Airborne Skin Diseases

11

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Airborne dermatoses are complaints linked to external environmental, chemical and biotic agents carried through the air (Table 11.1) [1–12]. In general, because they are so common in work environments, airborne dermatoses tend to cause diagnostic problems that are challenging for both the patient and the doctor. It should also be borne in mind that since the external culprit agents are present in the environment, they do not only come in contact with the skin and mucosa, but can also be inhaled or ingested, thus also causing respiratory (bronchitis, asthma, rhinitis) and systemic symptoms [4, 6–8, 10].

The occurrence of airborne dermatoses was underestimated in the past. In 1950, Pirilä was the first to introduce the concept of airborne dermatoses, describing cases of thiokol dermatitis that he had observed in Finland after the Second World War [13]. In 1963, the same author reported cases of occupational dermatoses due to airborne skin offenders [14]. Nowadays, cases of airborne skin afflictions are reported all over the world, reflecting the complexity and diversity of the problems encountered as a result of new causal agents and/or particular technical procedures.

Airborne dermatoses can be subdivided into two groups [4, 5]:

1. Airborne contact dermatoses, directly linked to skin contact with environmental causal agents carried through the air. These forms are by far the most common and well documented.
2. Dermatoses brought on by inhaling substances that are then absorbed into the system. These are rarer, less documented forms.

Within each group, mixed forms can also be observed linked to different pathogenic mechanisms. In the first group, for example, pictures induced by contemporary airborne and direct skin contact with the causal agent are very frequent, especially in industrial settings. Such situations are observed in cases of contact dermatitis due to epoxy resins in powder form, as well as to fiberglass and to phosphorus sequisulfide.

Instead, in the second group the skin manifestations follow airborne contact skin as well as inhalation and/or ingestion of the causal agent, as occurs in the case of chloracne induced by dioxin. Skin forms induced by a triple pathogenic mechanism (direct contact, airborne contact and contemporary inhalation) are also possible as after exposure to powdered mercury, for instance.

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Table 11.1 Airborne skin diseases

A. *Chemical agents*
Airborne contact dermatitis
Airborne photocontact dermatitis
Noneczematous erythema multiforme-like eruptions (tropical wood dust and fumes of combusted plants)
Chloracne (chlorinated compounds)
Extrinsic aging
Atopic dermatitis (in some cases)
Occupational skin cancer
Occupational scleroderma-like diseases (vinyl chloride, epoxy resins, pesticides)
Contact urticaria
Subcorneal pustular eruptions (trichloroethylene)
Purpura (epoxy resin)
Fixed drugs eruption (pyrazolones)
Paresthesia (pyrethroids)
Telangiectasia (corticosteroids)
B. *Biotic agents*
Atopy (animal epidermal derivatives)
Papular and urticarial dermatitis (pine caterpillar)
Miscellanea

11.1 Airborne Agents

There is considerable variation in the nature of airborne contactants, especially at work but also in non occupational environments, and in their form of presentation (Table 11.2).

11.1.1 Vapours and Gases

Chemical substances that come in contact with the skin may be in the form of vapours or gases. Vapour is defined as a diffuse, poorly visible substance suspended in the air, like mist, fumes or smoke. Gas has a more restricted meaning.

11.1.2 Droplets

Liquid products present as droplets in the air are a major source of harmful airborne agents. There are numerous examples on the market, such as sprays, paints, cosmetics (perfumes), insecticides, pesticides, and other hairsprays.

11.1.3 Solid Nonbiotic Particles

This group includes dust particles and fibers. In most cases, the agents responsible are in the form of "dust" of various chemical origins. These may be substances in a pure state or else

Table 11.2 Examples of the most common airborne agents

1. *Vapours and gases*
Formaldehyde, fumes of burning plants, metal soldering fumes, phosphorus sequisulfide fumes, mustard gas
2. *Droplets*
Sprays such as insecticides, perfumes, paints, hairsprays
3. *Solid non biotic particles*
Dust particles: resins, cement, anhydrite
Fibers: fiberglass, rock wood, carbon fibers
4. *Solid biotic particles*
Particles of vegetal origin: pollen, exotic woods dust
Particles of animal origin: scales, caterpillar hairs

particles with a complex chemical composition (compounds with numerous constituents). Dust particles are ubiquitous in work environments: they are transported by air and can agglomerate, visibly or invisibly, on the surface of the skin. Some dust particles are chemically inert and provoke only mechanical (friction) injury to the skin, whereas others have a chemical base that may be dissolved by sweat and cause irritation or chemical allergy. Some examples of dust particle are cement, resins, and anhydrite [2].

Various types of fibers can be involved [15]. The classic example is fiberglass; others include rock wool, carbon fibers, and plastic materials (polypropylene fibers). Many fibers are chemically inert but they can still cause harm through mechanical trauma of the skin. Others, such as epoxy-coated fiberglass, can induce allergic reactions.

11.1.4 Solid Biotic Particles

In some cases, airborne agents can be solid biotic particles of vegetable (pollen, dust from exotic woods) or animal origin (scales, caterpillar hairs).

11.2 Predisposing Physical and Constitutional Factors

Particular physical conditions can often predispose to the development of airborne dermatoses (Table 11.3) [4, 16]. Low environmental humidity alters the skin barrier as a result of reduced ceramide levels in the stratum corneum [17]; when it is lower than 35%, it fosters the spread of the substances in the environment [18]. At high temperatures there is increased perspiration, that facilitates the adhesion and absorption of harmful contactants through the skin. High temperatures also make some substances volatile (dimethylthiourea) [19], promote the passage from the liquid to the gas state (liquid mustard gas) and the desiccation of plants, dispersing their particles. In this regard, in fact, airborne contact dermatitis from plants is reported above all in hot countries where plants wither very easily and the dry fragments become volatile. The same dermatitis is infrequent in Europe, and in more humid countries in general [20–22].

In particular in cases of persistent atopic dermatitis, airborne proteins (house dust mites, cockroaches, pet dander, and plant pollen) can act as exacerbating factors. The impairment of the natural skin barrier present in the same complaint induces a greater penetration of the airborne particles in the epidermis and consequently leads to airborne contact dermatitis [23].

Seborrhoeic dermatitis of the face and dermographism can also favor skin penetration of substances dispersed in the environment. Finally, a facial eruption has been reported in visual display operators, which favours the onset of airborne contact dermatitis from particles present in the workplace [24].

Table 11.3 Risk factors in airborne dermatoses

1. *Environmental factors*
Low humidity (<35%) alters the skin barrier, reducing ceramide values in the stratum corneum, and favours dispersion of substances in the environment
High temperatures increase perspiration, make some substances volatile, promote the passage from liquid to gas and favour plant dehydration
2. *Constitutional factors*
Sweating favours substance agglutination and absorption
Atopic dermatitis
Seborrhoeic dermatitis of the face
Dermographism
3. *Physical factors*
Friction
Pressure

11.3 Airborne Contact Dermatitis

Airborne contact dermatitis is an inflammatory reaction linked to various contactants suspended in the air. The diagnosis of this complaint is based on the patient history and on follow-up, observation of the presence of dust or of volatile causative agents, on the distribution of the lesions and on the results of patch tests [25]. Although the clinical-morphological diagnosis of airborne contact dermatitis is not generally difficult, identifying the causative contactant and selecting appropriate treatment often pose a considerable challenge for the dermatologist.

Epidemiology and Pathogenic Mechanism. The prevalence of airborne contact dermatitis is difficult to estimate, for various reasons. First of all, detailed organic descriptions of the complaint date back only to the end of the 1980s and early '90s [1–4]. The etiological diagnosis is usually challenging as it involves recomposing a puzzle; sometimes the clinical diagnosis is difficult too, especially in cases where not only sites exposed to airborne contact are affected but also covered sites, as frequently occurs.

Further complicating the situation, different pathogenic mechanisms may be triggered, depending on the various types of contact with the particles suspended in the air. As stated above, in fact, the same substance very often comes in contact with the skin contemporarily via direct and airborne contact, thus confusing the clinical picture and making an immediate diagnosis very difficult. Sometimes, for example, when the hands are affected by direct contact and the face by airborne contact with the same substance (e.g. various dusts and powders), there may be a tendency to interpret the disorder as a primitive contact dermatitis of the hands with id-like manifestations on the face, excluding the diagnosis of airborne contact dermatitis. Moreover, the same substance suspended in the air can be simultaneously inhaled and/or ingested, causing systemic symptoms in various organs as well as objective skin manifestations that may be attributed to a systemic contact dermatitis.

From the epidemiologic standpoint, airborne contact dermatitis can be classified as occupational and non occupational. The common belief is that occupational forms are more frequent than non occupational, in the same way as airborne irritant contact dermatitis is thought to be more common than allergic form of airborne contact dermatitis. Although the disorder can be caused by a great number of agents, many of which have been reported in the literature as case reports or small case series, the prevalence of a particular etiological agent varies widely from nation to nation, depending also on the degree of industrialization and the climatic conditions. For all these reasons, it seems evident that the incidence of airborne contact dermatitis is likely underestimated. Indeed, bearing in mind the great variety and notable ubiquity of causal agents present in the environment, it is bound to be more common than would appear from the literature.

As regards airborne skin diseases, another important problem is that of percutaneous absorption: it is not clear why a substance that simply settles on the skin should be absorbed without any appropriate vehicle. However, recent studies in vivo and in vitro have inequivocably demonstrated that apart from the classic passive horizontal absorption through the multilayer intercellular lipid structures and the transcellular corneocytes route, there is a third absorption route, this time vertical, through the appendices (follicular apparatus of air follicles and sweat glands) and through microlesions in the interfollicular horny layer [26–31]. These structures can offer a vertical pathway for percutaneous absorption, i.e. a "shunt". In the past, hair follicles and sweat glands were considered of little importance since they account for only a small and insignificant percentage of the skin surface: only approximately 0.1% of the skin surface area [26]. But actually, the hair follicle shows a surprisingly high influence on the penetration process, that may serve in particular in the case of airborne contactants [26].

Clinical Features. The skin symptoms of airborne contact dermatitis do not generally have any special or peculiar morphologic

Table 11.4 Clinical diagnosis of airborne contact dermatitis

No peculiar clinical-morphologic characteristics
History of airborne origin of the dermatitis
Sites of lesions:
1. Sites exposed to the air
a. Face ("shaded" areas): upper eyelids, behind the ears, submandibular region, nasolabial folds
b. Neck, nape of neck, scalp, hands, wrists, forearms, lower legs (in women)
2. Non exposed areas
a. Major body folds (axillae, groin, popliteal and antecubital fossae)
b. Occluded sites (gloves, shoes, boots, rings, glasses)
Generally symmetrical lesions with faint edges
Possible conjunctivitis, systemic symptoms, prevalently of the airways

characteristics and can thus be confused with those of common contact dermatitis of the corresponding category. The clinician must base the diagnosis of the airborne origin of the dermatitis mainly on two factors: the case history and the site of the lesions. It must be remembered that airborne contact can affect both exposed and covered sites, whatever the chemical-physical nature of the contactants, because all such agents (droplets, gases, dust, powder) can cross or impregnate clothing (Table 11.4).

The most common sites for airborne contact dermatitis are the parts of the body that are exposed to the air: the face (Fig. 11.1), neck (Figs. 11.2, and 11.3), upper aspect of the chest ("V" region of the neck), hands, wrists, underarms, and sometimes lower legs in women. Dermatitis affecting these sites must firstly be differentiated, often with some difficulty, from photocontact dermatitis. In photocontact dermatitis, however, "shadowed" anatomic areas such as the upper eyelids, behind the ears

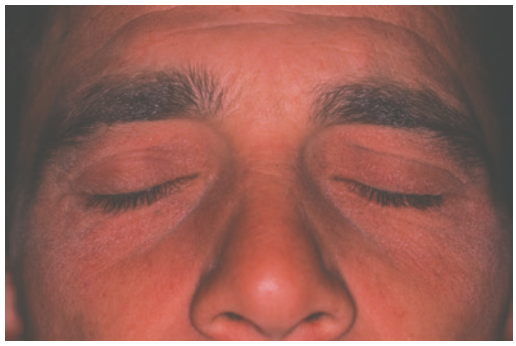

Fig. 11.1 Airborne contact dermatitis

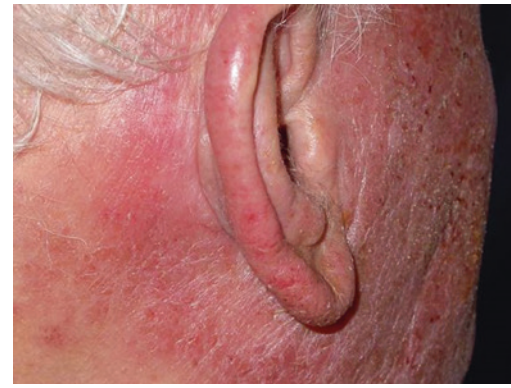

Fig. 11.2 Airborne contact dermatitis of the "Wilkinson's triangle"

("Wilkinson's triangle"), the submandibular region and under the hair (scalp and nape of the neck) are not affected [1, 2, 4, 5, 9, 10, 12]. The nature of the causal agent and the results of photopatch tests can guide differential diagnosis with classical contact photodermatitis.

The upper eyelids are particularly susceptible to airborne irritants or allergens, which can easily become trapped and so accumulate in this area. Moreover, the skin of the eyelids is particularly thin and so easily penetrated by chemicals. The upper eyelids are sometimes the only area affected and, on occasion, are associated with acute conjunctivitis. In cases of nickel allergy, for example, skin lesions around the eyes only can be observed. These lesions are sometimes so symmetrical that it is difficult to believe the allergen is simply carried on the hands, as is normally postulated. Apart from the possibility that

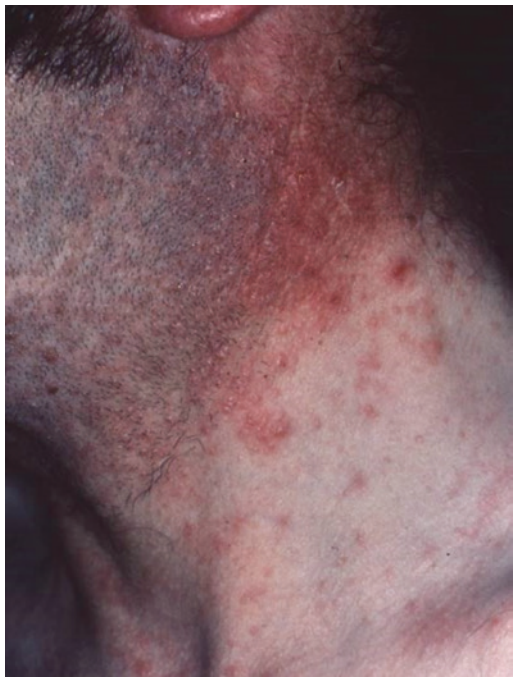

Fig. 11.3 Airborne contact dermatitis with irregular borders on the neck (Courtesy of Prof. Jean-Marie Lachapelle)

they may be an id-like manifestation from hematogenic spread of the allergen, it is likely that nickel present in the air as dust may contribute to the onset of this clinical picture [1, 14, 32–34]. In fact, in working environments the monitoring of nickel and chrome in the air in plants working areas processing these metals has revealed levels well beyond those recommended [32].

