Environmental effects and skin disease

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The skin is the largest organ in the body and one of its main functions is to protect the body from noxious substances, whether they are ultraviolet radiation, toxic chemicals or prolonged/repeated exposure to water. It is the level of exposure that determines if damage to the organism will result. The harm that can occur to the skin with sufficient exposure will be considered. Contact dermatitis, halogen acne, chemical depigmentation, connective tissue diseases and skin cancer are the conditions that will be covered in this chapter, as environmental exposure is important in their aetiologies. Systemic absorption will not be dealt with. Most environmental exposure to harmful substances will occur at work, but exposure may occur at home or during normal day-to-day activities.

Dermatitis

Contact dermatitis is an eczematous eruption caused by external agents. The causes can be broadly divided into irritant substances that have a direct toxic effect on the skin, and allergic chemicals where immune hypersensitivity reactions occur.

Irritant contact dermatitis

Irritant contact dermatitis (ICD) is caused by direct damage of the skin by the irritant substance. It develops if the exposure of the substance or substances is sufficient or the skin is particularly susceptible as is found in atopic dermatitis (AD) patients. The commonest irritants found in the environment are: soaps, detergents, water, solvents and a dry atmosphere. The occurrence of irritant contact dermatitis depends upon the degree of exposure. Most of us do not develop ICD when washing our own hair but an apprentice hairdresser is at high risk of developing dermatitis because the exposure to shampoo and water is so great. Irritant contact dermatitis is very common with at least 10% of the population suffering from hand dermatitis1. An infant's skin is more susceptible to irritant damage than adult skin.
Allergic skin reactions

There are two allergic mechanisms that can commonly affect the skin. They are immediate (IgE driven) and delayed (cell mediated) allergic reactions. The T cell lymphocytes involved in these allergic mechanisms can be subdivided into two functional subsets by their differing cytokine profiles. Immediate allergic reactions involve the central immune organs releasing B lymphocytes which are then stimulated to differentiate into plasma cells producing allergen specific IgE. This is the T helper 2 (Th2) response with cytokine profile of interleukin 4 and 5. Delayed allergic reactions involve lymphocyte-mediated mechanisms called the T helper 1 (Th1) response with cytokine profile of interleukin 2 and gamma interferon.

Hay fever, asthma and contact urticaria are examples of immediate allergic reactions. Common causes are: house dust mite, grasses, pollens, natural rubber latex, dairy products and peanuts. These allergenic proteins do not penetrate normal skin particularly well but can penetrate damaged skin such as AD and hence aggravate it. Sometimes exposure to these allergens can lead to anaphylaxis. Peanuts and natural rubber latex are good examples.

Allergic contact dermatitis (ACD) is caused by delayed allergenic mechanisms Th1 response. It takes the immune system a few hours to react. Common causes are: nickel, fragrances, rubber additives, preservatives, plants and medicaments (Table 1). The immune system of atopics tends towards Th2 responses and so is less likely to develop ACD even though their exposure to certain delayed allergens will be greater than for non-atopics.

Atopic dermatitis

There has been a three-fold increase in patients suffering from AD in the past 30 years. The reason for this is not clear but the hygiene hypothesis seems to be the best explanation\(^2\). The incidence of childhood AD in the UK is at least between 15 and 20\% and some countries even higher\(^3\). There has been an increase in frequency in first generation immigrants to western industrialized countries and there was a substantial increase in prevalence of atopic disease in Eastern Germany following reunification of Germany in 1990\(^4\). It would therefore appear that exposure to pollutants in some way protects against the development of atopy or that the exposure to infectious diseases associated with poorer, less developed nations protects against atopy. This is the basis of the hygiene hypothesis.
Chloracne (halogen acne)

Acne is a very common skin disease in adolescence but on rare occasions environmental pollution can result in a variant of acne called chloracne. Environmental acne results from various chemical exposures and the eruption may be mild, involving localized exposure, or covered areas of the body or severe, explosive and disseminated with involvement of almost every follicular orifice. Chloracne almost always represents a cutaneous sign of systemic exposure to highly toxic chemicals. Chloracne results from environmental exposure to certain halogenated aromatic hydrocarbons and is considered to be one of the most sensitive indicators of systemic poisoning by these compounds.

