

Review

Fragrance: emerging health and environmental concerns

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Received 17 September 2001

Revised 22 November 2001

Accepted 22 November 2001

ABSTRACT: Products containing scent are a part of daily life. The majority of cosmetics, toiletries, household and laundry products contain fragrance. In addition, there is exposure to fragrance from products that are used to scent the air, such as air fresheners and fragranced candles. In spite of this widespread use and exposure, there is little information available on the materials used in fragrance. Fragrance formulas are considered trade secrets and components that make up the fragrance portion of the product are not revealed on labels. Fragrance is increasingly cited as a trigger in health conditions such as asthma, allergies and migraine headaches. In addition, some fragrance materials have been found to accumulate in adipose tissue and are present in breast milk. Other materials are suspected of being hormone disruptors. The implications are not fully known, as there has been little evaluation of systemic effects. There are environmental concerns as well, as fragrances are volatile compounds, which add to both indoor and outdoor air pollution. Synthetic musk compounds are persistent in the environment and contaminate waterways and aquatic wildlife. At present there is little governmental regulation of fragrance. The fragrance industry has in place a system of self-regulation. However, the present system has failed to address many of the emerging concerns. Industry needs to responsibly address concerns and ensure that scented products are safe for users, those inadvertently exposed and the environment. It is essential that an industry that is, and wishes to continue to be, self-regulated should identify and address concerns in a forthright and responsible manner. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS: allergies; aroma chemicals; asthma; consumer products; cosmetics; dermatitis; fragrance; indoor air pollutants; migraines; olfaction; perfume/adverse effects; synthetic musk; volatile organic compounds; water pollutants

Introduction

Few would want to live in a world without the smell of flowers, the air after rain, or the subtle perfume worn by a loved one. Scents have the ability to alter mood and trigger powerful memories that are embedded in our minds. Research indicates that the sense of smell impacts not only psychological but physical health as well. During the past three decades the use of scented products has soared. Scented products are used by every segment of the population. The popularity of fragrance demonstrates that pleasant scents enrich our lives.

Fragrance is added to toiletries, cosmetics, household products, and a wide variety of other consumer products. In addition, the use of products to scent the environment, such as air fresheners and scented candles, is also very popular. There is exposure from flavours in foods and beverages as well.

It is because of this immense popularity of scented products that problems have surfaced. With increased usage and exposure there are increased anecdotal and clinical accounts of fragranced products causing, triggering and exacerbating health conditions. Further concerns relate to the bioaccumulation of fragrance chemicals in human tissue and the long-term impact. In addition, there are environmental concerns, as fragranced products add to both air and water pollution.

There are relatively few studies available in relationship to the widespread use and exposure to fragranced products. Many of the raw fragrance materials have little available health and safety data. Testing by the industry focuses on skin effects without taking into account respiratory, neurological or systemic effects. There are no industry-wide monitoring programs to gather data on adverse reactions. There is little regulation of monitoring of fragrance by regulatory agencies.

The industry contends that fragrances are safe and have a long history of use. Furthermore, there is in place a system of self-regulation for testing and determining the safety of fragrance materials. The industry contends that

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it follows existing regulations and laws; in relationship to use, negative effects are few and the products are safe.

Considering the tremendous use and exposure, there is limited information available related to health effects of fragrances. The information available is widely scattered throughout medical, scientific and industry literature and is rarely considered as a whole. Economic, political and social aspects further complicate the issues. A review of the literature and available information is needed to access and evaluate concerns. The primary focus of this review is fragrance use.

Regulation

While governmental agencies have some authority over fragrances, this authority is rarely invoked. In the USA, fragrances that are considered cosmetics come under the jurisdiction of the Food and Drug Administration (FDA). Health Canada is the agency responsible for cosmetic safety in Canada. In Europe, the European Commission (EC) is more actively monitoring fragrance.

US Regulation

Authority over fragrances is shared between the FDA and the Consumer Products Safety Commission (CPSC), with some regulatory aspects regarding air and water contamination involving the Environmental Protection Agency (EPA).

FDA

In the USA, fragrances and scented products that are considered cosmetics come under the jurisdiction of the FDA:

The FD&C Act [Food, Drugs and Cosmetics Act] defines cosmetics as articles intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structure or functions (FDA: Cosmetic Labeling Manual, October 1991; <http://vm.cfsan.fda.gov/~dms/cos-lab1.html>).

