the consumer and the aerosol industry. Other than the toxicity of the ingredients in a specific preparation, some of the factors contributing to the toxicity of the household aerosols include the pattern produced by aerosol spray (5) and the cooling action of the propellants (12). If the spray pattern of a product is not well controlled, particles intended for application in one place may well penetrate into the eye or impact on the skin. The impaction of particles from these products, because of the relatively high pressure exerted at release, may cause aerosol particles, that would otherwise be harmless, to penetrate the surface of the skin or the cornea of the eye, thus

making removal of the material difficult and increasing the likelihood of foreign body tissue reactions (5, 9). Spray keratitis, such as that just described, has been reported for hair sprays, insecticides, paint sprays, and deodorants (5, 9). Furthermore, the cooling and drying action of the propellants and/or solvents in a product may aid in the penetration of aerosol particles into the eye (5).

Predicting the toxicity of household aerosols in humans, as a result of screening studies in animals, is not easily accomplished. The anatomy and physiology of the respiratory structures in lower animals is different from man (34); also, diseased humans will often respond differently to a product than will healthy laboratory species. Another problem is the design of a suitable exposure chamber; assuming that the environment can contribute to the potential hazards of a household aerosol product, there is little equivalency between the exposure chambers commonly used in the testing laboratories to evaluate the potential toxicity of aerosol products and the actual rooms that humans live in when using such products (34). In general, though, despite the millions of units of household aerosol products consumed each year in this country, few toxic reactions are reported and, of those that are reported, approximately half are probably due to consumer error in following the instructions for use printed on the package.

Toxicity and Hypersensitivity

Toxicity is a function of a chemical compound and its reaction with biological tissues and can usually, but not always, be predicted from animal studies. It is the responsibility of the manufacturer of cosmetic and household aerosols to market products with a low order of toxicity; in general, this responsibility has been adequately accomplished. Hypersensitivity, or allergic, responses only occur in a small percentage of users of aerosolized products and, in general, cannot be adequately predicted from animal investigation. It is known, however, that persons with certain allergic diseases and/or a hereditary tendency towards respiratory and skin diseases may be more likely to elicit allergic reactions to many types of products commonly used in the home, including aerosols. There is little a manufacturer can do to reduce such adverse reactions to commercial aerosols, except to use ingredients which have been shown, through years of use or extensive laboratory and clinical testing, to produce a low incidence of hypersensitivity reactions. Other suggestions to reduce the incidence of aerosol-related allergy would be: pooling of reported allergic responses to products and ingredients; clinical testing on a wider scale to determine ingredients causing allergic responses; and limited marketing of new cosmetic or household aerosols, containing new ingredients, until the allergy profile is well established.

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References

(1) Nevins, M. A., Stechel, G. H., Fishman, S. I., Schwartz, C., and Allen, A. C., Pulmonary granulomatosis. Two cases associated with inhalation of cosmetic aerosols, *J. Amer. Med. Ass.*, **193**, 86–91 (1965).
(2) DeNosaquo, N., Hair sprays and blood dysrasias, Ibid., **188**, 197 (1964).
(3) Bergmann, M., Flance, I. J., and Blumenthal, H. T., Thesaurosis following inhalation of hair spray. A clinical and experimental study, *N. Engl. J. Med.*, **258**, 471–6 (1958).
(4) Kramer, R. A., and Pierpaoli, P., Hallucinogenic effect of propellant components of deodorant sprays, *Pediatrics*, **48**, 322–3 (1971).
(5) MacLean, A. L., A common epithelial keratitis from noncorrosive household sprays, *Trans. Amer. Acad. Ophthalmol. Otolaryngol.*, **71**, 330–40 (1967).
(6) Masters, E. J., Allergies to cosmetic products, *N.Y. State J. Med.*, **60**, 1934–40 (1960).
(7) Gowdy, J. M., Feminine deodorant sprays, *N. Engl. J. Med.*, **287**, 203 (1972).
(8) Kaye. B. M., Hazards of hygenic deodorant sprays for women, *J. Amer. Med. Ass.*, **212**, 2121 (1970).
(9) MacLean, A. L., Aerosol keratitis, a common epithelial foreign body reaction to household chemical sprays, *Amer. J. Ophthalmol.*, **63**, 1709–19 (1967).
(10) Zucker, A., Investigation of purified pyrethrum extracts, *Ann. Allergy*, **23**, 335-39 (1965).
(11) Teitelbaum, D. T., Vegetable oil aerosol spray intoxication, *Rocky Mt. Med. J.*, **66**, 62–3 (1969).
(12) Bernstein, I. L., Medical hazards of aerosols, *Postgrad. Med.*, **52**, 62–77 (1972).
(13) Sulzberger, M. B., Warshaw, T., and Herrmann, F., Studies of skin hypersensitivity to lanolin, *J. Invest. Dermatol.*, **20**, 33 (1953).
(14) Gloxhuber, C., Phototoxicity testing of cosmetic materials, *J. Soc. Cosmet. Chem.*, **21**, 825–33 (1970).
(15) Keil, H., Contact dermatitis due to oil of citronella, *J. Invest. Dermatol.*, **8**, 327 (1947).
(16) Osbourn, R. A., Tusing, T. W., Coombs, F. P., and Moorish, E. P., Dermatologic standardization of perfumes, *N.Y. State J. Med.*, **57**, 1069 (1957).
(17) Birmingham, D. J., Clinical aspects of cutaneous irritation and sensitization, *Toxicol. Appl. Pharmacol.*, **7**, 54–9 (1965).
(18) Spoor, H. J., Skin reactions to cosmetics—classification and diagnosis, *N.Y. State J. Med.*, **60**, 1940–6 (1960).
(19) Rand, M. J., Toxicological considerations and safety testing of cosmetics and toiletries, *Amer. Cosmet. Perfum.*, **87**, 39–48 (1972).
(20) Jacobi, O., More on skin respiration and cosmetics, *Ibid.*, **85**, 25–30 (1970).
(21) Taylor, G. J., and Harris, W. S., Cardiac toxicity of aerosol propellants, *J. Amer. Med. Ass.*, **214**, 81–5 (1970).
(22) Editorial, Cardiac toxicity of aerosol propellants, *Ibid.*, **222**, 827–9 (1972).
(23) Egle, J. L., Putney, J. W., and Borzella, J. F., Cardiac rate and rhythm in mice affected by haloalkane propellants, *Ibid.*, **222**, 786–9 (1972).
(24) Tronnier, H., Cosmetic agents for general skin care and for feminine hygiene: dermatologists viewpoint, *Seifen-Oele-Fette-Wachse*, **96**, 794–7 (1970).
(25) *Physicians Desk Reference to Pharmaceutical Specialties and Biologicals*, Medical Economics, Inc., Oradell, N.J., 1972, pp. 1374-5.
(26) Sterling, G. M., and Batten, J. C., Effect of aerosol propellants and surfactants on airway resistance, *Thorax*, **24**, 228–31 (1969).
(27) Editorial, Cardiac toxicity of aerosol propellants, *J. Amer. Med. Ass.*, **214**, 136 (1970).
(28) Reinhardt, C. F., Azar, A., Maxfield, M. E., Smith, P. E., and Mullin, L. S., Cardiac arrhythmias and aerosol sniffing, *Arch. Environ. Health*, **22**, 265–79 (1971).
(29) Idson, B., Topical toxicity and testing, *J. Pharm. Sci.*, **57**, 1–11 (1968).
(30) Downing, R. C., and Madinabeitia, D., The toxicity of fluorinated hydrocarbon aerosol propellants, *Aerosol Age*, **5**, 25–8 (1960).
(31) Aerosol Education Bureau, Warning against deliberate misuse of aerosol products, *Amer. Cosmet. Perfum.*, **87**, 53–4 (1972).