Chloracne was first observed by Von Bettman in 1897 and by Herxheimer in 1899. Since that time, a number of chloracnegenic chemicals have been identified. Before World War II, most cases were thought to be caused by chloronaphthalenes and polychlorinated biphenyls (PCBs). More recently, trace contaminants formed during the manufacture of PCBs and other polychlorinated compounds, especially herbicides, have been causally linked to chloracne development. These include polyhalogenated dibenzofurans in association with PCBs, polychlorinated dibenzo-p-dioxins, and chlorinated azo- and azoxybenzenes which are contaminants of 3,4-dichloraniline and related herbicides.

Table 1 Commonest allergens causing ACD and their sources

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Source</th>
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<tbody>
<tr>
<td>Potassium dichromate</td>
<td>Leather, cement, etc.</td>
</tr>
<tr>
<td>Neomycin</td>
<td>Antibiotic</td>
</tr>
<tr>
<td>Thiruam mix</td>
<td>Rubber additive</td>
</tr>
<tr>
<td>Paraphenylenediamine</td>
<td>Permanent hair dye</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Metal</td>
</tr>
<tr>
<td>Caine mix III</td>
<td>Local anaesthetic</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>Biocide</td>
</tr>
<tr>
<td>Rosin</td>
<td>Colophony, resin from spruce trees</td>
</tr>
<tr>
<td>Balsam of Peru</td>
<td>Fragrance</td>
</tr>
<tr>
<td>Isopropyl-phenyl-paraphenylenediamine</td>
<td>Industrial rubber additive</td>
</tr>
<tr>
<td>Wool alcohols</td>
<td>Lanolin</td>
</tr>
<tr>
<td>Mercapto mix</td>
<td>Rubber additive</td>
</tr>
<tr>
<td>Epoxy resin</td>
<td>Two part adhesive</td>
</tr>
<tr>
<td>Paraben mix</td>
<td>Preservative</td>
</tr>
<tr>
<td>Paratertiarybutyl phenol formaldehyde resin</td>
<td>Adhesives</td>
</tr>
<tr>
<td>Fragrance mix</td>
<td>Fragrance</td>
</tr>
<tr>
<td>Quaternium 15</td>
<td>Biocide</td>
</tr>
<tr>
<td>Nickel</td>
<td>Metal</td>
</tr>
<tr>
<td>Methylchloroisoo thiazolinone + methylisothiazolinone</td>
<td>Biocide</td>
</tr>
<tr>
<td>Mercaptobenzothiazole</td>
<td>Rubber additive</td>
</tr>
<tr>
<td>Primin</td>
<td>Primula</td>
</tr>
<tr>
<td>Sesquiterpene lactone mix</td>
<td>Compositae plant allergy</td>
</tr>
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The chloracnegenic compounds are structurally similar, all sharing relative molecular planarity and containing two benzene rings with halogen atoms occupying at least three of the lateral ring positions. The position of halogen substitution appears to be critical, as substitution to positions that lead to molecular nonplanarity reduces biological activity. Stereo-specific binding of these compounds to a receptor is implicated in their toxicity.

Most cases of chloracne have resulted from environmental exposure in chemical manufacturing or rarely from end-use of products. Exposure is usually through direct contact, but inhalation and ingestion may also be operative in some cases. Non-occupational chloracne has resulted from industrial accidents, contaminated industrial waste, and contaminated food products. A widely publicized example was the extensive environmental contamination with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (Fig. 1), which occurred on July 10, 1976, at the ICMESA chemical plant near Seveso, Italy. During production of trichlorophenol, an explosion resulted in the formation and ultimate discharge into the atmosphere of an estimated 2 kg of TCDD. The contaminated area encompassed more than 200 acres of land, and 135 cases of chloracne, mostly in children, were confirmed among some 2000 inhabitants. Other examples were the widespread ingestion of tainted rice cooking oil that occurred in Japan in 1968 and in Taiwan in 1979. Popular brands of oil were contaminated with PCBs and dibenzofurans resulting in the largest epidemics of chloracne to date. Over 1000 patients were affected with oil disease called Yusho in Japan, and Yucheng in Taiwan. For a listing of known chloracnegens, see Table 2.

Although chloracne tends to slowly resolve upon cessation of exposure to chloracnegenic compounds, the duration of chloracne correlates with the severity of the disease, which is usually a reflection of the degree and extent of exposure. Thus, in severely exposed victims of the Yusho incident in 1968, lesions characteristic of chloracne continued to develop for as long as 14 years after the initial exposure. Treatment has, in general, been disappointing, but the retinoids seem to hold some promise.