Apart from photoinduced contact dermatitis, the differential diagnosis of facial and neck airborne contact dermatitis must include contact dermatitis due to directly applied agents, connubial (consort) dermatitis, an id-like spread of a dermatitis elsewhere on the body, systemic contact dermatitis limited to the face, and an ectopic dermatitis (usually an asymmetric dermatitis, displaced from its usual site due to the transfer of allergenic particles from other sites of the body). Other eczematous diseases that must be taken into consideration in the differential diagnosis are atopic dermatitis and seborrhoeic dermatitis limited to the face (Table 11.5).

The skin lesions can also occur on parts of the body not exposed to the air. Volatile substances (dust, gases, solid particles of animal and vegetal origin) and droplets can, in fact, penetrate the clothes. Dust particles accumulate in occluded sites, such as the genital area, and particularly in the major body folds (axillae, poplital and antecubital fossa). Of course, these cases need to be differentiated from atopic dermatitis, clothing dermatitis, or an id-like spread of contact dermatitis from other areas, all events that can also affect the major body folds.

In some exceptional cases, the clinical lesions can even be generalized, resembling erythrodermia, as a result of the high concentration of the causal agent in the air (for example, the expression of a Compositae dermatitis) [36], or as a result of heavily contaminated articles of clothing. In cases of contemporary inhalation of the causal agents, (sub)erythrodermic cases can be observed, simulating a systemic contact dermatitis [37].

Apart from the above-described skin symptoms, there can often be involvement of the mucosa (conjunctivitis, for example) and airways (in cases of inhalation of the same substances). Systemic symptoms are also possible (fever and the involvement of various internal organs) in cases of ingestion of the airborne agents.

Table 11.5 Differential diagnosis of airborne contact dermatitis of the face and neck

Contact dermatitis from directly applied agents
Photocontact dermatitis from directly applied agents
Connubial (consort) dermatitis
Ectopic contact dermatitis
Id-like spread of contact dermatitis from elsewhere on the body
Systemic contact dermatitis
Atopic dermatitis
Seborrhoeic dermatitis (worsened by work conditions: irritant fumes or dusts, increased sweating)
Polymorphic light eruptions

At clinical observation it is important to remember that it is fairly common to see patients who are affected contemporarily by direct contact dermatitis and by airborne contact dermatitis. This event is more commonly observed in occupational settings, when workers come in contact with the same substance both directly (while manipulating it) and in an aero-mediated manner (because it is present in the environment). In this context, the most common culprit substances are epoxy resin dusts, metal dusts, cement powder, fiberglass and medicaments in powder form. The same substance may also be present in the environment in different forms (powder and vapour, solid form and smoke, liquid form and gas), passing from one form to the other for natural reasons (temperature) or due to particular processing: various such examples are described below.

Apart from classic eczematous lesions (acute, subacute or chronic), airborne contact dermatitis can manifest with peculiar papulo-follicular pictures (fiberglass dermatitis) or as multiforme-like erythema (wood dust and the fumes of plants in combustion). In rare cases the disease can present as actinic reticuloid (parthenium dermatitis) [38] or prurigo nodularis (parthenium dermatitis) [39]. Airborne droplets from acids or alkalis can cause burns in exposed areas [7].

Finally, again from the clinical standpoint, it should be borne in mind that the same agent can induce different clinical pictures. Thus, airborne formaldehyde can cause contact urticaria [40], irritant reactions, and allergic contact dermatitis [41]. Airborne particles from *Parthenium hysterophorus* can cause both allergic and photocontact dermatitis [42]. Finally, airborne phosphorus sesquisulfide can cause contact urticaria [43] and allergic contact dermatitis [44].

11.3.1 Airborne Irritant Contact Dermatitis

Great numbers of airborne irritant contact agents have been identified up to now, nearly all in occupational environments (Table 11.6) [1–8, 10–12, 16]. In many cases, they are highly alkaline substances (pH > 10) whose irritant effect is both chemical and mechanical. Some examples of airborne contact irritation are reported below.

Table 11.6 Common airborne irritants

Acids and alkalis
Urea-formaldehyde insulating foam
Glass fibers
Epoxy resins
Rock wool fibers
Calcium silicate
Formaldehyde
Domestic cleaning products
Cement dust
Industrial solvents
Aluminium powder
Phenol-formaldehyde resins
Tropical wood dusts
Anhydrite
Perchloroethylene
Arsenical dust
Mica dust
Dyes
Mustard gas
Food additives
Caterpillar hairs
Sewage sludge
Paper, no carbon required (NCR) paper
Slag
Benzoyl peroxide
Trona
Trichloroethylene
Ammonia
Pesticides

11.3.1.1 Fiberglass Dermatitis

This is a classic and common example of irritant airborne contact dermatitis. Today, fiberglass is used in many different fields [45, 46]: principally for thermal and acustic isolation purposes in the building industry, for fireproofing, as chemical filters, as an "armature" for plastic items, as "reinforcement" for rubber materials, in air conditioning filters, supports of electric circuits, in the textiles industry (in draperies and curtains, for instance).

Fiberglass is obtained by means of various processing systems, through fusion and the subsequent spinning of vitrifiable raw materials, such as silica sand, kaolin, calcium carbonate, dolomite and feldspar [46]. Various additives can be mixed with the glass fibers depending on

the various uses: phenol-formaldehyde resins, epoxy resins, melamino-formaldehyde resins, polyvinyl acetate, silicones, urea, dyes, mineral oils.

The glass fibers that can provoke skin lesions are those with a diameter exceeding 4.5 μ [2, 47]. In the epidemics reported in work environments, the diameter of the incriminated fibers ranges from 8 to 20 μ. In fact, the pathogenic effect on the skin of glass fibers is directly proportional to the diameter (>4.5 μ) and inversely proportional to the length. By contrast, the risk of bronchopneumonia is inversely proportional to the diameter and length. Fiber glass-induced dermatitis is one of the most common occupational pictures of mechanical irritation. It generally arises in subjects after brief exposure, whereas in subjects with routine contact with fiberglass a certain tolerance seems to develop, that allows these workers to continue with their working activities without developing problems. In fact, very few of these workers apply for a job change [46].

The entity of the dermatitis differs according to various factors: individual susceptibility (in comparable working conditions, atopics are more prone to develop the dermatitis; there is a good correlation between the symptoms of fiberglass friction and the intensity of the dermographism; phototype I subjects are more susceptible); environmental conditions (high temperatures, low humidity, poorly aired environments and the concentration of fibers in the air foster the onset of the dermatitis); the duration of the exposure; the mode of contact of the fibers with the skin (direct, localized contact or indirect airborne contact, so more extended); the pathogenic mechanism of the dermatitis (mechanical-traumatic irritation through contact or intracutaneous penetration of the fibers, or else contact allergy to the resins employed in the fiber glass work process).

In an occupational setting, the skin manifestations can follow direct manipulation of the fibers; in these cases the dermatitis will feature pruritus and punctiform excoriations on the backs of the hands. The penetration of the fibers under the peronychium can cause chronic paronychia, and under the nailbed, onycholysis. Other clinical signs have sometimes been reported: eczematous lesions or others of nummular eczema type, purpura, folliculitis, urticaria and telangiectasia.

Most often, fibers suspended in the air reach the uncovered sites, but also some particular covered sites by insinuation under workers' clothing. The subjective signs of the dermatitis will be pruritus and pricking sensations; objective signs are erythematous papules measuring 0.1–0.5 mm in diameter, excoriations, lesions due to scratching and occasionally pustules. The same micropapules, with a purpuric hue, can also interest the hair follicles. The preferential sites are the skin folds (axillae, groin, popliteal fossae, elbow folds), the extensory faces of the limbs and the belt zone (Figs. 11.4, and 11.5). Sweating fosters agglutination of the fibers.

The dermatitis sometimes follows the release into the environmental air (in both occupational and non occupational settings) of fibers released from defective air conditioners. The symptoms are largely subjective, consisting of pruritus of the face and neck. Small epidemics due to this problem can arise in office, schools and families. A pruritus that affects small groups of subjects must always suggest the possible diagnosis of a fiberglass dermatitis.

Exceptionally, glass fibers can penetrate into the derma and provoke the formation of foreign body granulomas. Sensitization to the resins covering the fibers is rarely observed. The onset of fiberglass dermatitis occurs after 2–3 hours from the contact and it resolves within a few days if exposure is eliminated; a chronic course is rarely observed.

Histopathologic examination demonstrates erosion of the distal epidermal layers and the formation of scabs, the presence of fiberglass fragments in the stratum corneum and spinosus, subepidermic detachment and a perivasal mononuclear lymphocytes infiltrate. In rare cases, some aspects of spongiforme dermatitis are observed, more frequently in atopics, and the picture of a foreign body granuloma. Polarized light inspection of slides allows a better identification of the fiberglass fragments.

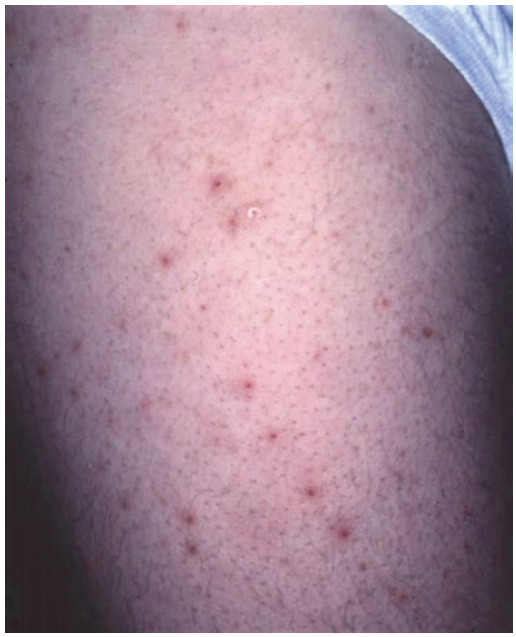

Fig. 11.4 Airborne irritant contact dermatitis due to glassfibers

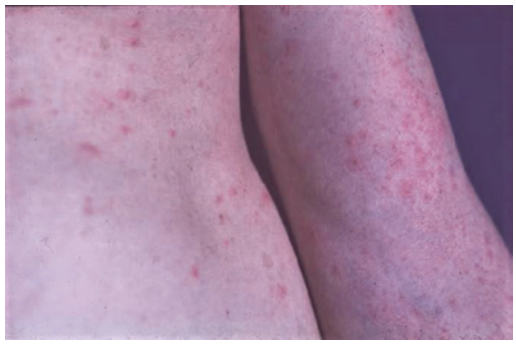

Fig. 11.5 Airborne irritant contact dermatitis due to glassfibers

The diagnosis relies largely on the medical history and clinical examination. A search for glass fibers is made by surface biopsy, consisting of stripping of the corneal layer by chemical (with one or two drops of 20% potassium hydroxide) or physical means (using adhesive tape), that is then directly observed at the microscope. Differential diagnosis needs to be made with various other pruriginous and extensive forms of dermatitis due to exogenous causes (Table 11.7) and sometimes, especially in chronic and peculiar cases, with Hodgkin's disease and aspecific chronic leukemia pictures.

Table 11.7 Differential diagnosis of fiberglass dermatitis

Eczema prurigo
Animal acariasis
Pediculoses
Epidermal zoonoses
Papular urticaria
Actinic prurigo
Scabies
Phytodermatoses
Hodgkin's disease
Cutaneous lesions in chronic leukaemia
Cereal acariasis

In general, workers fitting fiberglass products are those most exposed and hence at risk of the disease, more so actually than those working at fiberglass factories, because the fiberglass concentrations in the environmental air can vary greatly depending on the application method and the air saturation in the work area. Table 11.8 [48] lists some fiberglass dermatitis prevention criteria. Treatment is based on low potency corticosteroids. Barrier creams, siliconated or not, are not found to offer efficacious prevention of the dermatitis.

It should be remembered that patch test reactions to mineral fibers, although secondary to mechanical irritation, can simulate an apparently allergic reaction [49] and so are not recommended. Possible allergy to mineral fibers is more often linked to epoxy and phenol-formaldehyde resins. Nevertheless, in many cases it may be necessary to analyze the chemical substances in the fibers to ensure a correct diagnosis of the related contact allergy [49].

11.3.1.2 Dermatitis Due to Other Fibers

Rock wool dermatitis is comparable to fiberglass dermatitis. Rock wool is composed of minerals, coal and limestone, added with mineral oils, silicone compounds and phenol-formaldehyde resin.

Other types of fibers that can induce dermatitis, generally of milder type, are *cellulose* and *cardboard fibers,* used in packaging, *mica fibers* and *synthetic polypropylene fibers* (synthesized

Table 11.8 Criteria for the prevention of fiberglass dermatitis

1. Closed cycle production must be ensured, to minimize dispersion of the fibers and hence exposure
2. Storage and transport of fiberglass products must be done in special sealed containers
3. Products must be prepared in advance in the forms required for installation, to reduce to a minimum the subsequent dispersion during cutting and modeling
4. Felts must be applied using suitable tools and must be cut at the application site with hand tools not electric machinery
5. Except when specifically stated otherwise, spray isolation procedures must be done using wet not dry techniques
6. The working areas, both for production and processing, must be regularly cleaned with a proper aspiration system or vacuum cleaning. Normal cleaning can leave glass fiber residues in the environment
7. Perfectly sealed plastic containers must be used for the transport of fiberglass products and processing residues
8. It is essential that the removal of isolation materials comply with the above-stated norms, especially as regards wetting the materials and vacuum cleaning work areas
9. Appropriate overalls ensuring proper protective isolation must be used, and properly cleaned, frequently and separately from other clothing to avoid contamination

as fiberglass replacements for some uses; the fiber particles are 10 μ in diameter). *Carbon fibers* can also be used as partial or complete substitutes of fiberglass, as already done for tennis rackets, for instance. They induce a dermatitis characerized by pruritus of a more or less intense type and excoriated papules; they too have a diameter of about 10 μ.

11.3.1.3 Dust Dermatitis

In such cases the dust consists of a pulverulent blend of solid particles light enough to remain suspended in the air. They can be chemically inert (such as aluminium dust) or else, after agglutinating on the skin, they release irritant chemical substances (such as cement). Some have a crystalline structure with sharp edges, others an amorphous appearance. The most common dusts mentioned in the literature are listed in Table 11.6. The clinical picture is comparable to that induced by glass fibers.