Cosmetics are not required to be safety tested before marketing; however, if the safety has not been substantiated, a warning label is required:

Sec. 740.10. (a) Each ingredient used in a cosmetic product and each finished cosmetic product shall be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not adequately substantiated prior to marketing is misbranded unless it contains the following conspicuous statement on the principal display panel: 'Warning—The safety of this product has not been determined' (FDA: Prohibited Ingredients and Related Safety Issues, 30 March 2000).

There have been no standards established by the FDA as to what constitutes 'substantiating safety'. Interpretation has been left up to manufacturers, although it is generally accepted that products should be safe for intended use and that any incidental exposures may be reasonably anticipated from that use.

The primary purposes of fragrance are to impart a scent to a product, mask the odour of other materials in the product or, in some cases, alter mood. In using these products there is exposure to the skin, the upper airways, olfactory pathways to the brain, and the lungs. All of these pathways are also entry points into the body, so there is systemic exposure as well.

Most available health and safety data on fragrance chemicals focus on skin effects. Respiratory, neurological and systemic data are not generally available. Although Material Safety Data Sheets on many fragrance chemicals clearly state they have not been thoroughly tested, virtually no fragranced product carries a warning label.

Other than a few materials prohibited, any material may be used as a fragrance ingredient. The individual components that make up the fragrance portion do not have to be listed on the label. Only the word 'fragrance' must appear. The fragrance portion of the product may contain over 100 different materials, some of which are only present in tiny amounts. Secrecy is often required to protect the formula. It also would be difficult to have such a large number of ingredients on the label and still meet the requirements of labelling laws, such as size of lettering.

Products that contain fragrance used to mask or cover up the odour of other materials in the product may not have fragrance listed in the ingredients. Masking fragrance is often used in 'unscented' and 'fragrance-free' products. Usually these masking materials are at low levels. However, they could be problematic to someone that already has an allergy to them—the very people that are most likely to seek out products without fragrance.

The FDA does have in place a program to report adverse reactions to cosmetics.¹ There has been an increase in the number of reported adverse reactions to fragrance.

EPA

The EPA has some developing interest in environmental aspects of fragrance production and use. Fragrances can impact indoor air quality and there is suggestive evidence that fragrance, as an indoor air pollutant, may play a role in exacerbating asthma.

There has also been some activity by the EPA in reducing the volatile organic compounds, or VOCs, in consumer products. Virtually all the materials used in fragrances are volatile or semi-volatile compounds.

These materials play a role in the development of smog. The EPA has taken little regulatory action.

Pesticide products must be registered with the EPA and all ingredients, including fragrance, must be revealed. However, the EPA cannot reveal the ingredients contained in the fragrance portion of pesticides or any other information deemed to be confidential business information.

In the fall of 1999, two products designed to kill or control dust mites were introduced in the marketplace. There were hundreds of complaints filed regarding adverse reactions to the products. There was a recall in January of 2000. It was determined by the EPA and the manufacturer that the 'fragrance' in the product was responsible for the adverse effects. The products were recalled from the marketplace.² The specific materials responsible for the adverse effects were not pinpointed. An opportunity to pinpoint fragrance materials that are problematic for asthmatics was missed.

High production volume (HPV) chemicals are those designated by the EPA as being produced or imported at levels of 1 million pounds or more. Of the approximately 3000 materials that meet this definition, 43% have no publicly available basic toxicity information and only 7% have a full set of basic toxicity information. Basic toxicity information covers acute toxicity, chronic toxicity, development and reproductive toxicity, mutagenicity, ecotoxicity and environmental fate.

The EPA HPV Chemical program asks industry to provide basic toxicity information for the chemicals on that list. There are over 50 materials on the EPA's HPV chemical list that the fragrance industry has signed up to provide information on.³

CPSC

The Consumer Product Safety Commission or CPSC is responsible for the safety of consumer products that are not considered cosmetics. There is no program in place within this agency through which the fragrances in products are evaluated for safety.

Canadian Regulation

Canadian law requires that labels warn of any avoidable hazards associated with the product that the consumer should be aware of:

Avoidable Hazard: Section 24 of the Cosmetic Regulations (Food and Drugs Act): (a) danger to the health of the user of a cosmetic that can be predicted from the composition of the cosmetic, the toxicology of the ingredients, and the site of intended application; (b) that can reasonably be anticipated during normal use; and that can be eliminated by specified limitations on the use of the cosmetic.

Materials used in fragrances are known to be skin sensitizers and are a frequent cause of skin allergies. Scented products also cause respiratory and airway irritation in those with asthma and other respiratory disorders. At present, fragranced products in Canada do not carry a warning of these known avoidable hazards and cosmetics are not required to list ingredients on the label.

European Commission

The (EU) is the regulatory body of an alliance of European nations. It formulates policies that are in the best interest of its member nations to facilitate trade, travel between member states, and protect shared resources.