The prevention and control of chloracne require a totally enclosed manufacturing process with no opportunity for direct skin contact or inhalation of the toxic chemicals—a difficult environmental engineering challenge.
task. The only other alternative is to attempt to alter the chemical synthetic process to eliminate or minimize exposure to the contaminant chloracnegens.

Chemical depigmentation

Chemical leukoderma is defined as pigmentation or hypopigmentation of the skin due to industrial exposure to a chemical or chemicals known to have a destructive effect on epidermal melanocytes. Certain chemicals, particularly the substituted phenols, are destructive to functional melanocytes. Many of these compounds cause permanent depigmentation of the skin, resembling vitiligo. The most commonly implicated chemicals are para-tertiary butyl phenol, para-tertiary butyl catechol, monobenzyl ether of hydroquinone, hydroquinone and related compounds. A list of chemicals known to cause occupational leukoderma is shown in Table 3.

The diagnosis of occupational vitiligo should be suspected if a worker who potentially has been exposed to depigmenting chemicals develops leukoderma on the dorsal aspects of the hands or in a more widespread distribution. There should be particular suspicion if more than one worker is involved. The chemicals to which the worker is exposed should be identified and investigation made to see if it or they are known to cause depigmentation.
There is no specific treatment for chemical leukoderma. Removal of the offending chemical may result in partial repigmentation but this process may take years and may not occur at all. Treatment should be aimed at preventing further exposure. Camouflage cosmetics may be used and the depigmented skin protected from ultraviolet irradiation by sunscreens.

### Scleroderma-like disease

Scleroderma-like diseases have been observed increasingly over the last few decades\(^\text{10}\). These comprise diseases that in addition to skin changes similar to those of scleroderma also involve other organ systems, but are not consistent with classical scleroderma. The most important aetiological factors and clinical manifestations are summarized in Table 4. A common factor in these diseases is that they generally show definite clinical improvement when exposure to the relevant agent ceases apart from quartz induced systemic sclerosis.

### Quartz induced scleroderma

Quartz is widely distributed in nature (silicon dioxide, \(\text{SiO}_2\)). Silicon-derived materials predominantly as quartz) account for 27% of the earth’s crust. Silicon dioxide is present in over 90% of all minerals. Quartz is chemically virtually inactive and can remain unaltered for decades in human tissues. The principal medical significance of the substance is as the causative agent of pulmonary silicosis.
The first suggestion of a possible association between occupational exposure and the development of systemic sclerosis came from the Scottish physician Bramwell in 1914. He observed nine patients of whom five had worked as stonemasons. In 1957 Erasmus reported 16 cases of scleroderma amongst 8000 miners in South African gold mines, in comparison to a control group of 25,000 hospital patients without a single case of scleroderma. Since then similar case reports and studies have been published in the USA, France, Italy, Japan, Switzerland, Canada and Germany.

Quartz exposure occurs particularly in the following industries and occupations: mining, stone industry, slate industry, foundry industry, fire-clay manufacture and processing, construction, rubber industry (talc is heavily contaminated with silicon dioxide), ceramic and glass industries.

Treatment of scleroderma is unsatisfactory as there is no specific therapy and the course is almost always progressive. Death usually results from general debility or from renal, myocardial or pulmonary sclerosis. In quartz industry-related cases, removal of the patient from exposure does not usually result in clinical improvement.

**Vibration white finger**

Vibration white finger (VWF) consists of the episodic appearance of white-finger skin patches (Raynaud’s phenomenon) in response to environmental cold and is accompanied by secondary loss of sensation caused...
by vascular ischaemia. It can be part of but is not synonymous with the hand-arm vibration syndrome. The pathogenesis of VWF is poorly understood. Chronic vibration exposure may damage endothelial vasoregulatory mechanisms by disturbing the endothelial-derived relaxing factor-mediated vasodilatory function. Operatives using vibrating tools, such as lumberjacks, coal miners and road and construction workers, are at risk of developing VWF. Affected individuals develop symptoms of Raynaud’s phenomenon on exposure to cold or vibration, usually after many years of working with vibrating tools. The diagnosis is usually made by history alone; ice provocation tests are not always reliable in precipitating attacks of VWF.