C*ement dust* dermatitis is fairly common in cement factories. Being very pulverulent, cement insinuates under workers' clothing and overalls, and also agglutinates on the face. Irritation is particularly severe in cases of excessive sweating, that dissolves some alkali cement components. Dry cement irritation is frequent in cement factories but less so at building sites, where damp cement diseases are prevalent (burns, irritant contact dermatitis, allergic contact dermatitis). In all cases, air-induced irritation is favored by a relatively low rate of environmental humidity in the air.

Trona dermatitis has been described in miners and trona workers [50]. Trona, or sodium sesquicarbonate, is extracted from mines in Wyoming in the USA and processed to make glass, paper, detergents, as well as for chemical applications. It is an alkaline dust (pH 10.5) and can have irritant effects on the airways, mucosae and skin. Trona dermatitis is characterized by pruritus, and dry erythematous lesions of the hands (direct contact), face and limbs (airborne contact).

Anhydrite is an anhydrous calcium sulfate dust with traces of calcium fluoride and hydrofluoric acid. It is very highly alkaline (pH 11.2), and is used in coal mines to fix metal railings to the rock. Anhydrite-induced skin irritation has been observed in coal miners performing this procedure. The only manifestation is subjective signs of pruritus or burning of the face, neck, forearms and thighs. No erythema or eczematous lesions develop [51]. The irritant action of alkaline anhydrous paste has been demonstrated by laser Doppler flowmetry: repeated application of the substance on the flexory face of the forearm in healthy volunteers induced an increased blood flow in the more distal dermal layers. This dermatitis is a classic example of a purely subjective airborne irritant contact dermatitis with no objective clinical signs. Replacing anhydrite by a less alkaline paste (hemihydrate) was successful in solving the problem.

Slag dermatitis is observed in the metallurgic industry [52]. Slag (a mixture of silicium and

calcium oxides, or other oxides) is poured onto melted steel in the procedure known as continuous steel casting. While the slag is poured, being extremely pulverulent it raises a thick cloud of dust. The particles insinuate under workers' overalls from the wrists or ankles and accumulate in the skin folds and extensory faces of the limbs. The objective and subjective clinical signs are comparable to those of fiberglass dermatitis. Microscopic examination of the dust particles shows crystals in various sizes and shapes (about 10–80 μ long) and cutting edges. The latter characteristic suggests a skin insult of mechanical type. Replacing these with larger, rounded slag particles resolves the problem. Cases of airborne irritation due to sewage sludge [53], indigenous and exotic woods dust, and food additives dusts [54] have also been reported.

The diagnosis of airborne dusts-induced dermatitis is based on the medical history, clinical examination and other specific procedures (Table 11.9). Microscopic examination of the dusts is done under polarized light. In the case of dusts in crystal form or with sharp edges, the shape itself may play an irritant role, even if this has not yet been experimentally verified. The presence of dust particles on the skin can be established using the stripping method and subsequent polarized light examination. It is essential to determine the dusts pH, by suspending the particles in bidistilled water and determining the pH of the supernatant. Some dusts are highly alkaline (cement, dyes in powder form) but, more rarely, they can be acid. The acidity or alkalinity is an important irritation factor. Finally, it is essential to control the percentage of environmental air humidity.

Table 11.9 Diagnostic procedures in dust-carried airborne irritant contact dermatitis

Microscopic examination of the dusts (polarized light)
Determination of dusts on the skin (stripping with adhesive tape)
Determination of dusts pH
Control of environmental humidity percentage
Exposure tests

The treatment is the same as for fiberglass dermatitis, while prevention relies on proper aspiration systems, ventilation and hygrothermal control of the work area, and when possible, automation of the work cycles. Individual prevention measures are only appropriate overalls because barrier creams are inefficacious.

11.3.1.4 Airborne Dermatitis from Sprays, Vapours, and Gases

A less frequent observation is airborne irritation due to vapours and gases. In general, the dermatitis affects the face; however, some vapours and gases impregnate clothing and so are responsible for lesions on covered body areas.

Dermatitis from Vapours

Among vapours, some acid and alkali substances producing them are well known and common irritants. Ammonia is widely used. Exposure to formaldehyde can occur in industrial, crafts and domestic environments. Emanations of formol stem from various preservatives present in soluble oils and isolation materials with a urea-formaldehyde resins base [55]. Peroxides, like benzyl peroxide, are released into the air during the manufacture of plastic materials, and are particularly irritant.

Some organic solvents used to dry clean clothing can also be culprits. Those best known are perchloroethylene (tetrachloroethylene: $Cl_2C{=}CCl_2$), the solvent most commonly used in closed cycle machines, trifluorotrichloroethane (F_2 Cl CC Cl_2 F) and trichloroethylene (Cl HC$=$$CCl_2$), that is least used owing to its high toxicity. Occupational dermatitis forms caused by organic solvents are due to defective machines at laundries, giving rise to perchloroethylene emanation or to perchloroethylene residues from clothes that have been dry cleaned [5].

It is no rare occurrence for vapours and gases to be released from solid substances at high temperatures. To disinfect rubber pacifiers, for example, they are usually boiled but rubber chemicals can become volatile and cause airborne contact dermatitis in sensitized subjects. In fact, a substance that is not harmful at normal temperatures can become very volatile

and hazardous at higher temperatures. Indeed, if plastics are heated, they may decompose into approximately 50 different products, some of which are irritants and/or allergens [7]. In the paint and printing industries, various solutions of paints and printing inks are spread, casting vapours and droplets in the air [7].

In the literature, there have been reports of skin damage due to self-defence sprays, that are sometimes wrongly used as weapons. In many countries these tear gases are freely available on the market; they are considered not to induce severe complications, and their effects are assumed to last about half an hour and leave no sequela. This is not actually true. Some tear gases (lachrymators) contained in them are the same as those used for military and civilian (by the police force) defence purposes in order to neutralize a subject through the immediate lachrymogenic effect, and ensure his immobilization for a few minutes. About fifteen different substances are used for lachrymogenic purposes in self-defence sprays [56]. The most common and harmful are chloroacetophenone (CN) ($C_6H_5COCH_2Cl$) and ortho-chlorobenzylidene malonitrile (CS). Other synthetic tear gases, much less commonly used, include bromobenzyl cyanide (CA), ethyliodoacetate, bromoacetone, benzyl iodide, benzyl bromide and some others.

The oleoresin of capsicum (Cayenne pepper from *Capsicum frutescens*, or "poivre rouge" in French) is a natural lachrymogenic used in sprays. For some times, the US government has issued aerosol sprays containing this oleoresin to postal carriers for their defence against animals, especially dogs. It is also contained in self-defence 'objects' (like lipstick or a fountain pen) present on the market. Oleoresin is a dark red liquid, extremely bitter and pungent, that irritates the conjunctivae and nasal and oral mucosa; it is also an efficient repellent against man and beast (organic or synthetic lachrymators do not affect animals).

CN (or phenacyl chloride), that has been known since the First World War, is a powder that is insoluble in water but soluble in alcohol and ether; it is very irritant for the skin, eyes and respiratory tract. In self-defence sprays it is dissolved in 1,1,1-trichloroethane. CS (named after Carson and Stoughton who invented it in 1928), that is also insoluble in water, is an irritant with a faster action than CN, but is less toxic; in sprays it is present in concentrations of 2–8% and dissolved in methylethylketone. The effects of CN and CS have been studied in animals and in man [56]. Skin irritation or sensitization phenomena have been observed in industrial environments among workers at a chemical factory producing them [57] and in subjects sprayed with a lachrymogenic [56–62].

In fact, lachrymogens can have two skin effects: most cases are due to airborne contact irritation, but some are due to airborne contact allergy. In the case of subjects sprayed with a lachrymogen in the street, the skin lesions appear immediately, and immmobilize the subject due to erythema and intense burning of the face, which is often affected only on one side because the spray is activated from the side. By the next day there is remarkable facial edema, especially of the eyelids, of Quincke type, and blisters with skin detachment. The dermatitis resolves within about two weeks.

However, a different clinical evolution has also been described: after an initial improvement, by the fifth to the eighth day the skin manifestations reappear in the previous sites and also at a distance. Perhaps an immunoallergic mechanism can be attributed to the event in such cases, arising from systemic effects of the lachrymogen, or else a situation comparable to the allergic dermatitis induced by dinitrochlorobenzene owing to intrinsic properties of the substance itself. The phenomenon could also be linked to the persistence of the lachrymogens in powder in the hair or on clothing, or else in the pilosebaceous follicles. Because CN and CS are not hydrosoluble, and CS has some affinity for oily substances, it is important that the initial copious washing be done with solvents of grease and oily substances.

Ocular complications, that can be of variable severity and persistence, are frequent, such as conjunctivitis, corneal lesions and even sight disturbances. In black-skinned subjects CN can provoke skin depigmentation.

Skin tests, even if they are not recommended, can be done with CN and CS crystals in a pure state; the substances are solubilized in acetone at a dilution of 1:100.000. The tests must definitely not be done with substances present in the sprays available on the market.

Lachrymogens released in the air deposit in the form of powder, so it is necessary to change all clothing, accurately cleanse the eyes, and the skin with a facial milk or detergent. Lesions can be treated with corticosteroid and antibiotic creams.

Mustard Gas Dermatitis

We observed an exceptional, practically unthinkable irritant airborne contact dermatitis in 12 deep-sea fishermen [4, 8, 63, 64]. The disease was due to mustard gas or yperite (2,2'-dichlorodiethylsulfide, $C_4H_8Cl_2S$), one of the most aggressive war gases. The name derives from the city of Ypres (Belgium), where it was used for the first time in bombs in July 1917. The British and Americans call it mustard gas because of the characteristic smell. Yperite is an oily, odorless and colorless liquid in the pure state, and it is the impurities (ethylsulphides) that cause the yellowish-brown color and the smell of mustard. Poorly soluble in water, it dissolves readily in organic solvents and fats. This feature facilitates its penetration in the cells, where it has toxic effects. Mustard gas evaporates slowly owing to the low tension of the vapour, even if it increases as the temperature rises. It is toxic in both liquid and vapour form; in the first case it damages the skin; in the second, the skin, conjunctivae and respiratory mucosa. Its effects appear after a latency period ranging from 4 to 6 hours up to 24 hours.

Since the First World War, intoxication by yperite has been almost exclusively associated with occupational contact in producers, except for its wide use in the Iraq-Iran war (1980–1988) [65]. In the 1950s, cases of acute or chronic intoxication were reported in workers at factories producing yperite or at retrieving ferrous residues of unused war materials [66, 67].

The 12 cases of yperite dermatitis we observed were fishermen in the Adriatic sea, working in deep waters off the coast of Molfetta, 30 km to the north of Bari. More than one hundred cases of dermatitis of variable severity have been reported to the Coastguard at the port of Molfetta. The concentration of such cases in the same Adriatic zone is due to the fact that a company packaging and depackaging war weaponry was located in Molfetta. After the Second World War, war surplus weaponry was thrown into the sea a few miles off the coast. These residues are brought back up to the surface by fishermen in their trawling nets during the summer months when this fishing activity is practiced. All the fishermen tell the same story. They find bombs in their nets together with the fish (in fact, the risk is well known in the profession) and throw them back in the sea. However, owing to erosion, the bombs leak non hydrosoluble liquid that impregnates the nets and after a few hours, direct irritant contact dermatitis of the hands and forearms develops. This features erythemato-vesico-bullous lesions of various sizes, with a pale serous content (Fig. 11.6). Owing to the high summer temperatures, the liquid evaporates and also induces an irritant airborne contact dermatitis of exposed sites (facial erythema and blisters, eyelids edema and severe conjunctivitis with lachrymation and photofobia), as well as some covered sites because mustard gas clings to clothes (Figs. 11.7, and 11.8). In three cases we observed intense erythema and edema of the genitals, and the subsequent onset of bullous lesions with a necrotic and escharotic evolution (Fig. 11.9). Intense pruritus and burning accompany these skin lesions.

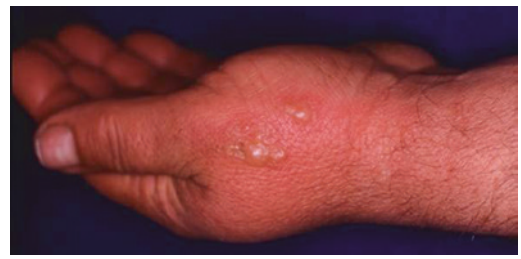

Fig. 11.6 Blistering direct irritant contact dermatitis from mustard gas (Reproduced with permission by Bonamonte and Coll [68])

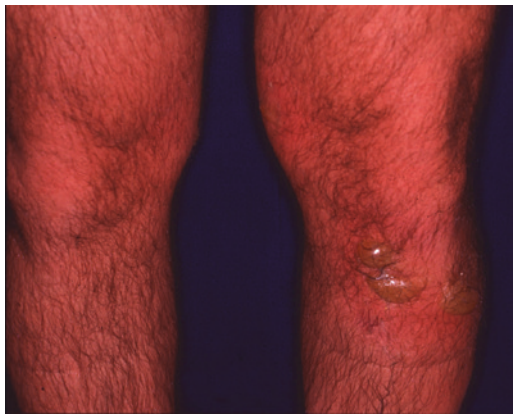

Fig. 11.8 Blistering airborne irritant contact dermatitis from mustard gas (Reproduced with permission by Bonamonte and Coll [68])

In six patients, the skin symptoms were associated with headache, coughing, nausea and vomiting [68]. The dermatitis resolved in 10–15 days leaving hyperchromic marks. In one case localized on the genitals, scars were left. The conjunctivitis resolved with washing using 2% sodium bicarbonate and antiseptic eye-drops. Systemic symptoms, due to inhaling the gas, regressed rapidly with symptomatic treatment. Controls after 20–30 days excluded any re-presentation of the dermatitis [68].

Although chemical bombs are present in all European seas, similar cases of dermatitis from mustard gas have only occasionally been reported [69, 70], probably because it is practically impossible to connect the disease with contamination by fishing nets unless the bombs are actually seen in the nets. Otherwise, the skin symptoms may be attributed to the harmful action of some marine flora and fauna [71].

Fishermen should be informed of the risk of fishing up bombs in particular areas, and must be instructed to throw them back into the water without opening them and in cases of inadvertent contamination, to go straight to hospital for proper treatment. All the contaminated areas of the boat must be thoroughly cleaned and the fishermen's clothes and personal effects must be destroyed. Mustard gas can impregnate clothes and leather objects and persist for a long time. In fact, we have also observed cases of contamination of members of the family due to contact with the fisherman's clothing.