Products do not have to reveal individual ingredients in the fragrance portion of the product. The word 'perfume' substitutes for a detailed listing of fragrance ingredients. Other than materials specifically prohibited from being used, any material may be used as a fragrance ingredient. A list of over 2000 fragrance chemicals is available, which does not reflect all of the materials in use by the industry. The list provides chemical name and identification numbers.⁴

In Europe, concerns related to fragranced products as skin sensitizers have been reviewed. The Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) has recommended that known skin sensitizers be listed on the label to allow consumers to avoid products that contain known allergens. This recommendation is in response to the continuing increase in dermal allergies to fragrance materials. It is likely that the EC will adopt in some form these recommendations.⁵

Since fragrances are an international commodity, it is likely that other countries, such as the USA and Canada, will follow the lead of Europe and eventually require similar labelling. In addition, concerns related to fragrances in the environment, such as the persistence in the environment of synthetic musk compounds, are being explored. Nitro-musks are used less in Europe because of these concerns. Two synthetic musks were withdrawn from use by the industry when potential health concerns were discovered.

The EU has also set criteria for labelling of dishwashing detergent and cleaners that are considered environmentally friendly. To qualify for the 'eco-label', among other criteria, the products must not contain nitro-musks or polycyclic musks that have been shown to persist in aquatic environments.⁶

Japanese Regulation of Fragrance

Japan has more restrictive regulation of fragrances. Uses of nitro-musk compounds were banned in the early

1980s because of environmental concerns. Some common sensitizers are prohibited from being used. These measures have reduced allergies to common fragrance sensitizers in Japan.

Self-regulation

By all accounts, the fragrance industry is primarily self-regulated. The Cosmetic, Toiletry, and Fragrance Association (CTFA) is the leading US trade association for the personal care products industry.⁷ The CTFA assesses the safety of cosmetics via various programs. It has in place a program to help dermatologists determine specific allergens, including fragrance, in a product. In real-use situations, the program is awkward and time consuming, making it difficult to use in clinical settings. It was reported at the 1999 CTFA Conference that the CTFA would conduct studies of their own regarding fragrance and asthma.⁸

The self-regulatory system for the fragrance industry is composed of the Research Institute for Fragrance Materials (RIFM) and the International Fragrance Association (IFRA).⁹ RIFM tests and compiles data on raw fragrance materials, not final formulations. Approximately 1200 materials have been evaluated by the RIFM. Monographs on these substances have been published in *Food and Chemical Toxicology* (formerly *Food and Cosmetic Toxicology*). It is the RIFM's policy that materials used by, or under control of, one company are not assessed, as it is that company's responsibility to ensure the product is adequately evaluated. According to Richard Ford of the RIFM: 'It has always been the policy of the RIFM that if a material is used only by one company, it is that company's responsibility to see that the material is adequately tested and evaluated.'¹⁰

In early stages of testing by the RIFM, it was found that if similar materials were tested on the same panel there was a higher incidence of positive allergic reactions. When these materials were then tested individually, the results were negative. Testing protocol was subsequently changed so that similar materials were not used on the same panels.¹¹

Testing by the RIFM does not reflect real-use situations, as products are a combination of many materials. Products may contain several known sensitizers. Even though only one company may manufacture a material, it is often widely used. A material may be in common use for close to 20 years before it is evaluated by the RIFM. The last monographs were published in 1992. There are no published monographs from the RIFM on materials introduced in the past 20 years.

The results of the screening of these materials are submitted to the International Fragrance Association. The IFRA then evaluates the data and formulates guidelines

for safe use of the materials. The IFRA has made recommendations on about 100 fragrance materials, and publish their recommendations or Code of Practice and makes it available in printed form or at their web site (<http://www.ifraorg.org/>). The IFRA has no authority to enforce the recommendations. Companies that do not follow them can be expelled from the organization, but to date no company has been expelled and there is no monitoring to ensure that recommendations are followed.

Health Concerns

With increased usage and exposure, problems have emerged regarding fragrances. There are concerns for both those that use scented products and those exposed from others' use. Many of the concerns regarding skin allergies are well recognized. Other concerns, such as those surrounding phthalates as possible hormone disruptors, and the impact of this on respiratory health, are emerging issues on which there are limited data available.

Skin

The vast majority of medical literature available on the health effects of scented products is in the realm of dermatology. Fragrances have been long recognized as skin allergens and irritants. The skin was thought of as the primary route of exposure from scented products, and until the late 1970s the skin was thought to be an effective barrier to fragrance materials entering the body. Most health and safety concerns related to fragrance were focused on effects on the skin. It is now recognized that the skin is not an effective barrier to many substances. The skin is an entry point for materials into the body. Once entry has been gained, there is potential for systemic effects.