(32) Clayton, J. W., The toxicity of fluorocarbons with special reference to chemical constitution, *Freon Tech. Bull.* S-22.
(33) Clayton, J. W., Fluorocarbon toxicity and biological action, *Fluorine Chem. Rev.*, **1**, 197–252 (1967).
(34) Wiberg, G. S., Evaluating the toxicology of household aerosols, presented at the Society of Toxicology, 11th Annual Meeting, March 1972.
(35) McClure, D. A., Failure of fluorocarbon propellants to alter the electrocardiogram of mice and dogs, *Toxicol. Appl. Pharmacol.*, **22**, 221–30 (1972).
(36) Azar, A., Zapp. J. A., Jr., Reinhardt, C. F., and Stopps, G. J., Cardiac toxicity of aerosol propellants, *J. Amer. Med. Ass.*, **215**, 1501–2 (1971).
(37) Flowers, N. C., and Horan, L. G., Nonanoxic aerosol arrhythmias, *Ibid.*, **219**, 33–7 (1972).
(38) Rubin, J., Slepyan, A. H., Weber, L. F., and Neuhauser, I., Granulomas of the axilla caused by deodorants, *Ibid.*, **162**, 953–5 (1956)
(39) Asby, N., Consumerists and feminists vs. the vaginal spray, *Product Management*, 30–4 (March 1973).
(40) Medical News, Feminine hygiene sprays controversial despite FDA action, *J. Amer. Med. Assoc.*, **219**, 449–52 (1972).
(41) Parisse, A. J., Recent changes in formula technology of aerosol personal products, *Amer. Cosmet. Perfum.*, **86**. 46–8 (1971).
(42) Brunner, M. J., Giovacchini, R. P., Wyatt, J. P., Dunlap, F. E., and Calandra, J. C., Pulmonary disease and hair-spray polymers: a disputed relationship, *J. Amer. Med. Assoc.*, **184**, 851–7 (1963).
(43) Calandra, J., and Kay, J. A., Inhalation of aerosol hair sprays, *Drug Cosmet. Ind.*, **84**, 174–7 (1959).
(44) Giovacchini, R. P., Becker, G. H., Brunner, M. J., and Dunlap, F. E., Pulmonary disease and hair-spray polymers: effects of long term exposure of dogs, *J. Amer. Med. Ass.*, **193**, 298–9 (1965).
(45) John, H. A., Thesaurosis: a survey of those at risk, *Med. Office*, **109**, 399 (1963).
(46) McLaughlin, A. I. G., Bidstrup, P. L., and Konstam, M., The effects of hair lacquer sprays on the lungs, *Food Cosmet. Toxicol.*, **1**, 171–88 (1963).
(47) Larson, R. K., A study of midexpiratory flow rates in users of hair spray, *Amer. Rev. Resp. Dis.*, **90**, 786–8 (1964).