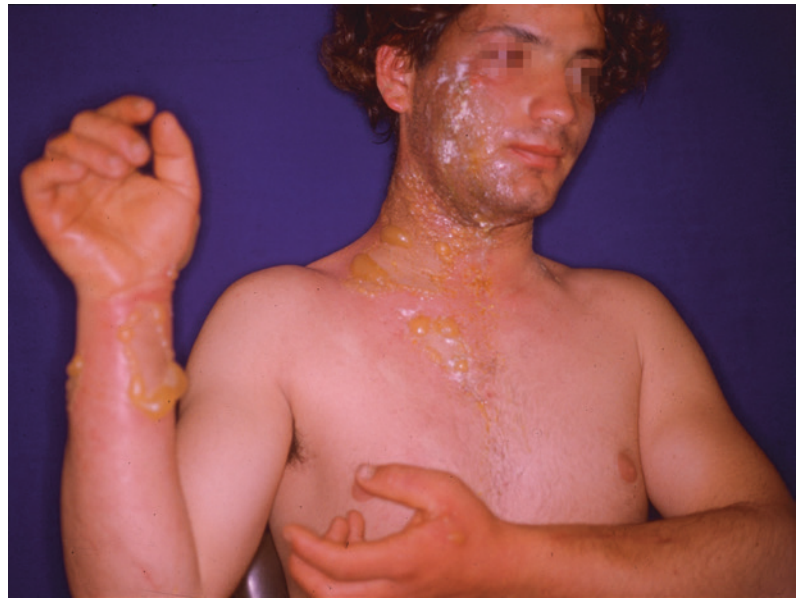

Fig. 11.7 Blistering airborne irritant contact dermatitis from mustard gas (Reproduced with permission by Bonamonte and Coll [68])

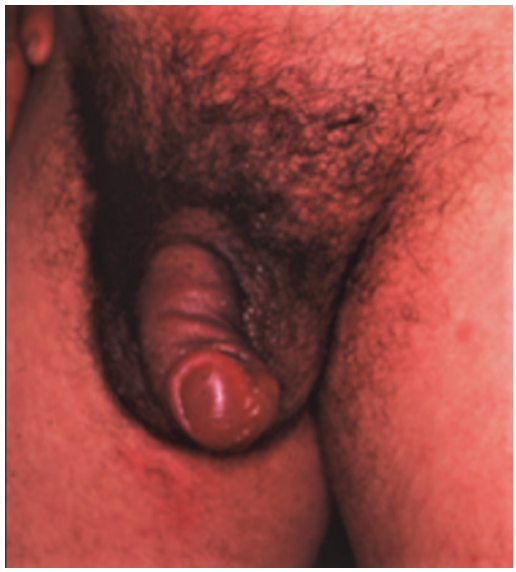

Fig. 11.9 Erythemato-edematous airborne irritant contact dermatitis from mustard gas (Reproduced with permission by Bonamonte and Coll [68])

Volatile Products of Photocopying Paper

The symptoms provoked by emanations of volatile products from photocopying paper include irritation of the skin, eyes and respiratory tract (obstruction of the upper airways), asthenia, nausea and headache. At skin level there is pruritus and burning, above all of the face but sometimes also of the oral and nasal mucosa. These complaints are observed in office workers. The nature of the irritant substances varies according to the types of paper [5, 72, 73].

In some cases formol emanations occurred while handling photocopying paper. Tests with various constituents of the paper were negative. It was observed that the symptoms developed above all when handling new packs of paper, likely due to the release of an organic solvent still present in the freshly opened paper [5]. Occasionally, such symptoms are observed in workers at photocopying paper factories. On one occasion, whose physiological agent was not identified, the pruritus was accompanied by irritation of the upper airways, asthenia, contact urticaria and increased PGF-2 prostaglandins [74].

Propellant and Ethylene Oxide Dermatitis

Halogenated hydrocarbons (freons) were widely used in the past but have now been replaced by various other substances because they were poorly biodegradable and so concentrated in the atmosphere, lasting for hundreds of years. They were rarely sensitizing (trichloromonofluoromethane, dichlorodifluoromethane, tetrafluoromethane) [75–77] but highly irritant. The propellents most commonly used nowadays are butane, propane, isobutane liquified petroleum gases (LPGs) gelled propellants, and compressed gases (nitrogen or carbon dioxide) [76].

Ethylene oxide is a colorless, gaseous, simple epoxy compound whose sterilizing action is due to an irreversible toxic effect on living cells. It is therefore essential to remove any trace of ethylene oxide from sterilized items before the products come in contact with human tissue [78]. Gaseous ethylene oxide is one of the most common sterilizing agents used for medical equipment and materials. Given its harmful properties (it is also genotoxic) [79], in the US precise recommendations are made regarding its use [78]. Various cases of irritation and burns, and of contact allergy from ethylene oxide have been reported in hospital and industrial settings [80–82].

11.3.2 Airborne Allergic Contact Dermatitis

Airborne contact allergy has a lower incidence than airborne irritation but is more often reported owing to the notable symptoms. These are those of common allergic contact dermatitis. The lesions are generally symmetrical, with an acute or chronic evolution, depending on the nature and concentration of the allergen and the frequency of airborne contact. The localization of the dermatitis is fairly characteristic. The sites most often affected are those exposed to the air: the face, neck, décolleté, hands, forearms and legs in women. On the face, the lesions affect the eyelids most severely, in the form of edema, the conjunctiva (pruritus,

reddening, lachrymation, photofobia), retroauricular regions and submandibular region. In some cases only the eyelids and conjunctiva are involved but covered areas can also be affected, such as the folds, where solid particles can insinuate under clothing and accumulate.

There are many culprit agents (Table 11.10) [1–11]. Classic examples of the most commonly observed causal agents of airborne contact allergy are epoxy resins, present in many industrial sectors in the form of dusts or droplets (in the metalmechanical industry). Cement dust (Fig. 11.10), in particular in cement factories, can cause allergic airborne contact dermatitis owing to its chromium or cobalt content. Such cases affect the face, generally inducing a dry, lichenified dermatitis associated with conjunctivitis (Figs. 11.11, 11.12, and 11.13).

Dermatitis from vapours, usually of occupational origin, can be induced by amines used as epoxy hardeners and resins [83, 84]. In the past dermatitis of the face caused by vapours from turpentine, a solvent used in various occupational sectors, including woodworking, was common. The picture, that features intensely erythemato-edemato-exudative lesions, is rarely seen today (Figs. 11.14, and 11.15).

Additionally, rubber, glues, metals, pesticides and insecticides, and many other industrial and pharmaceutical substances have been reported as causes of airborne dermatitis. Forms due to pesticides droplets sprayed on plants are often observed in agriculture, showing clinical manifestations in both exposed and covered sites, since the drops impregnate clothing. The main culprits are thiourams, that can also be used in the production of medicaments. Nobecutane® spray, containing tetramethylthiouramdisulfide, a fungicidal and bactericidal aerosol whose use was recommended for disinfecting the skin and protecting wounds, could induce airborne allergic reactions on the face in subjects previously sensitized to thiourams by direct contact. We have observed two such cases, in a mechanic (Fig. 11.16) and a housewife who developed facial rashes after using the spray to treat contact dermatitis of the hands due to thiourams [8].

Table 11.10 Most common airborne allergizing substances

1. *Metals*
Chromates in cement and welding fumes
Cobalt
Nickel
Silver
Mercury
Gold
Arsenic salt
Beryllium
2. *Solvents*
Formaldehyde
Turpentine
3. *Pharmaceutical chemicals*
Albendazole
Chloroquine sulfate
Spiramycin
Chlorpromazine
Semisynthetic penicillins
Streptomycin
Virginiamycin
Quinolone compounds
8-Methoxypsoralen
Benzalkonium chloride
Apomorphine
Chloracetamide
Chloroquine sulfate
Quinoline compounds
Vincamine tartrate
Diphencyprone
Ethylenediamine
Paracetamol
Propacetamol
4. *Insecticides and animal feed additives*
Carbamates
Pyrethrin
Pesticides
Captan
Captafol
Dyrenium
Ethoxyquin (antioxidant)
Oxytetracycline
Penicillin
Tetrachloroisophthalonitrile
Tetrachloroacetophenone
Tylosin
5. *Aquatic animals*
Bryozoans

Among non occupational forms, airborne contact dermatitis can develop due to fragrances in sprays. We observed two young women with contact allergy at the axillae caused by

Table 11.10 (Continued)

6. *Plastics,* rubbers, glues
Acrylates
Cyanoacrylate
Benzoyl peroxide
Diaminodiphenymethane
Dibutylthiourea
Epoxy acrylates
Epoxy resins
Formaldehyde resins
Phenolformaldehyde resins
Isocyanates
Rubber additives
Unsaturated polyester resins
Polyurethane
7. *Plants* and wood allergens
Lichens (d-usnic acid)
Compositae (sesquiterpene lactones)
Frullania (sesquiterpene lactones)
Poison ivy (urushiol)
Poison oak
Poison sumac
Parthenium hysterophorus
Acacia melanoxylon
Alstroemeria (tulipalin A)
Apuleia leiocarpa (wood)
Citrus fruits (lemon essential oils)
Pine dust
Dalbergia latifolia
Essential oils
Garlic
Helianthus annuus
Primula obconica
Chlorophora excelsa (iroko)
Machaerium scleroxylon
Barley dust
Sawdust
Tulipalin A in tulip bulbs
Soybean
Tea tree oil
Tropical woods
Anthemis nobilis

Table 11.10 (Continued)

8. *Miscellanea*
Color developers
Bromophthalide
Hydrogen sulfide
Cytosine arabinoside
Bromomethyl-4-nitrobenzene
Cigarettes and matches
Phosphorus sesquisulphide
Pig epithelia
Penicillium
Isothiazolinones
Methyl red
Isofluorene
Hydroxylammonium chloride
Pyritinol
Pyritinol hydrochloride
Tyrophagus putrescentiae
Glutaradehyde
Chloracetamide
Propolis
Colophony
Hair sprays
Deodorants
Chloroacetophenone
Fragrances
Halogenated compounds
NCR paper
Dimethylthiourea
Persulfates
Allylphenoxyacetate
Dimethoxane
Paraphenylenediamine
Persulfates
Thiourea
Dimethylthiourea

fragrances (intense positive patch tests reactions to cynnamic aldehyde). They developed an intense erythemato-edematous reaction on the face and especially the eyelids, after visiting a perfumery where fragrances were continually sprayed into the environment (Figs. 11.17, and 11.18). In one of the two cases, an exposure test to a perfume containing cynnamic aldehyde was followed by eyelids erythema and edema [8]. In both cases, the women were, of course, subjects with a very low sensitization threshold to fragrances. Similar cases have been reported by other authors [1].

Cleaning products [1] often trigger allergic airborne contact dermatitis together with various other household products. A notable example is the dermatitis from isothiazolinone, increasingly used as a preservative in many household products [16, 85].

11.3.2.1 Plants and Woods in Airborne Dermatitis

Woods and plants are often causal of airborne contact dermatitis: the allergens are dried botanical material and smoke from burning plants. The plants families most often responsible for airborne allergic contact dermatitis are the

Fig. 11.10 Ciment dust as cause of airborne contact dermatitis

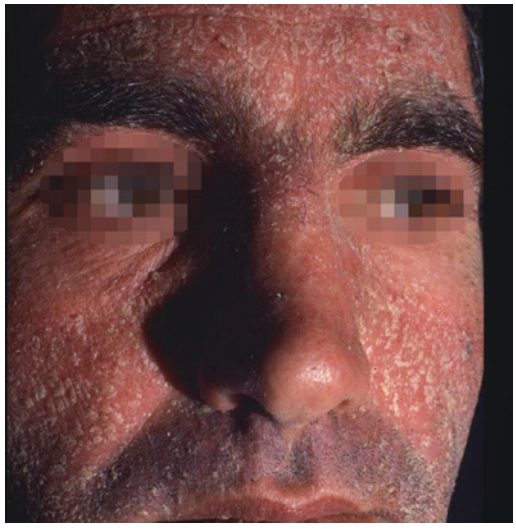

Fig. 11.11 Airborne allergic contact dermatitis due to chromium in ciment dust

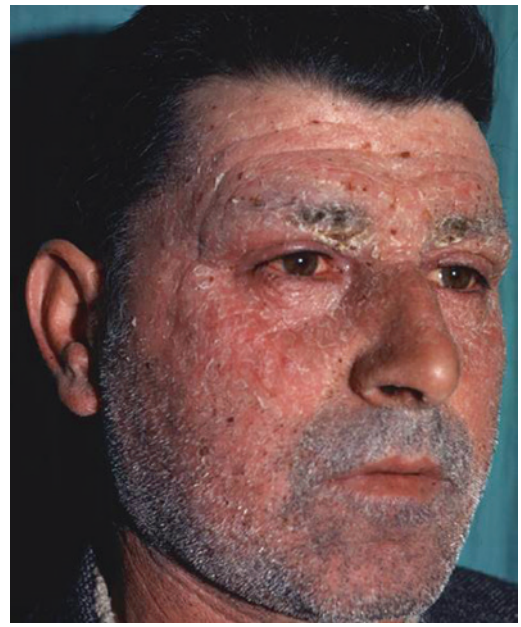

Fig. 11.12 Airborne allergic contact dermatitis and conjunctivitis due to chromium in ciment dust

Compositae family and the Anacardiaceae family [11, 86–88]. Among the Compositae, well known causal plants are ragweed, sunflowers, goldenrod and chrysanthemums. Their flowers, leaves, stems, and pollens contain sesquiterpene lactones, responsible for the allergic reactions.