Fragrance ingredients can be irritants, allergens, photosensitizers or phototoxins and they can have other negative effects on the skin. In spite of the fragrance industry's focus on skin safety of fragrance materials, dermatologists are usually the ones to pinpoint problematic materials. Actual real-use situations reveal much more than tightly controlled laboratory testing of singular materials. The incidence of skin allergy to fragrance has increased with exposure. A conservative estimate is that 1–2% of the population has skin allergy to fragrance. There is a direct correlation between the use of scented products and development of skin allergy to fragrance.¹²

Fragrances are complex mixtures of substances whose interactions with the skin are affected by many factors. Even though there may be sensitization to a specific substance, other substances can impact penetration, distribution, metabolism and interaction. Singular materials

may have a far different effect than complex mixtures. Some materials used in perfumes alter the surface tension of the skin and thus can more deeply penetrate the skin. Combinations of materials can have an impact on absorption. Materials commonly used in fragrance formulae can increase penetration of the skin. Some terpenes have been found to significantly enhance dermal absorption of pharmaceuticals. It is thought that they disrupt the stratum corneum to allow increased penetration of the skin. Terpenes are common in scented products and are likely to increase the absorption of other materials in products and in the fragrance portion of the product.¹³

Testing by the RIFM is usually done on healthy adult volunteers whose skin is intact. It fails to account for more vulnerable populations. One in ten eczema patients have allergies to fragrances. The rate has doubled since 1979. Perfume allergy is one of the most frequent types of contact allergy among children with eczema. Children, especially those with eczema, should not use perfume, to avoid developing perfume allergies. Generally, pediatricians and dermatologists recommend that scented products not be used on children, yet there are many scented products available for children, many of which contain known skin allergens, sometimes at levels that exceed industry's recommended use level.¹⁴ In addition, children are exposed to fragrance in many of the same products as adults, such as soaps, laundry products and toiletries and, particularly if they have perfume allergies, should avoid scented products. Also, as is the case with adults, those with eczema should avoid skin contact with perfumes to avoid developing fragrance allergies.

It has been found that there is an additive and probably synergistic effect when multiple allergens are used in fragrance. By changing testing protocols so that similar materials were not tested on the same panel, the RIFM has missed an opportunity to better evaluate real-use situations. In actual use, formulae may contain several known sensitizers, and in some instances higher than industry recommended levels are used. Such formulations increase the potential for allergies to develop. Further use of multiple products can expose the skin to numerous combinations and levels of allergens. It has also been found that inhalation of some fragrance materials alters the immune response of the skin. Interestingly, it was found that application of the materials to the skin did not have this same effect.¹⁵

Problems from fragrance are not limited to people that use scented products. Airborne contact dermatitis occurs due to exposure to fragrance materials in the air.¹⁶ These cases are much more difficult to manage, as simply avoiding the use of scented products will not solve the problem. Those seriously impacted often have to greatly alter their lives to prevent exposure. It has been found there are other problems as well from fragrance in the air.

Respiratory

Fragrance can induce or worsen respiratory problems. There are increasing anecdotal and clinical accounts of fragrance triggering and exacerbating respiratory problems. Fragrances are thought to trigger asthma and other respiratory conditions, due to their irritant effect. Those with asthma, allergies, sinus problems, rhinitis and other such conditions are more susceptible to the effects of irritants, often at levels that are many times lower than what would cause problems in the general population.

There are some subsets of the population that seem to be specifically triggered by fragrances often at levels that are too low to be considered irritants. Whether there is sensitization to specific materials or some other mechanism is involved is difficult to tell. There are no commercially available tests to determine whether specific fragrance chemicals are respiratory allergens. Lack of information on what is contained in a fragrance makes it extremely difficult to determine whether specific materials are involved.

In other industries, it has been found that chemicals can act as a hapten, binding with body proteins to form allergens. Some of these materials are known to cause both skin and respiratory sensitization. It has also been found that skin contact may play a role in respiratory sensitization.¹⁷

Fragrance chemicals are known to act as haptens in the skin and bind with body proteins to form allergens.¹⁸ This same mechanism is thought to be involved in development of respiratory sensitization to chemicals. Several fragrance materials are known to have the potential to cause respiratory sensitization. Limonene is a common terpene used in fragrances and cleaners; when it oxidizes, it forms substances that can sensitize both the lungs and the skin. Many manufacturers add antioxidants to prevent the formation of potentially sensitizing substances.