With widespread knowledge of the cause of VWF, controls over duration of use of relevant machinery and improved personal protective equipment have led to a reduction in the incidence of VWF. The treatment of VWF is the same as for Raynaud’s phenomenon. It is generally believed that symptoms of VWF regress some time after cessation of exposure.

### Skin cancer

In 1775, the first cancer of any type to be linked with environmental exposure was scrotal squamous carcinomas in British chimney sweeps reported by Percivall Pott. In the rest of Europe the disease was unknown because of wearing protective clothing and the reduced carcinogenicity of wood soot as opposed to coal predominantly burnt in Britain. Soot formed by burning wood has much lower levels of the polycyclic hydrocarbon, benzo(a)pyrene (Fig. 2), implicated in the aetiology of skin cancer. Skin cancer was still reported in chimney sweeps in Britain in the 1950s. By 1945 in Britain, almost 50% of industrial skin cancer was attributable to exposure to pitch and tar in occupations such as mule spinners and jute workers and in the engineering industry.

![Fig. 2 Benzo(a)pyrene.](image-url)
In the past, however, there have been several virtual epidemics of skin cancer, which were traceable to environmental exposures. The major environmental carcinogens recognized were polycyclic hydrocarbons, ionizing radiation and arsenic. Ultraviolet radiation is now the most important carcinogen in the aetiology of environmental skin cancer.

Polycyclic hydrocarbons are produced by incomplete combustion and distillation of coal, natural gas and oil shale. These chemicals are contained in tar, fuel oils, lubricating oils and greases, oil shale and bitumen (Table 5)\(^{16}\).

The diagnosis of skin cancer is similar to that of non-occupational skin cancers. Generally the exposed sites are involved. Previously the scrotum was involved frequently because of continuous exposure to carcinogens and the increased likelihood of skin absorption in that site. There may be co-existing signs of exposure prior to or in addition to evidence of skin cancer. These may include oil folliculitis and hyperkeratoses described in people working with mineral oil, and pitch or tar warts. Oil hyperkeratoses were described as being flat, white, circular, hyperkeratotic smooth plaques, small in diameter and often clustered. In addition there were verrucose pigmented round or oval irregular raised warts. Tar warts were pigmented small papules which were often seen around the face on the eyes, eyelids, cheek, forearms and back of the hands.

Prevention of skin cancers is most important. In the workplace it is important to consider substitution of carcinogens where possible; an example is the declining exposure to polycyclic hydrocarbons in recent decades. Protection of the skin, with either protective clothing or with engineering control such as machine guarding, is important. Daily washing is essential. Since most of the skin cancers are associated with a very long latency

<table>
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<tr>
<th>Table 5</th>
<th>Occupations with potential exposure to causative agents in environmental skin cancer</th>
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<tr>
<td><strong>Polycyclic hydrocarbons</strong></td>
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<td>Tar distilling</td>
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<tr>
<td>Coal gas manufacturing</td>
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<td>Briquettes manufacturing</td>
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<td>Shale oil workers</td>
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<td>Refinery workers</td>
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<tr>
<td><strong>Ultraviolet light</strong></td>
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<td>Outdoor workers</td>
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<td>Welders</td>
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<td>Laser exposure</td>
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<tr>
<td>Printers</td>
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<tr>
<td><strong>Ionizing radiation</strong></td>
<td></td>
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<tr>
<td>Nuclear power plant workers</td>
<td></td>
</tr>
<tr>
<td>X-ray technicians</td>
<td></td>
</tr>
<tr>
<td>Uranium mining</td>
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</table>
period, it is important to have continued surveillance of older or retired workers. Finally, the skin cancers need to be treated as appropriate.

**Sunlight effects on the skin**

Non-ionizing radiation, predominantly in the ultraviolet region (Fig. 3), from the sun is important in a variety of skin cancers and inflammatory skin diseases.

There is good evidence that sunlight (particularly ultraviolet B, and to a lesser degree ultraviolet A radiation) plays an important role in the aetiology of the commonest skin cancers, basal cell carcinoma$^{17,18}$ and squamous cell carcinoma$^{19}$ and its precursor lesions actinic keratoses$^{20}$ and Bowen’s intraepidermal neoplasia. There is more controversy about the role of sunlight in the development of malignant melanoma, but it is probable that sunlight exposure, perhaps particularly intermittent exposure in childhood, is important$^{21-24}$.