Airborne allergic contact dermatitis is commonly caused in the USA by plants of the *Toxicodendron* genus of the Anacardiaceae family: poison ivy, poison oak, and poison sumac. These plants exude a sap which contains a highly allergenic oil, urushiol [16], present in various portions of the plants (including

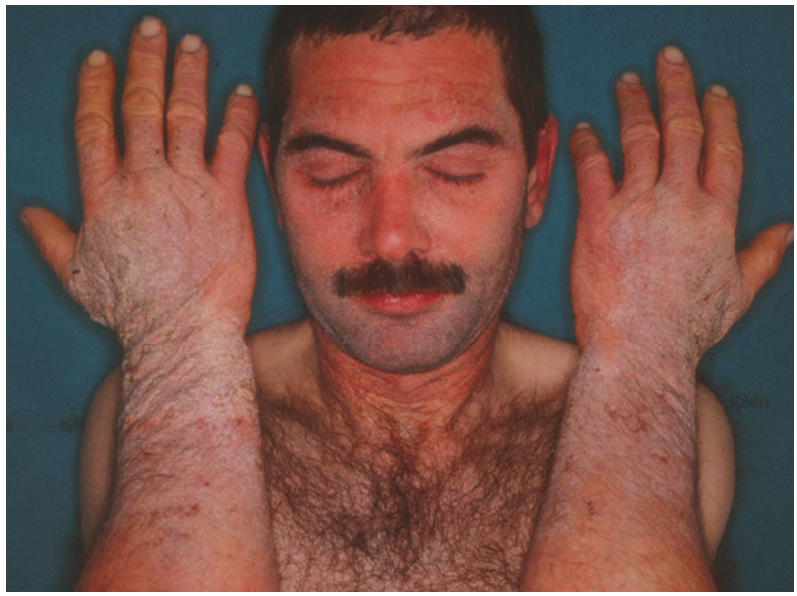

Fig. 11.13 Airborne allergic contact dermatitis due to chromium in ciment dust

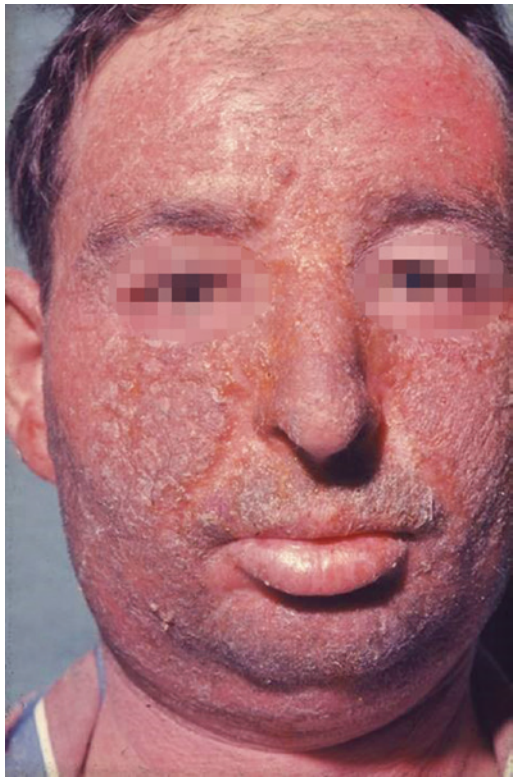

Fig. 11.14 Intensely erythemato-edematous airborne allergic contact dermatitis from turpentine vapours

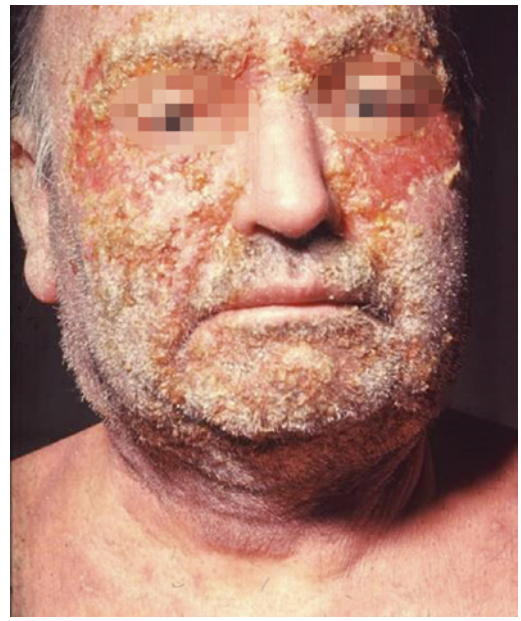

Fig. 11.15 Intensely erythemato-edemato-exudative airborne allergic contact dermatitis from turpentine vapours

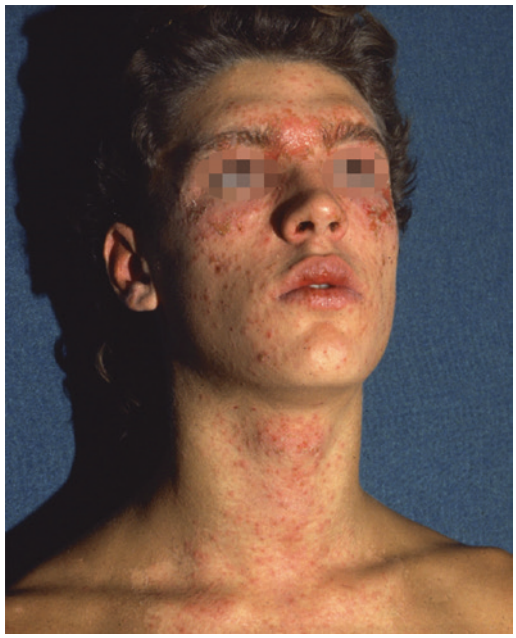

Fig. 11.16 Airborne allergic contact dermatitis from a thiurams-based spray in mechanic with contact dermatitis of the hands by tetramethylthiouramdisulfide

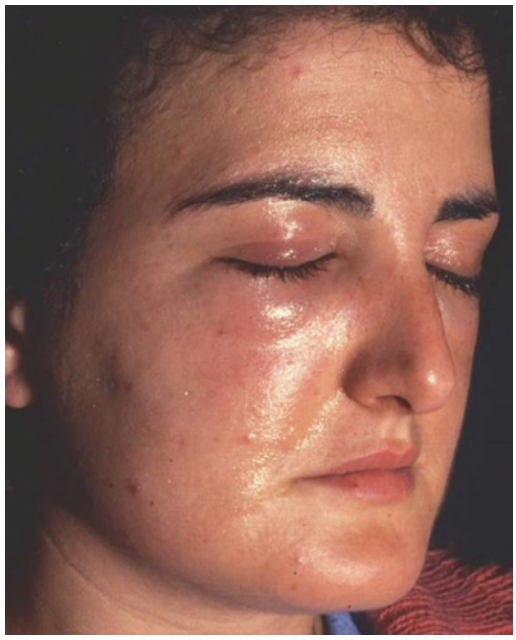

Fig. 11.17 Airborne allergic contact dermatitis to fragrances sprayed in the environment

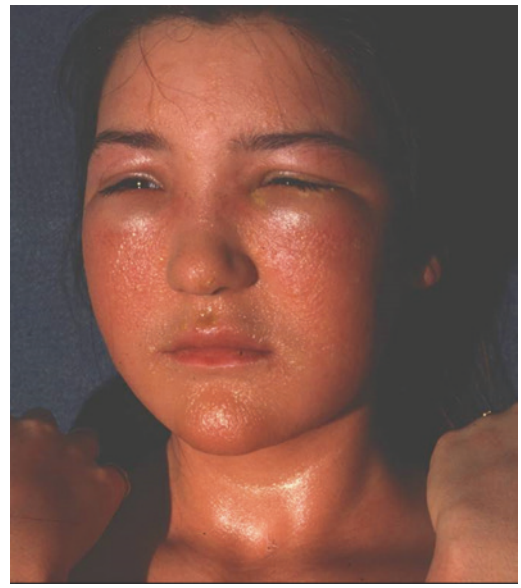

Fig. 11.18 Airborne allergic contact dermatitis to fragrances sprayed in the environment

the roots, stems and leaves), even when they are dried. Dead poison ivy plants are still toxic, because urushiol remains active for several years. Although poison ivy rash is usually a summer complaint, cases sometimes occur also in winter, when people burn wood containing urushiol or cut poison ivy vines for wreaths [87]. In short, these plants are toxic in all seasons. Urushiol penetrates the skin a few minutes after contact, and in allergic subjects the reaction appears within 12–48 hours. In cases of airborne contact dermatitis, the rash affects both sites exposed to the smoke, and covered sites because urushiol clings to clothing, which must be immediately removed and machine washed or else dry cleaned. The rash lasts 10–15 days, and is particularly severe on the face, with intense eyelid edema. It is often of erythema multiforme-like type. Exposed sites must be washed with running water and soap within a few minutes of contact. For preventive purposes, barrier creams used on uncovered sites are sometimes helpful [87]. Some patients' claims that they developed a reaction to poison ivy simply by walking through the woods are absolutely true. It is important to be

aware of the fact that patients allergic to plants of the genus *Toxicodendron* may develop cross-reactions to various other substances, including mango skin, cashew nut oil, and the fruit of the ginkgo biloba tree [16].

Poison ivy, poison oak and poison sumac grow almost everywhere in the USA, except Hawaii, Alaska and some desert areas of Nevada. Poison ivy usually grows east of the Rocky Mountains and in Canada. Poison oak grows in the Western US, Canada, Mexico, and in the southweastern states. Poison sumac grows in the eastern states and Southern Canada [87].

Florists are often exposed to various plants families, including the Compositae (Asteraceae), the plants most often causal of airborne contact dermatitis [21]. A study by Hausen and Oestmann showed that 50% of florists have dermatitis of the face; the plants most often to blame are chrysanthemums, tulips, and *Alstroemeria* [88].

Florists and homemakers are also exposed to plant oil sprays, which are used to make the leaves look more shiny. These sprays contain a rubber chemical, tetramethylthiuramdisulfide, which may cause allergic airborne contact dermatitis in pre-sensitized people [7].

Various airborne dermatitis forms due to contact with woods are occupational in carpenters, joiners, cabinet makers, and associated trades subjects [89]. The most sensitizing woods are of tropical and subtropical origin; dusts from these woods can cause airborne contact dermatitis as well as an erythema multiforme-like eruption [90].

In hot and dry regions, pulverized parts of dead plant material become windborne and can induce dermatitis of the exposed skin, that may be mistaken for a photocontact dermatitis [91]. Although in many cases pollens are inculpated, in the case of ragweeds and related members of the Asteraceae family finely pulverized material from dead plants is more likely the causative agent [36, 92]. Various species of lichens (consisting of a fungus and an algae growing together in symbiosis), present on walls, roofs, trees, and rocks, are sensitizing: an airborne contact dermatitis of the face was reported in subjects allergic to these lichens [93].

11.3.2.2 Airborne Skin Lesions Due to Pesticides

Pesticides are the only toxic substances intentionally released into environments to kill living things [94]. As well as their use in agriculture for the control of pests (pesticides), weeds (herbicides), fungi (fungicides), and rodents (rodenticides), they are also used in horticulture, forestry, and livestock production, but their use is not limited to these sectors, and also comprises homes, schools, buildings, roads, and parks: indeed, it is difficult to find any place where pesticides are not used. They can also be present in the air, in foods and in the water we drink. Pesticides, herbicides and fungicides are the major groups (Table 11.11) [94–98].

Many pesticides are potentially very harmful to human health (Table 11.12) [94–102]. They have been linked to a wide range of health hazards, ranging from short-term impact (headaches, diarrhea, fatigue, nausea) to chronic impact (cancer, reproductive harm, endocrine disruption). They are potentially hazardous to other organisms in the environment and may also cause damage to ecosystem.

Pesticides are normally classified according to their specific activity, while the active ingredients are often indicated by their common name or even a trivial name. The WHO classification by the degree of acute hazard to humans is widely used: class Ia (extremely hazardous), Ib (highly hazardous), II (moderately hazardous), and III (slightly hazardous). They are formulated in different ways: solid or liquid concentrates, solutions or emulsion in water or organic solvents, aerosols, granules, powders, mixed with sand, dusts and fumigants [97]. Together with the active ingredients, pesticides contain other non active ingredients and possibly contaminants, many of which are toxic substances while some are known skin irritants and allergens (organic solvents, formaldehyde, isocyanates) [97].

Many subjects suffer skin exposure to pesticides at work, above all sprayers, mixers, loaders, packers, and mechanics. Workers may be exposed to pesticide residues on treated plants and wood, because although some are

Table 11.11 Most common pesticides and repellents

Insecticides and acaricides
Organophoshate compounds (malathion, parathion)
Pyrethroids
Pyrethrum (natural compound from *Chrysanthemum cinerariaefolium)*
Methylcarbamates
Organochlorates (lindane)
Herbicides and desiccants
Thiocarbamates
Organonitrogens (triazines, phenylureas, nitroanilines, anilides)
Dipylidium compounds (paraquat)
Aliphatic chloroacids (diquat)
Dinitrophenols
Phenoxycarboxylic acids
Fungicides
Inorganic compounds (sulfur, copper, iron sulfate, barium polysulfide)
Dithiocarbamates (zineb, ziram, maneb, mancozeb)
Organonitrogens (benomyl)
Thiophthalimides (captan, captafol, difolatan, folpet)
Rodenticides
Coumarin compounds (warfarin, ANTU)
Fumigants
Halogenated hydrocarbons
Repellents
N,N-diethyl-*m*-toluamide (DEET)
Wood preservatives
Chlorothalonil (also a fungicide)
Tributyltin oxide
Glutaraldehyde (also slimicide)
Methylchloroisothiazolinone/methylisothiazolinone (together with arsenic, chromium, and copper compounds, also slimicide)

Table 11.12 Health hazards of pesticides

Bone-marrow effects (leukemia, Hodgkin's disease, non-Hodgkin lymphoma)
Cancer (brain, bone, breast, ovarian, prostate, testicular, liver)
Endocrine system effects
Reproductive system effects
Birth defects
Behavioral disorders
Enzymes induction
Eye lesions
Respiratory effects
Systemic poisoning
Immunological effects
Skin diseases
· Chloracne
· Chemical burns
· Contact dermatitis (irritant and allergic)
· Hyperpigmentation
· Hypopigmentation
· Photosensitivity
· Nail dystrophy
· Porphyria cutanea tarda
· Squamous cell carcinoma

rapidly degraded others persist in the air for variable periods of time. Various different methods are employed to assess exposure [103]. Cholinesterase activity in erythrocytes or in plasma must be determined in workers using organophosphorus compounds. Some pesticides and their metabolites need to be measured in the urine. Skin exposure can be assessed by the fluorescent tracer technique, and by analyzing pesticide levels in patches on the skin. The body sites most strongly exposed are the face and hands but all unprotected areas can be affected (Figs. 11.19, and 11.20). Percutaneous absorption of pesticides varies remarkably from one product to another. The sites of greatest absorption are the scrotal skin, head and neck. The degree of percutaneous absorption also relies on occlusion, the duration of contact, the concentration, preexisting skin damage, humidity and the environmental temperature.