Concerns surfaced during the 1970s regarding the effects of aerosols. It was found that hair spray triggered respiratory symptoms in susceptible populations. The adverse reactions were attributed to the fragrance in the hair spray.¹⁹ Results from aerosol testing by the industry from the mid-1970s to the early 1980s concluded that the products were safe. However, the formulations tested are no longer in use and present formulations are often quite different (Fukayama *et al.*;²⁰ this summary was published in December of 1999. It is the only published article on respiratory concerns from the fragrance industry).

A MEDLINE search using the search terms 'perfume' and 'asthma' pulls up 22 articles. One was published before 1980; three were published during 1986–1987, the rest since. Clearly, fragrance is an emerging respiratory concern.

A 1986 survey of asthmatics found that 72% were triggered by perfume and/or colognes.²¹ Four patients with a history of sensitivity to fragrance underwent respiratory

challenges to cologne. Pulmonary function using forced expiratory volume in one second (FEV₁) was evaluated before, during, and after the challenge. FEV₁ declined 18–58% below the baseline period during the 10-min exposure. There was a gradual increase in FEV₁ over the next 20 min.

Twenty-nine asthmatics and 13 without asthma were exposed to perfume strips found in magazines, filter paper impregnated with the perfume identical to that in the perfume strips, 70% isopropyl alcohol, or normal saline. It was found that 20.7% of asthmatics experienced chest tightness and wheezing from the perfume exposures. Those with severe and atopic asthma were the most severely affected.²²

Results from a Tulane University study found that popular perfumes are cited as triggers for asthma. Challenge tests with six of these perfumes caused a significant decrease in FEV₁ in the 15 asthma patients studied. There was a 20 min perfume exposure, with FEV₁ being measured in the last 10 min.²³

Decreases were less than what was expected from their clinical histories of sensitivity to fragrances. There are several things that may account for this. If smaller airways were involved, clinical symptoms would not be accurately reflected by FEV₁, as it is not an accurate reflection of small airway involvement. The exposures were only for 20 min, whereas actual exposures are often much longer. There was no assessment of longer exposures or of effects that might persist or be delayed.

Since fragrances are odorous substances, it is very difficult to determine whether the odour of the product or other properties are responsible for the effects. Odours are known to trigger adverse reactions even if the material responsible for the odour is considered harmless. Eliminating awareness of the odour in order to determine which properties are responsible for the adverse effects is difficult.

A Swedish study addresses the aspect of odour. Nose clips were used to block the passage of air through the nose. Patients with a history of sensitivity to perfumes were introduced into rooms in which fragrance was present or in rooms where fragrance was not present. Triggering of respiratory symptoms was reported when the patients were exposed to fragrance. Further testing revealed that carbon filter masks did not prevent symptoms in these patients. This suggests that either such masks did not filter out the fragrance materials or that the symptoms were triggered through other pathways.²⁴

Eleven patients with histories of respiratory symptoms from fragrance exposure were exposed to fragrance or placebo via the eyes and the airways. During exposure to the eyes, the nose was clamped and fresh air was breathed. During exposure to the airways, the nose was clamped and the eyes were covered. It was found there was a gradual but significant increase in respiratory symptoms when exposed to fragrance by both routes.

The conclusion was that respiratory symptoms can be triggered by exposure via sensory pathways, and that further study was needed on the role of the sensory nervous system.²⁵

Another study found that exposure to five commercially available fragrances for 1 h caused pulmonary irritation and decreases in airflow velocity in mice.²⁶

If fragrance triggers and exacerbates asthma, does it play a role in causing asthma? There are accounts that implicate fragrance as a cause of occupational asthma. Perfume in cat litter was cited as a cause for one case of occupational asthma.²⁷ A woman who worked demonstrating perfumes developed asthma to fragrance.²⁸ A clinical study found that workers in the perfume industry were among groups with the highest rate of occupational asthma.²⁹ A woman sprayed in the face with perfume developed occupational asthma.³⁰ No specific agents were identified.