Non-ionizing radiation from the sun is important in the clinical expression of the idiopathic photodermatoses (Table 6), the cutaneous porphyrias, and drug-induced photosensitivity. It is also important in the rare genophotodermatoses, such as the many types of xeroderma pigmentosum which share the common feature of impaired ability to repair ultraviolet induced DNA damage. Many other dermatoses can be photoaggravated, including cutaneous lupus erythematosus, Jessner’s lymphocytic infiltrate, melasma, pemphigus vulgaris, and actinic lichen planus. The effects of sunlight on the skin are not all adverse, and are beneficial for the majority of those with some common inflammatory skin diseases including psoriasis and atopic dermatitis.

How might environmental pollution alter the transmission of ultraviolet radiation and visible light to the skins of people living in different parts of the world? And what are the possible effects, for good or ill, on the prevalence and severity of common and serious skin diseases?

![Fig. 3](https://academic.oup.com/bmb/article-abstract/68/1/129/421238) Ultraviolet and visible rays (and the longer infrared rays) reach Earth. The ultraviolet rays are most relevant in causing, triggering, aggravating and relieving skin diseases.
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Possible effects of pollutants: effects on high atmospheric ozone

Depletion of ozone in the upper atmosphere (stratosphere), thought largely to be due to human activities particularly the release of chlorofluorocarbons (CFCs), has resulted in an increase in shorter wavelength ultraviolet B (UVB, see Fig. 3) reaching the Earth’s surface. The actual increase in shorter wavelength UVB reaching ground level has been most marked in the southern hemisphere. In the northern regions studied, counteracting effects of air pollutants in the lower atmosphere have generally limited such an effect, although an increase in UVB at ground level in Scotland did coincide with reduction in stratospheric ozone.

Mathematical modelling has estimated that the actual increase in skin cancers seen in the northern hemisphere as a result of ozone depletion will be small, although not insignificant when we consider that non-melanoma skin cancers are the commonest cancers in peoples with constitutively pale skin. Yet the effects of ozone depletion might be expected to cause more problems in the South. An increase in patients with sunburn, and other photodermatoses, presenting to the dermatologist serving Punta Arenas, the most southerly city in South America, has been noted to coincide with increased ground-level UVB measurements associated with movements of the Antarctic ‘ozone hole’. While confounding factors, particularly media attention to the ozone hole likely to increase the probability of someone
with sunburn seeking a dermatologist’s opinion, could not be excluded in this observational study, this was an important report as it showed for the first time a possible real association of skin disease and changes in stratospheric ozone.

Overall, small changes in stratospheric ozone, increasing shorter ultraviolet wavelengths reaching ground level, particularly in the southern hemisphere, may be expected to increase the frequency of sunburn episodes, and skin cancers, although the evidence that this is actually happening is limited. If there are effects on other common conditions such as polymorphic light eruption (PLE), it is unclear what these will be: possibly PLE will even decrease in frequency as this condition is generally provoked more readily by longer wavelength ultraviolet (UVA) radiation, and it is likely that its relative rarity near the equator is due to greater UVB exposure.

**High atmospheric ozone and lower atmospheric pollution**

Pollutants, such as the smoke from forest burning in South East Asia\(^3\), would be expected to reduce the frequency of conditions caused or aggravated by ultraviolet exposure.

It is theoretically possible that worry about the possible risks of CFC pollution affecting the ozone layer will lead to increased sunscreen use. Recently, several widely used absorbent sunscreens have been shown to have oestrogenic activity comparable to that of other xenoestrogens released into the environment and entering the food chain\(^3\), raising concern about possible effects on ecology and human health.

**Key points for clinical practice**

- Irritant contact dermatitis is the commonest dermatosis caused by environmental exposure.
- Chloracne, chemical depigmentation and certain connective tissue diseases can be caused by environmental pollution.
- Ultraviolet radiation is the most important carcinogen in the aetiology of skin cancer.
- Ultraviolet radiation can aggravate certain dermatoses and cause photosensitivity.
- There is as yet little hard evidence that atmospheric pollution has had (or will have) an effect on skin diseases influenced by ultraviolet radiation from the sun.
References

26 Frederick JE. Ultraviolet sunlight reaching the Earth’s surface: a review of recent research. *Photochem Photobiol* 1993; 57: 175–8

27 Moseley H, Mackie RM. Ultraviolet B radiation was increased at ground level in Scotland during a period of ozone depletion. *Br J Dermatol* 1997; 137: 101–2