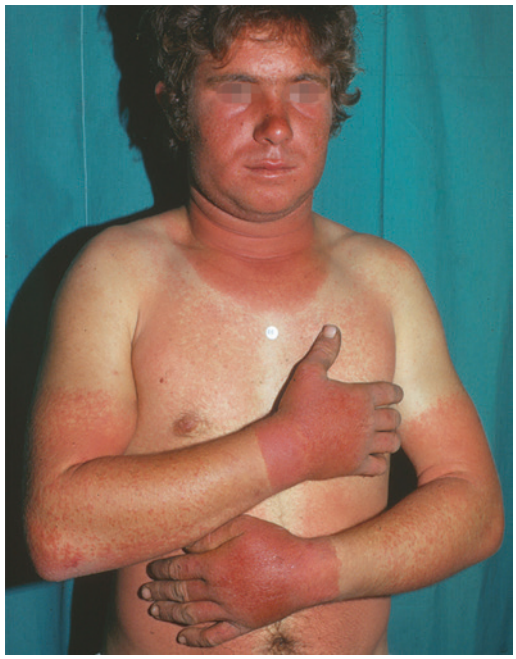

Fig. 11.19 Airborne allergic contact dermatitis of uncovered and not well covered areas due to pesticides

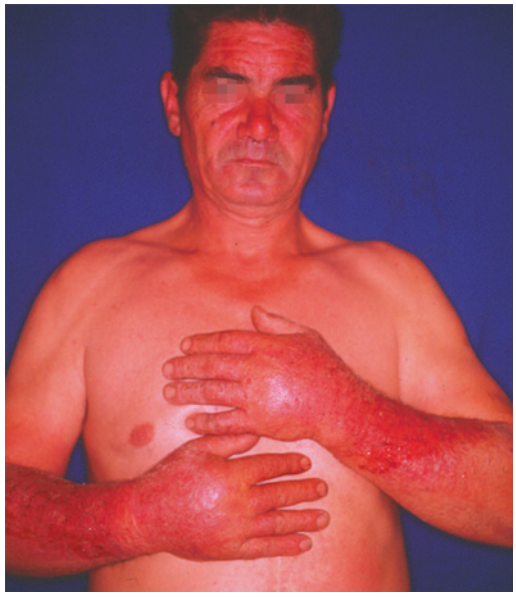

Fig. 11.20 Airborne allergic contact dermatitis of uncovered areas due to pesticides

The prevention of skin exposure must take into account various important rules, especially in subjects at high risk, such as pesticides applicators, mixers, and producers. Protective equipment must be properly used, cleaned and maintained in good shape. The gloves offering the best protection are nitrile/butyl rubber gloves or laminate gloves. Barrier creams are not effective as protection measures [97]. Protection norms vary in different parts of the world and are, of course, worst in the poorest developing countries, where the most harmful pesticides are often used without any protective measures at all. Aerial application can be extremely harmful in various occupations (pilots, ground crew, field workers) and for residents near sprayed fields. In this regard, it is important to reduce the duration of the spray season, ban the use of "flaggers" (workers in the fields who guide the pilot during spraying) and favor tractor spraying [102]. Guidelines for personal protection and for field surveys have been published by the WHO and other organizations.

The prevalence and incidence of skin reactions to pesticides are not known but are surely higher than reports in the literature would suggest [104–107]. Irritant contact dermatitis is believed to be more frequent than allergic contact dermatitis (linked particularly to insecticides and fungicides). Fatal effects have been linked to acute toxic reactions to the percutaneous absorption of organophosphorus compounds.

Patch tests must be carried out with active ingredients and with other ingredients the patient is known to be exposed to, but it may be extremely difficult to obtain the various ingredients. In general, some patch test clinics have their own pesticides series, related to the pesticides most commonly used in that geographic area [107]. A pesticide can be tested at appropriate dilutions from 1 to 0.1% in water or petrolatum. The active and other ingredients sometimes need to be further diluted. In any case, it is mandatory to check the pesticides implicated in the most recent reports and reviews to ascertain the safety and proper dilutions of the single ingredients. It is also important to patch test the same substances on control persons.

The health hazards from pesticides do not only depend on the toxicity of these chemicals but also on other factors, such as environmental conditions (hot weather, humidity, wind), methods of application, incorrect use of formulations, and failure to use adequate skin protection. Therefore, it is essential to promote specific widespread campaigns providing information and warnings in order to reduce the risk of skin and systemic damage in the various workers who come in contact with these substances in one way or another.

11.3.2.3 Airborne and Direct Allergic Contact Dermatitis

Very frequently, airborne and direct skin contact occur simultaneously. This is due to the fact that especially in occupational sectors, workers can come in contact with the same substance via different routes, particularly in the case of substances in powder form. Practical examples are dermatitis due to cement and powdered resins: the workers have both direct and airborne contact with these, owing to the strong concentrations in the air.

Sometimes the same substance can be present in the environment in different chemical-physical forms, for instance in solid form but also as fumes, or both in solid form and in droplets. A classic example of the first type is dermatitis due to phosphorus sesquisulfide contained in a particular type of matches (called "zolfanelli" in Italy, that are similar to the "strike anywhere" type) [8, 44, 108, 109]. The most common and well known complaint is allergic contact dermatitis due to direct contact, affecting the anterolateral face of the thighs and/or the anterior region of the chest, attributable to the habit of carrying the matches in a trouser or shirt pocket (Figs. 11.21, and 11.22). This picture is observed largely in males, usually agricultural workers and manual workers in general. Allergic airborne contact dermatitis, instead, affects the face and is linked to the phosphorus sesquisulfide fumes rising when lighting a cigarette (Figs. 11.23, and 11.24). The latter

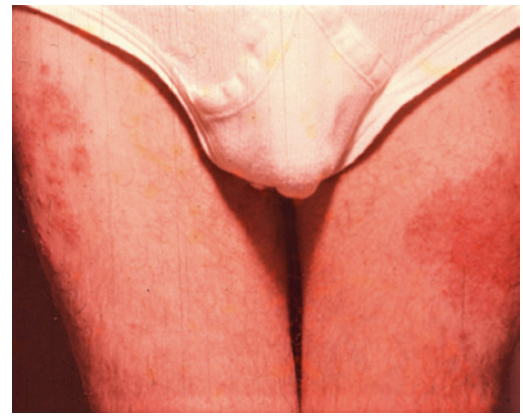

Fig. 11.21 Direct allergic contact dermatitis to phosphorus sesquisulfide in matches carried in trouser pockets

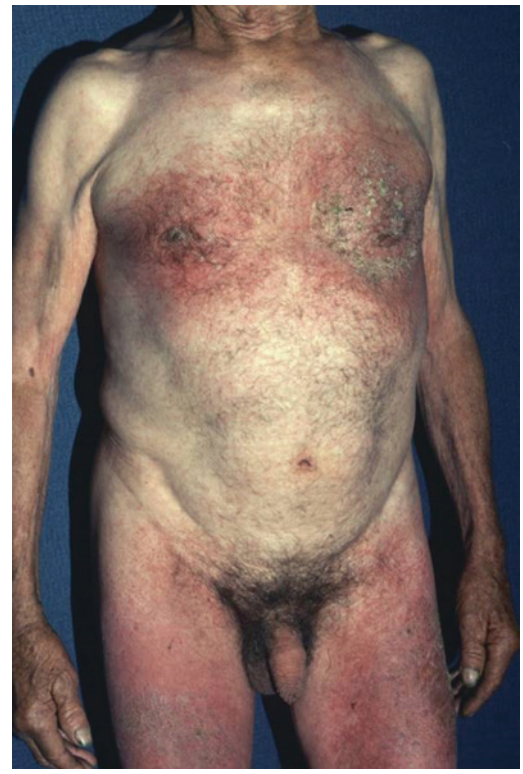

Fig. 11.22 Direct allergic contact dermatitis to phosphorus sesquisulfide in matches carried in trouser and shirt pockets

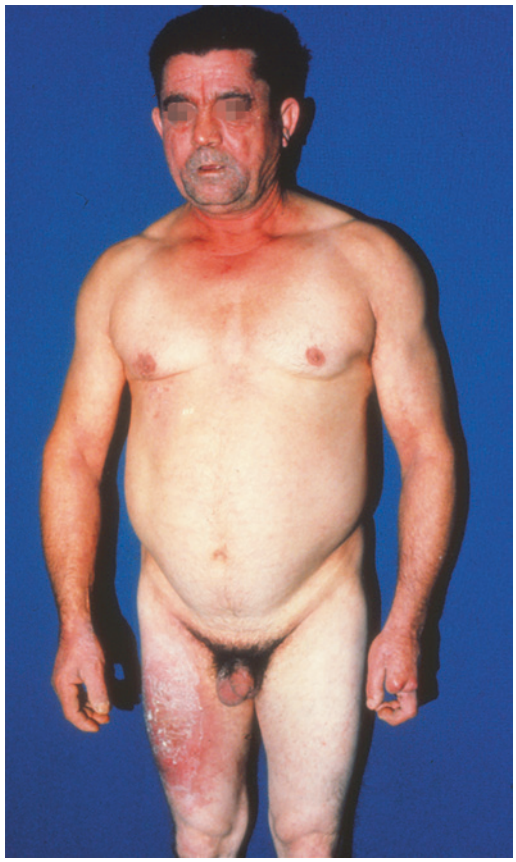

Fig. 11.23 Direct (right thigh) and airborne (face and neck) allergic contact dermatitis to phosphorus sesquisulfide

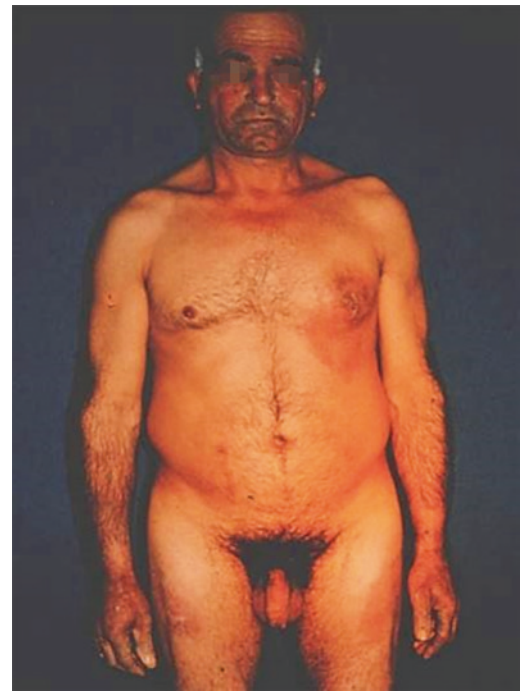

Fig. 11.24 Direct (thighs and left breast) and airborne (face and neck) allergic contact dermatitis to phosphorus sesquisulfide (Reproduced with permission by Angelini and Coll [44])

observation has also been described in women in Anglosaxon countries, provoked by "strike anywhere" matches (for pipes) [110]. Facial forms include erythema, often accompanied by eyelids edema, that can be asymmetrical, affecting only one side of the face. The affliction can in rare cases also affect the palms, again in asymmetrical fashion, due to the habit of cupping the hands around the flame when lighting a cigarette.

An example of the second type is contact dermatitis from Bryozoans [111]. It affects fishermen and was first observed in the North Sea (hence its first name "Dogger Bank Itch", from the Dogger Bank area in the North Sea) and then reported also in the eastern part of the Channel [112–114] and in the Bay of the Seine [115, 116]. Fishermen come in contact with "sea moss" or "seamats" when they pull their nets on board the boat and find them jumbled in with the fish. The hands and forearms are first affected through direct contact with the Bryozoans; the face and neck may be involved through airborne contact with drops of sea water containing the allergenic material. The allergen responsible is 2-hydroxyethyl dimethylsulphoxonium present in *Alcyonidium gelatinosum*, a filament-like zooarium that looks like a yellow-green-brown alga and that lives in colonies attached to hard substrates (rocks, shells, gravel, stones) in filaments about 20–30 cm long [106]. Patch tests can be made with fragments of live Bryozoans just after harvesting, with seawater containing the allergen and aqueous and acetonyl extracts of seamoss.

11.3.2.4 Direct and Airborne Contact Dermatitis Associated with Inhalation

Pulverulent substances, present in both occupational and non occupational settings, can come into direct or airborne contact with the skin while also being inhaled. In this event, owing to the multiple pathogenic mechanism, dermatitis is usually accompanied by systemic symptoms that can also be severe. Various examples include that of mustard gas in liquid form and giving off vapours, as already described [63, 64], while another example is chloric acne as described below.

A particular dermatitis caused by contact with mercury was observed [37]. This form had a triple underlying pathogenic mechanism, observed in subjects following the use of MOM ® in powder form (with an ammoniated mercury and metallic mercury base) for pubic phthiriasis. The intense erythemato-exudative lesions of the genitalia, pubic region, and internal plane of the thighs (due to direct contact during the application of the powder), were associated with involvement of the face, neck, folds, and trunk (airborne contact resulting from airborne spread of the powder) (Figs. 11.25, 11.26, 11.27, and 11.28) and with systemic clinical signs (fatigue, high temperature and leukocytosis) due to inhaling the powder [37, 117].

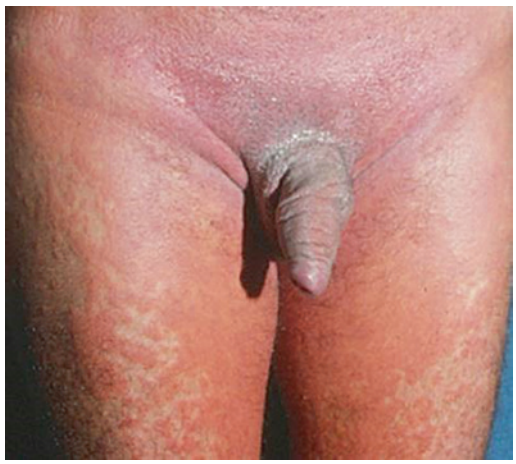

Fig. 11.25 Direct and airborne allergic contact dermatitis due to ammoniated mercury used for pubic phthiriasis

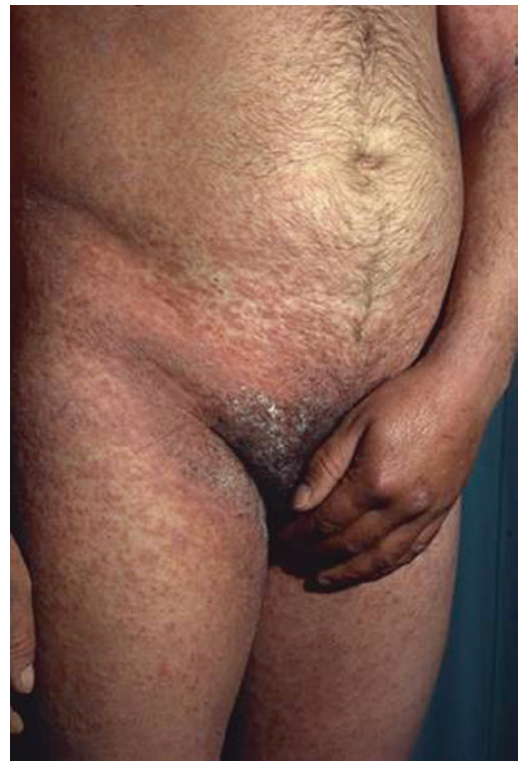

Fig. 11.26 Direct and airborne erythema multiforme-like eruption due to ammoniated mercury used for pubic phthiriasis (Reproduced with permission by Angelini and Coll [117])

11.3.3 Airborne Photocontact Dermatitis

Airborne photocontact reactions affect sites exposed to light. In theory, there are no clinical signs enabling a clear differentiation between photodermatits due to direct or to airborne contact. In practice, however, in non airborne forms some parts of the face are relatively or completely spared (region under the chin, retroauricular regions, upper eyelids), whereas in airborne forms no part of the face is spared. Nevertheless, there are many exceptions to this rule, so the diagnosis must be based on an accurate medical history, analysis of subjective symptoms and objective signs, and the results of patch and photopatch tests.