Perfume was found to be an environmental factor associated with the development of asthma in children in the United Arab Emirates.³¹ An epidemiological study of bronchial asthma among children in Moscow found that children living near perfume factories had a higher incidence of asthma.³²

A review of the literature by the Institute of Medicine categorized exposures as to their impact on triggering and causing asthma. The conclusion of the study was that their medical literature supports limited and suggestive evidence that 'second-hand smoke' (for school-age children and adults), fragrances and formaldehyde trigger and exacerbate asthma. There was insufficient evidence to associate fragrances with causing asthma. The IOM recommended that further studies be done.³³

There are only a few studies on the impact of fragrances on the respiratory system. Clearly, this is an area that needs to be further explored. Asthma rates have soared since the 1970s. It is important to look at changes that have taken place during this time period that might contribute to the rising rates. In the past three decades, fragrance has gone from 'special occasion' to use of multiple scented products on a daily basis. According to fragrance industry demographics, Blacks and Hispanics are more frequent users of fragrance than other segments of the population.^{34,35} They are also more likely to suffer from the effects of asthma. While these things are not proof of the impact fragrance has had on asthma, they certainly support the need for further and more extensive examination of respiratory effects of fragrance.

While there is a scarcity of information in medical and scientific journals regarding the impact of fragrances on respiratory health, there seems to be an abundance of clinical and anecdotal accounts of fragrance exacerbating respiratory conditions. Virtually every health organization and agency concerned with respiratory health lists fragrances as triggers for asthma.^{36,37} Even fragrance

industry information acknowledges that fragrances can trigger asthma due to their irritant effects.³⁸

There is limited data regarding the specific long-term effects of irritants on the airways. In the short term, irritants can cause inflammation and increase mucus production. This can increase susceptibility to allergens, other irritants and pathogens. It is known that those with asthma and other respiratory disorders are much more impacted by irritants. Continued exposure to irritants exacerbates these conditions by triggering attacks and contributing to the underlying inflammatory process.

Whether fragrances are specific allergens or irritants, or whether other mechanisms are involved, it is clear that a significant portion of the population is potentially impacted by their widespread use. There are over 17.3 million asthmatics in the USA. Some 35 million suffer from chronic sinus infections, and another 9 million suffer from rhinitis. There are millions more with chronic respiratory disease. While these conditions certainly overlap, they still represent millions of people and a significant portion of the population. The costs of these disorders in both economic factors and quality of life are tremendous.

Neurological

Fragrance can impact the brain and nervous system. Some of these effects are immediate and transitory, while others can be long-term. Olfactory pathways provide the most direct connection to the brain of any senses and also provide a means of toxic materials entering the brain.

The olfactory epithelium also contains receptors for the trigeminal nerve. While olfactory receptors are only located in the nose, trigeminal receptors are located in the eyes, nose, mouth, face, scalp and airways. About 70% of odorants stimulate the trigeminal nerve to one degree or another. Trigeminal nerve stimulation is responsible for cold, hot, tingling or irritating sensations. Materials that stimulate the trigeminal nerve can cause tearing in the eyes, as well as irritation of the nose and airways.

The sense of smell is the most primitive sense. Odorants are volatile materials that have properties that allow them to be detected by olfactory receptors. From the receptors in the nose there is a direct pathway where nerve impulses travel to the brain and odours are interpreted. The sense of smell can detect very low concentrations of odorants. However, it cannot detect the same odour at the same concentration for an extended period of time.

Those that use scented products on a regular basis may not be able to detect their own fragrance shortly after applying it. They may apply increasing amounts or reapply frequently so that they can smell the fragrance. In many instances they are totally oblivious to the fact

that their fragrance is often overwhelming and intrusive to others.

The widespread use of scented products also creates a background of fragrance that is present all the time. In order for products to be detected over this background, they are formulated with intense and longer-lasting fragrance.³⁹ Traditionally, a good perfume lasted for 6–8 h. Scent from laundry products now lasts for weeks.

Olfaction has both physiological and emotional aspects and the two often overlap. This makes it difficult to assess where an effect is purely physical or is impacted by subjective factors. This has led to great debate as to whether the effects of fragrances are due to their odour or other properties of the materials. Setting up blinded assessments in which odours are not a factor is very difficult, as blocking the odour also blocks the sensory pathways.

The term 'AROMA-CHOLOGY®' has been coined by the Olfactory Research Fund to describe the concept of the psychological effects fragrance can have on feelings, i.e. the ability of fragrance to transmit though odour-specific feelings directly to the brain.⁴⁰

It is highly unlikely any substance that has a direct effect on the brain and nervous system has only psychological effects. Autonomic nervous system (ANS) parameters were measured during inhalation exposures to two forms of limonene and carvone. Subjective assessments of mood and alertness were also gathered: inhalation of (+)-limonene caused an increase in systolic blood pressure and reports of alertness and restlessness; (–)-Limonene caused an increase in systolic blood pressure, but no mood alteration; (–)-Carvone caused increases in pulse, diastolic blood pressure and restlessness; (+)-Carvone caused increases in both systolic and diastolic blood pressure. It is suggested that prolonged inhalation of these materials affect both ANS parameters and mental and emotional status. The differences in response to varying forms of the same chemicals indicate that the chirality of the material is an important factor in the biological effects of the materials.⁴¹

Other research indicates that fragrance materials can act on receptors in the brain and affect frame of mind in a similar manner to alcohol and tobacco, raising the intriguing possibility that there could be addiction to fragrance.⁴² Research supports the claims that lavender contains substances that indeed do relax and calm. The motility of mice that inhaled linalool (a compound found in lavender) decreased 40%.⁴³ Even stimulation with caffeine did not return activity to normal levels.