Among the occupational phototoxic agents that can induce airborne contact dermatitis, polycyclic hydrocarbons and psoralens or

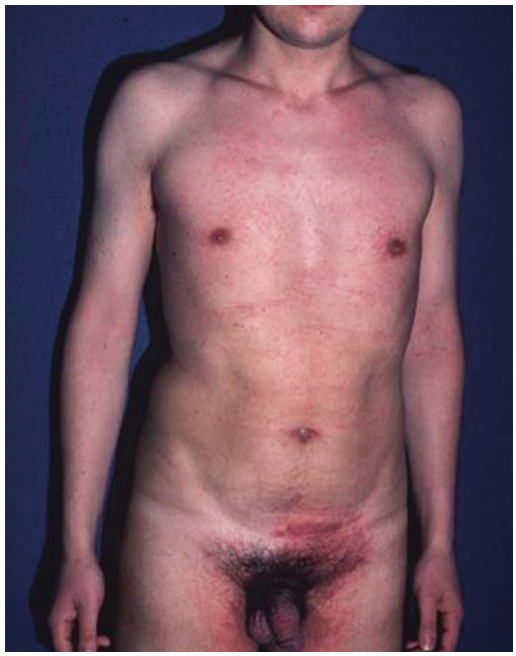

Fig. 11.27 Direct and airborne allergic contact dermatitis due to ammoniated mercury used for pubic phthiriasis

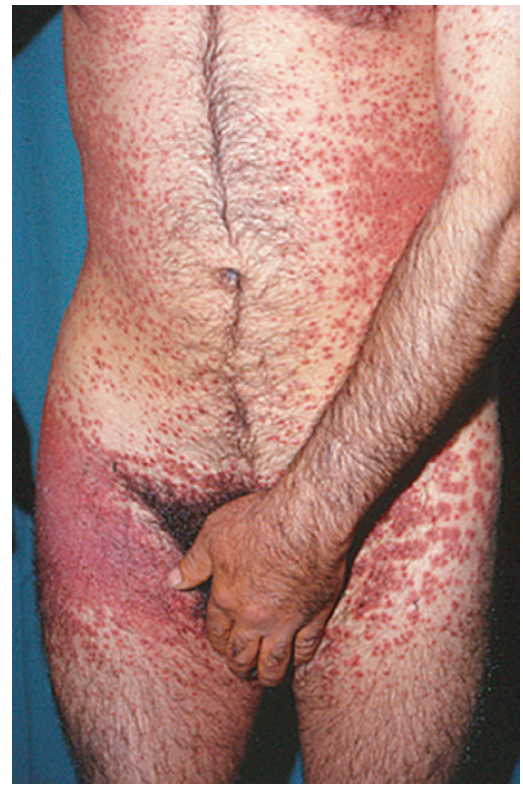

Fig. 11.28 Direct and airborne erythema multiforme-like eruption due to ammoniated mercury used for pubic phthiriasis (Reproduced with permission by Angelini and Coll [117])

furocoumarins are particularly important. The former (anthracene, pyrene, benzopyrene, and phenantrene) are present in carbon fossil tars, pitch and creosote. When heated, these compounds become volatile and on sunny days, can induce airborne phototoxic reactions in workers with asphalt, builders and railway workers. The eruptions, that sometimes appear in the form of small epidemics, can be prevented by applying total sunscreen products before starting work.

Furocoumarins are present in many plants. The presence of dry vegetable particles in the air during the summer favors the onset of the dermatitis (airborne phytophotocontact dermatitis) on uncovered skin sites. In a gardening concern sown with medicinal plants, an airborne phototoxic eruption due to *Heracleum sphondylium,* that contains methoxypsoralen, bergapten and imperatorin, was observed in a gardener [5]. Airborne phototoxic reactions to 8-methoxypsoralen were observed in three female workers confectioning tablets at a pharmaceutical company. After prolonged sunbathing at the end of the work, phototoxic lesions developed in the skin areas that were uncovered during work. The reaction was of mixed type, involving the hands (as a result of direct contact) and the face, décolleté, and arms (as a result of airborne contact). The airborne spread can be explained by the powdery nature of 8-methoxypsoralen tablets [118].

Airborne photoallergic contact reactions are very rare. Possible culprits are fragrance ingredients (in the cosmetic industry), coaltar derivatives, olaquindox, and several drugs (in the pharmaceutical industry).

Combined airborne and photoaggravated contact allergies are also possible, as observed for Compositae and lichens [119]. Vegetable particles of plants containing furocoumarins could also be implicated. In fact, in cases of direct contact dermatitis from *Ficus carica,* we also observed photoallergic reactions due to 8-methoxypsoralen [120].

11.4 Airborne Contact Urticaria

Among the various substances that can induce contact urticaria (immunological or non immunological), some are volatile or pulverulent, and these can undoubtedly cause airborne contact urticaria. Nevertheless, this mode of transmission has rarely been reported in the literature.

Allergy to natural rubber latex (usually derived from *Hevea brasiliensis*, of the Euphorbiaceae family) is an important health care issue today. Direct contact urticaria due to latex gloves involves the hands because natural rubber latex proteins are absorbed onto the cornstarch powder (derived from *Zea mais* L., family Graminaceae) in the gloves. When the packets are opened or the gloves are pulled out of multipack boxes, the proteins are released into the air and can induce various clinical problems, such as airborne contact urticaria of the face, conjunctivitis, rhinitis and even asthma [121, 122].

Other agents responsible for occupational airborne immunological contact urtcaria are cosmetics, vegetables, fruit, ammonium persulphate, animal hair, anhydrides [123]. Airborne contact urticaria reported in a warehouse worker resulted from exposure to dust derived from cinchona bark (*Cinchona* spp, family Rubiaceae) [124]. Processionary caterpillars can provoke various airborne reactions, mainly of urticarial type, both non immunological and immunological. The disease is common among foresters and also in non occupational situations (trappers and campers). Veterinarians, furriers and laboratory personnel working with furry animals can develop airborne contact dermatitis and airborne contact urticaria [7].

11.5 Airborne Atopic Dermatitis

The airborne nature of atopic dermatitis seems to be supported by some data, at least in a certain percentage of subjects, but the issue is still controversial [125].

Occasionally, the inhalation of dusts, pollens, and animal hair causes a flare-up of atopic dermatitis, and in some instances airborne allergens (dermatophagoides) produce positive patch tests reactions. Moreover, an alleviation of atopic dermatitis has been reported following the avoidance of aeroallergens [126]. In one study, a positive correlation was found between the severity of atopic dermatitis and the concentration of house dust mites in the home environment [127]. An exacerbation was observed following the inhalation or direct contact with algae and lichens [128]. In another study the inhalation of dermatophagoides was clearly correlated with worsening of the atopic dermatitis [129].

Langerhans cells express an IgE high-affinity receptor complex (FCεRJ) that is more than four-fold greater in the normal-appearing skin of subjects with atopic dermatitis than in non atopic control individuals [130]. This receptor activation leads to complete activation of Langerhans cells in atopic patients, but not in non atopic subjects.

11.6 Diagnostic Procedures and Prevention

Because there are huge numbers of irritant and allergizing agents carried through the air, and scattered widely in both outdoor and indoor environments, the skin diseases they induce are presumably very much more frequent than would appear from the literature. The problem is that the diagnosis of airborne contact dermatitis can be very difficult to make for various reasons. The approach to each individual case consists of various steps, that must take into account the physical-chemical environment (outdoor or indoor) for each patient and the availability of specific tests at the laboratory.

The classical tools available for diagnosing an airborne contact dermatitis include the medical history, clinical symptoms, any exacerbation of symptoms during work activities, determination of the presence of all possible causal agents at the workplace or in various outdoor environments, and a knowledge of the physical-chemical nature of these agents, as well as specific tests to be done in the patient or at the laboratory.

In general, as regards clinical-morphological aspects, airborne contact dermatitis should be suspected when faced with symmetrical lesions in sites exposed to the air, if the patient denies any use of topical agents and the symptoms improve or resolve when in a different environment. Meticulous inspection of the distribution of an eruption is critical for a correct diagnosis. "Exposed sites" in cases of airborne contact dermatitis are different from the "photoexposed sites" of photocontact dermatitis [131]. When observing a facial dermatitis, as a rough-and-ready rule, in non-airborne forms some parts of the face may be spared whereas no part will be spared in airborne forms but this is not an absolute rule and there are a number of exceptions, some of which are common. For example, allergic contact dermatitis to cosmetic products (fragrances, lotions, hair days) can mimic an airborne contact dermatitis, involving both exposed sites and photo-exposed sites. It can often be difficult to make a differential diagnosis between airborne contact dermatitis and atopic dermatitis limited to the face, bearing in mind that facial signs of atopic dermatitis could be triggered, worsened or even provoked by various allergens of high molecular weight (mainly proteins) present in house dust, pollens, moulds, etc., and it is also common to see contact allergy to topical medicaments or cosmetics superimposed on atopic dermatitis [132, 133]. In subjects allergic to liverworts or to lichens, the area under the chin may be spared, giving the appearance of a so-called pseudo-photodermatitis [7]. In doubtful cases a careful medical history should resolve the problem.

Individuating the etiological agent is a major problem, particularly in occupational settings [7, 10]. In this regard, the recommended steps are detailed in Table 11.13. In the occupational field, visiting the work place is of crucial importance, and should be conducted in cooperation with the factory doctor and occupational hygienists, to analyze the technical aspects of procedures carried out, and the work conditions. Samples of the airborne contaminants should be collected, namely air samples (to check for vapours and gases) and various other substances (fibers, dusts, liquids sprayed in the air). Different methods (gas chromatography, high performance liquid chromatography, ion exchange chromatography, infrared- and ultraviolet-spectrophotometry, nuclear magnetic resonance spectrometry or phase contrast microscopy) are adopted to analyze the samples (pH, physical-chemical properties of the substances).

Table 11.13 Diagnostic procedures in airborne contact dermatitis

Visit to the workplace
Analysis of technical aspects of the work procedure
Analysis of the work conditions
Collection of air samples (presence of vapours and gases) using specific absorption devices
Collection of samples of contaminants (fibers, dusts, liquids)
Evaluation of relative humidity in the air
Patient examinations
Patch and photopatch tests with the standard series, other relevant test batteries and with suspected products and chemicals from the work environment according to the patient's medical history and occupation
Open tests, repeated open-application tests, use tests
Atopy patch tests (in atopic subjects)
Prick tests (in suspected airborne contact urticaria)
Evaluation of irritant materials on the skin by means of non invasive techniques (transepidermal water loss, erythrometry, laser—Doppler flowmetry)
Determination of the presence of causal chemicals in the skin by skin surface biopsy
Laboratory tests
Analyses of samples of substances (pH and physical-chemical properties) by gas chromatography, high performance liquid chromatography, ion exchange chromatography, infrared- and ultraviolet-spectrophotometry, nuclear magnetic resonance spectrometry, phase contrast microscopy

The diagnostic procedures performed in patients are as follows (Table 11.13). Patch tests and/or photopatch tests, performed in the usual way, must include all the suspected substances (that are not always easy to obtained in a pure state) at suitable concentrations. Epicutaneous tests must include additional procedures: open test, repeated open-application tests and, obviously adopting proper precautions, use tests. In cases of airborne contact urticaria prick tests are warranted.

To evaluate the irritant potential of materials collected on the skin of patients or volunteers, non invasive techniques, such as transepidermal water loss, erythrometry, laser-Doppler flowmetry and others, are useful. The determination of the presence of particles (and, if necessary, of chemicals) in the skin can be done by skin surface biopsy [134]. Being a coadjuvant physical factor in determining airborne contact dermatitis, the relative rate of humidity in the air needs to be evaluated. In skin and respiratory diseases induced by airborne agents, the use of an exposure chamber designed for experiments with controlled exposure to airborne particles, mainly irritants, is the best solution. The aim is to study skin effects and to develop methods for the measurement of the deposition of the particles on the skin [135]. Finally, continual updating by means of reviewing the relevant literature is fundamental.

In general, prevention measures commonly used in occupational and non occupational dermatology can be applied to airborne dermatoses (Table 11.14). First of all, great attention must be paid to the chemical-biotic environment, both indoor (workplace, houses, schools, gyms) and outdoor. The severity of contact dermatitis depends on the degree of contact hypersensitivity and the quantity of antigen the patient is exposed to. These two factors need to be reduced, and since it is impossible to reduce the hypersensitivity, then one must operate on the quantity of antigen in the environment. Therefore, the ventilation and temperature in closed environments must be adjusted and monitored at work and elsewhere (houses, schools, gyms). In cases of airborne contact dermatitis due to parthenium, for example, the patient must avoid going outdoors on days when pollens are present in high concentrations in the air. Air conditioning decreases indoor pollens counts. Simple routines like bathing after coming indoors, wearing fresh clothes and eliminating weeds and grasses in the garden can be helpful. The use of barrier creams on exposed sites can contribute to slow down the skin penetration of the antigen, as also the use of sunscreens in cases of photosensitivity.

In the work environment vapours, gases and pollen need to aspirated. When doing some jobs indoors or outdoors, suitable masks, gloves and overalls should be worn. In extreme cases it may be necessary to consider a change of job.

11.7 Processionary Dermatitis

11.7.1 Pine Caterpillar Dermatitis

In Mediterranean coastal regions, each year pine trees are assaulted by an apparently inoffensive insect, the pine caterpillar *Thaumetopoea*

Table 11.14 Prevention methods in airborne skin diseases

Greater information about, and attention paid to physical and chemical-biotic environment (indoor and outdoor)
Proper ventilation (indoor)
Adjustment of temperature (indoor)
Adjustment of environmental humidity (indoor)
Avoidance of outdoor activities
Absorption of vapours, gases and pollens (indoor)
Use of appropriate masks, gloves and overalls (indoor and outdoor)
Frequent changes of clothing
Frequent washing, personal and clothing
Use of barrier creams, sunscreens
Change of job

pityocampa Schiff. Being strictly phyto- and xylophagous, this insect survives by eating parts of pine trees, destroying their branches and delaying their growth. The disruptive effects of the pine caterpillar extend to man and pets, inducing various pathological conditions. Pine caterpillar hairs can cause adverse reactions at the skin, ophthalmic and respiratory levels.