These studies support the idea that fragrances not only have the potential to affect emotion and feelings, but also have physiological or drug-like effects. This raises concerns that exposure may have unwanted consequences. There are often extensive differences in how individuals will react to the same substance at the same level. What

may be relaxing to one, may be sedating to another. And there are many instances where materials that decrease alertness would be undesirable and even dangerous.

Olfactory pathways not only provide a route for transmission of sensory information, but also a direct point of entry for toxins into the brain.⁴⁴ Solvents and other materials in fragrances can negatively impact the nervous system. Exposure to the nervous system can occur through materials inhaled, ingested or absorbed through the skin.

Acetyltetramethyltetralin (AETT) and musk ambrette, two materials in common use for decades, were found to be neurotoxic.^{45,46} AETT caused a bluish discoloration of the internal organs of laboratory animals and was severely neurotoxic. Musk ambrette was readily absorbed through the skin and also had neurotoxic properties.

Systemic Effects

Fragrance can enter the body through numerous routes, such as skin absorption, inhalation, ingestion and the olfactory pathways. Once inside the body, the materials can impact any organ or system.

Safrole was listed as reasonably anticipated to be a human carcinogen, according to National Toxicology Program studies in 1981. It occurs naturally in some essential oils and in sassafras roots. Safrole causes liver tumours in animal studies. The FDA banned safrole for food use. IFRA guidelines recommend that safrole should not be used as a fragrance ingredient. Essential oils containing safrole can be used with the restriction that safrole levels should not exceed 0.01% in consumer products.⁴⁷ Coumarin is widely used in fragrances. There was some evidence of it being a carcinogen in animal studies, where it was associated with an increase in lung, liver and renal tumours.⁴⁸ It has been banned from use in foods by the FDA, but continues to be used in fragrances. Methyleugenol is a common fragrance/flavours material. It also occurs naturally in spices and some essential oils. NTP studies found clear evidence of carcinogenic activity in studies of animal exposure to methyleugenol.⁴⁹ Musk xylene was found carcinogenic in animal studies.⁵⁰ Most fragrance chemicals have not been evaluated to determine whether they are carcinogens.

In single large doses, 6-acetyl-1,1,2,4,4,7-hexamethyltetraline (AHTN) caused liver toxicity and organ discoloration in animals. Similar but less prominent effects were also observed with hexahydro-hexamethyl-cyclopenta γ -2-benzopyran (HHCB). The cause and the implications of the discoloration were not known.⁵¹ Both AHTN and HHCB are synthetic musk compounds that are widely used at relatively high levels. AHTN may be used at 5–20% in the fragrance formula and HHCB at up to 50%.⁵² Both of these materials are common in

laundry products, which involves skin contact over large, often occluded areas.

Other areas of concern are the potential for fragrance chemicals to impact the reproductive system, fetal development and infants breast-feeding. Materials used in fragrances can cross the placental barrier and have the potential to impact fetal development.⁵³ Synthetic musk chemicals are known to bioaccumulate in human tissue and are present in breast milk.⁵⁴

Studies on musk ketone have suggested that it may increase susceptibility to carcinogens.⁵⁵ Since this material has been found in breast milk, it more than likely present in breast tissue. Studies need to be done to ensure that musk ketone and other fragrance chemicals that are present in breast tissue do not play a role in development of breast cancer.

Musk ambrette was found to cause atrophy of testicles in animal studies.⁵⁶ Citral, a common material in both fragrances and flavours causes enlargement of the prostate gland and is estrogenic.⁵⁷ Men working in perfume and soap manufacture in Sweden have a higher incidence of prostate cancer.⁵⁸ Two common fragrance materials have been found to have weakly oestrogenic properties.⁵⁹

A recent study found that metabolites of diethyl and dibutyl phthalate were common in women of childbearing ages.⁶⁰ Some phthalates have been found to be hormone disruptors in animal studies. Diethyl and dibutyl phthalate are common in scented products. In an analysis of a popular perfume, diethyl phthalate (DEP) made up over 10% of the fragrance portion of the product.⁶¹ DEP is a common solvent in raw fragrance materials.

The vast majority of fragrance chemicals have not been assessed for systemic effects. The acute and long-term impacts are not known.

Environmental Concerns

Fragrances are primarily volatile compounds that impact both indoor and outdoor air quality. Many compounds are not filtered out by water treatment and end up in waterways. These materials accumulate in aquatic wildlife and contaminate the food chain. They are an often overlooked source of pollution.

Impact on Air

Fragrances by design get into the air. In order to detect an odour, molecules of that substance must be airborne. Fragrances are complex mixtures of volatile organic compounds (VOCs), formulated to have a specific odour. Once in the air they break down, mix with other pollutants, and form new compounds that are often more irritating or allergenic than the original substance. VOCs are

associated with exacerbating respiratory disease, such as asthma. According to the California Air Resources Board 1990 statistics, some 265 tons of VOCs were released into California air from the use of consumer products each day.

Fragrance chemicals that are air-sensitive may form peroxides, respiratory irritants, and particles that cause inflammatory responses in the lungs. Particles of 10 µm or less are considered respirable. When D-limonene, a common fragrance material, was added to the air in an office environment, there was a 10× increase in sub-µm particles than measured in a comparable office without the added limonene.⁶²

There have been very few studies done specifically on the role of fragranced products in air pollution. A Norwegian study found synthetic musk compounds in outdoor air, not only in urban areas but also in remote areas.⁶³ The presence of these synthetic musk compounds was so ubiquitous in indoor air, even in the laboratory setting, that special procedures for preventing contamination of the samples of outdoor air had to be taken.

An examination of scented products by the EPA concluded that scented products contained some materials that were of toxicological significance at low levels; further work and study were needed in this area. Benzaldehyde and toluene were some of the materials found.⁶⁴ Benzaldehyde can cause both respiratory and skin sensitization, is a possible mutagen and targets the nerves and liver. Toluene is an eye, skin and respiratory irritant, has systemic effects via inhalation, and has neurological effects.

The words 'air freshener' suggest that such products would improve air quality. In actuality, the opposite is true. The toxicity of an air freshener was evaluated by allowing mice to breathe in the emissions from a commercially available solid air freshener for 1 h. The researchers concluded that 'emissions of this air, freshened at several concentrations, including concentrations to which many individuals are actually exposed, caused increases in sensory and pulmonary irritation, decreases in airflow velocity and abnormalities of behavior measured by the functional observational battery score.'⁶⁵

Presence in Waterways and Wildlife

Most soap, shampoos and other bathing products contain fragrance. In addition, fragrance is added to most household cleaners and laundry products. A large portion of these materials ends up in wastewater. Most wastewater treatment methods do not remove fragrance compounds. These materials end up in streams and rivers from discharge of water from sewage treatment.⁶⁶

In 1999, the EPA sponsored a review of the literature pertaining to the impact of pharmaceuticals and personal

care products on the environment. The review concluded that:

'Fragrances (musk) are ubiquitous, persistent, bioaccumulative pollutants that are sometimes highly toxic; amino musk transformation products are toxicologically significant'.⁶⁷ Even materials that do not persist in the environment may act as they do because the supply is constantly being replenished.

Musk compounds tend to accumulate and break down slowly. They persist in the aquatic environment and accumulate in the fatty tissue of aquatic wildlife. Shellfish and fish have measurable levels of synthetic musk compounds in their tissues. These materials can be considered 'persistent organic pollutants'.

Most of the work done regarding synthetic musk compounds has taken place in Europe. It is highly likely that findings would be similar in the USA. It is also likely that levels of nitro-musks in the aquatic environment would be higher, as those materials are in more common use in the USA. In Europe, the polycyclic musks have largely replaced nitro-musks.

Conclusion

There is widespread use and exposure to scented products. While there are frequent clinical and anecdotal accounts of adverse effects, there is limited research outside of the area of dermatology. The available information is widely scattered and needs to be considered as a whole. Fragrance is clearly an emerging health and environmental concern. There needs to be further study and evaluation of its impact. While it is true that the issues are very complex, this is not an excuse to dismiss them.

Emerging concerns have not been adequately addressed by the industry. In order for problematic materials to be pinpointed and suitable substitutes found, there must be a cooperative effort that involves the industry as well as the regulatory, scientific and medical communities. There needs to be a system in place where adverse effects are reported and evaluated. Furthermore, the industry needs to include testing for adverse effects via all routes of exposure. Assessment of concerns and addressing problems in a responsible manner is essential if the industry wishes to remain primarily self-regulated.

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