Many French [136, 137] and Italian [4, 8, 138–140] authors have examined the problem since it is widespread in certain areas of these countries. In Italy, the Apulia region is particularly burdened by these insects, so much so that they are sometimes referred to by the media as a true "nightmare". Today, the pine processionary is also expanding northwards as a direct effect of global warming [141].

The pine caterpillar is not the only urticarial species of the Lepidoptera order [142] (Table 11.15). Other caterpillar species are also urticarial (hence the term "erucism", from the Latin *eruca*=caterpillar), as also moths (hence the term "lepidopterism", from the Greck *lepìs*=scale and *ptéron*=wing). In the majority of cases, however, damage to human skin and mucosa occurs as a result of the penetration of caterpillar hairs. The Thaumetopoeidae family numbers 3 urticarial caterpillars with different biological cycles but indistinguishable clinical symptoms.

Table 11.15 Common Lepidoptera responsible for skin damage

Family	Species
Saturniidae	*Hylesia* species
Lasiocampidae	*Dendrolimus punctatus*
Arctiidae	*Hyphantria cunea*
Lymantriidae	*Euproctis crysorrhoea* *E. edwardsi* *E. similis*
Megalopygidae	*Megalopyge opercularis*
Cochlididae	*Sibine stimulea*
Thaumetopoeidae (Processionary caterpillars)	*Taumetopoea pityocampa*
	T. pinivora
	T. processionea

T. pityocampa (the term comes from the Greck *cámpa*=caterpillar, *pìtys*=pine, *poieo*=does, *thàuma*=wonders) has a biological cycle consisting of 2 phases: an aerial phase (larvae) and a ground phase (when the chrysalis transforms to a moth). While devouring the pine needles, the caterpillars weave a net creating "tent" nests, typically placed on tree tops (Fig. 11.29). The caterpillars move along branches and also among

Fig. 11.29 Nest of the caterpillar *Thaumetopoea pityocampa* on cluster pine (Reproduced by Bonamonte and Coll [139])

trees in order to feed; these movements occur in procession fashion (nose to tail columns), usually at night (Fig. 11.30). During the aerial phase, the pine processionary evolves through 5 instar stages (L1–L5). Climatic conditions are essential to larval development: the pine caterpillar does not tolerate temperatures above 25 °C or below 5 °C, the optimal temperature ranges between 20 and 25°C. For this reason, the aerial larval phase ends between March and June, and the biologic cycle is generally annual [139].

For protective purposes, processionary larvae have developed an urticarial apparatus. At the fourth and fifth instar stages, their tegument comprises two different kinds of hairs: true non removable hairs and removable urticarial hairs (setae) growing dorsally and medially on the first 8 abdominal larva segments. The setae, displaced on a "mirror-like" morphology apparatus, are laid out on the segments of 4 articular larva scales with a density of about 60,000/mm^2 per side, or 120,000 in all, and 1 million for each caterpillar [142]. The setae vary in length from 100 to 200 nm and present pointed spikes towards the distal end and a proximal extremity normally infixed in cuticular pads.

Urticarial hairs penetrate through human skin by means of the proximal extremity. They do not show any superficial holes but are hollow along most of their axis. They have a defensive action and are expelled in great quantities when the caterpillar is in any way threatened, through the contraction of intersegmental muscles. Given their size, these hairs are invisible; in such muscle contractions, thousands are projected into the air as a fine powder.

Clinical Symptoms. The pathogenic effects of pine processionary extend to the skin, eyes and, more rarely, to the respiratory system. The dual pathogenic mechanism includes direct contact with nests or caterpillars (that will only involve the skin) and airborne contact with urticarial hairs dispersed in the air, that causes skin, ocular and respiratory affections. Contamination is common in pine foresters (70% of cases), less frequent outside forests (26.8%), and exceptional in urban environments [138, 140].

Airborne contact forms are the most commonly observed; they take place in our region in spring from March to June, reaching a peak in April and May. Obviously, this pattern may differ in relation to weather and caterpillar biological cycle variations.

Processionary dermatitis is observed in occupational settings (forestry personnel, residential gardeners, lumberjacks, woodcutters, resin collectors, stockbreeders, and entomologists) and even more commonly in non occupational situations (tourers and campers).

Fig. 11.30 Caterpillars (*Thaumetopoea pityocampa*) in procession

Based on the mode of contact, there are two clinical forms. One with limited, figured lesions due to direct skin contact with a caterpillar, that is observed especially in children who play with the larvae and let caterpillars stroll on their skin (Fig. 11.31). Another form, with extensive lesions, is due to airborne skin contact with the hairs dispersed in the air, that can pass through clothes (Figs. 11.32, 11.33, 11.34, 11.35, and 11.36). The last form is favored by the wind. The face, neck, forearms, and backs of the hands are the body areas most commonly involved. The onset of the eruption occurs 1–12 hours from contact, or rarely, days after. Clinically, it manifests with pinkish to bright red, round macules and papules, 3–8 mm in diameter, overlapping an urticarial base. Papules can be surmounted by vesicles. Oftentimes, clinical characteristics mimic those of strophulus, sometimes with bullous lesions. At the eyelids there can be evident edema, of a more or less conspicuous type. Itching is intense and continuous; purpuric and scratching lesions are common findings.

Albeit rarely, the skin manifestations can parallel systemic symptoms, such as malaise, fever, and anaphylactic syndrome [143, 144].

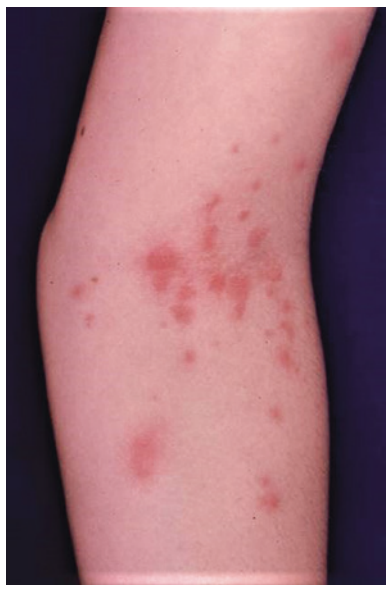

Fig. 11.31 Direct papulous contact dermatitis due to caterpillars

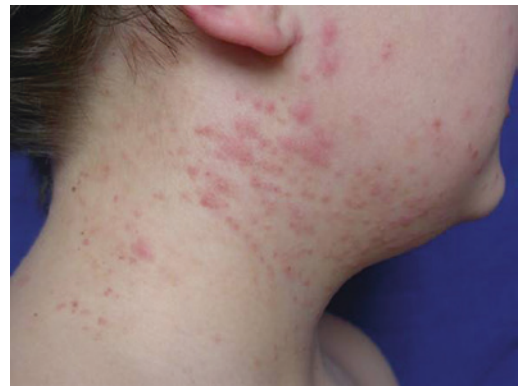

Fig. 11.32 Papulous airborne dermatitis due to the air-dispersed hairs of caterpillars (Reproduced by Bonamonte and Coll [139])

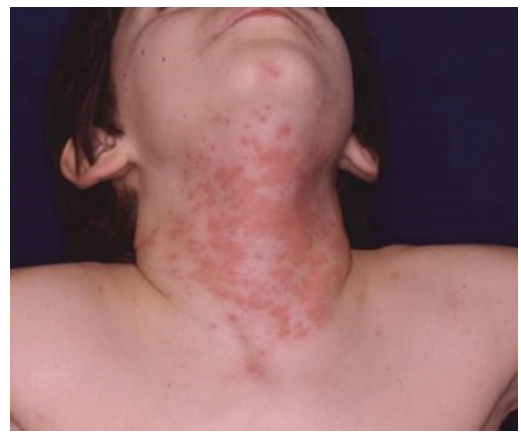

Fig. 11.33 Papulous airborne dermatitis due to the air-dispersed hairs of caterpillars (Reproduced by Bonamonte and Coll [139])

Cutaneous lesions evolve in 3–4 days and leave a brownish macule which resolves in 1–2 weeks. An atypical case has been reported in the Italian literature and cited in an international journal: a farmer who had developed an ulcerative dermatitis of the penis after he had manipulated pine processionary nests (*Cnethocampa pinivora*) and later masturbated [145].

In approximately 10% of cases, there is ocular involvement [138, 139] with early (a burning sensation, almost invariably unilateral, hyperemia and conjunctival edema) or late

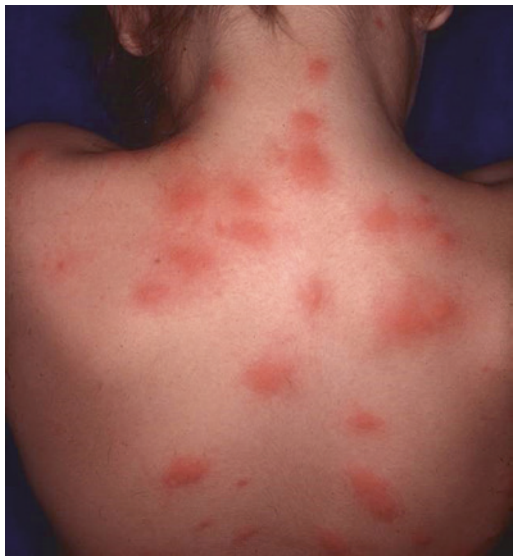

Fig. 11.34 Papulous airborne dermatitis due to the air-dispersed hairs of caterpillars (Reproduced by Bonamonte and Coll [139])

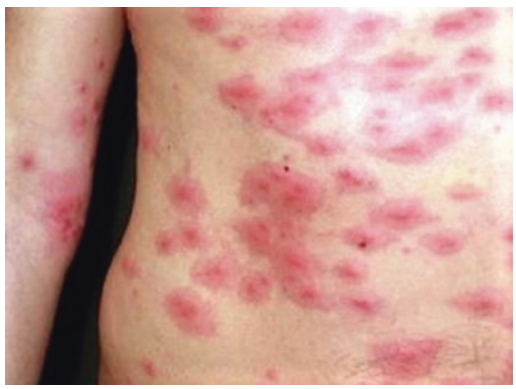

Fig. 11.35 Papulous airborne dermatitis due to the air-dispersed hairs of caterpillars

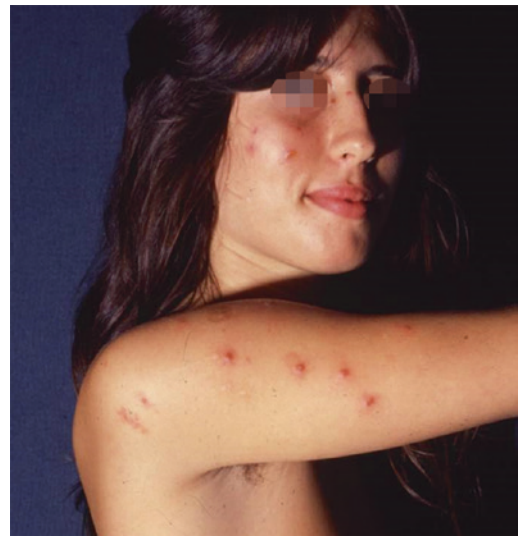

Fig. 11.36 Airborne papulo-bullous lesions due to the air-dispersed hairs of caterpillars (Reproduced by Bonamonte and Coll [139])

(photophobia, profuse tearing, and the formation of conjunctival yellowish nodules: ophthalmia nodosa) lesions. If there is hair migration towards the inner structures, sclera involvement, iris nodules, glaucoma, keratitis, uveitis, cataract, and panophthalmitis can be observed [137, 141, 146–151].

Respiratory involvement associated with pine processionary inhalation is rare, but the upper airways may be affected, with rhinitis, cough, dysphagia, and dyspnea. Asthma crises and the risk of asphyxia are possible, although rare, and require urgent treatment [137, 141, 146, 149].

Pathogenic Mechanisms. The mechanism is dual, being mechanical (skin infixion by hairs) and pharmacological [146, 152, 153]. It is likely that the mechanisms are valid for all the processionary species, although the hair venom composition in various Lepidoptera families has yet to be completely recognized. Shared venom components include histamine, histamine releasers, serotonin, and proteases [154, 155]. In 1986, Lamy and Coll isolated a protein, thaumetopoein (P.M. 28.000 D), from pine processionary hairs [156]. This protein acts directly on mast cells, inducing degranulation, validating a non specific urticarial effect of these caterpillars.

However, besides the direct histaminergic mechanism, reations to *T. pityocampa* have long been suspected to be associated to IgE-mediated hypersensitivity [157]. As a matter of fact, recently published studies have demonstrated through in vitro and in vivo tests that an IgE-mediated mechanism is involved in most *T. pityocampa* cases in adults [148, 149] and that the allergenic potency dramatically increases during larval development, peaking at the L5 instar

stage [158]. In particular, a 2012 study showed that setae contain a complex mixture of at least 70 proteins including 7 allergens, which are delivered to the skin by penetration of the setae [159]. The latter comprise minute amounts of proteins enclosed in a chitin-based envelope. Chitin exposure has been shown to induce the expression of interleukin (IL)-4 and IL-13 and so of eosinophils and basophils. Therefore, exposure to chitin has been proposed as the primary trigger in the development of the allergy [160]. In addition, data show that *T. pinivora* setae are able to penetrate the outer skin layer and remain there for up to 3 weeks, potentially releasing allergens that could trigger and/or enhance an immune allergic reaction in the host [161].

Diagnosis and Therapy. A history of residing, passing through or nearby pine forests is of prime importance, as also a history of direct contact with caterpillars, the presence of strophulus-like lesions, the distribution of the latter, and the development of dermatitis in the patient's friends and family (Fig. 11.37).

Stripping the lesions with tape and subsequent microscopic examination can demonstrate the presence of caterpillar hairs [162]. Histological studies on spontaneous lesions are scarce [163]. Focal disruption of the stratum corneum, along with epidermis cell lysis and consequent intraepidermic vesicles, has been described in experimentally induced lesions. Hair fragments are usually visible. Perilesional skin appears spongiotic, while edema and a perivascular lymphocyte, neutrophil, and eosinophil infiltrate are apparent in the dermis. In a later stage the same features become more discernible, with intense spongiosis and intraepidermic bullae formation; in the dermis the infiltrate extends to the hypodermis and becomes lymphohistiocytic in composition [163].

Patch tests with ether, alcohol, and saline filtrates result negative. Prick tests with a ground hair filtrate are positive, showing an urticarial reaction. These tests support the histaminergic urticarial activity of the substances, the need for skin scarification for the reaction to take

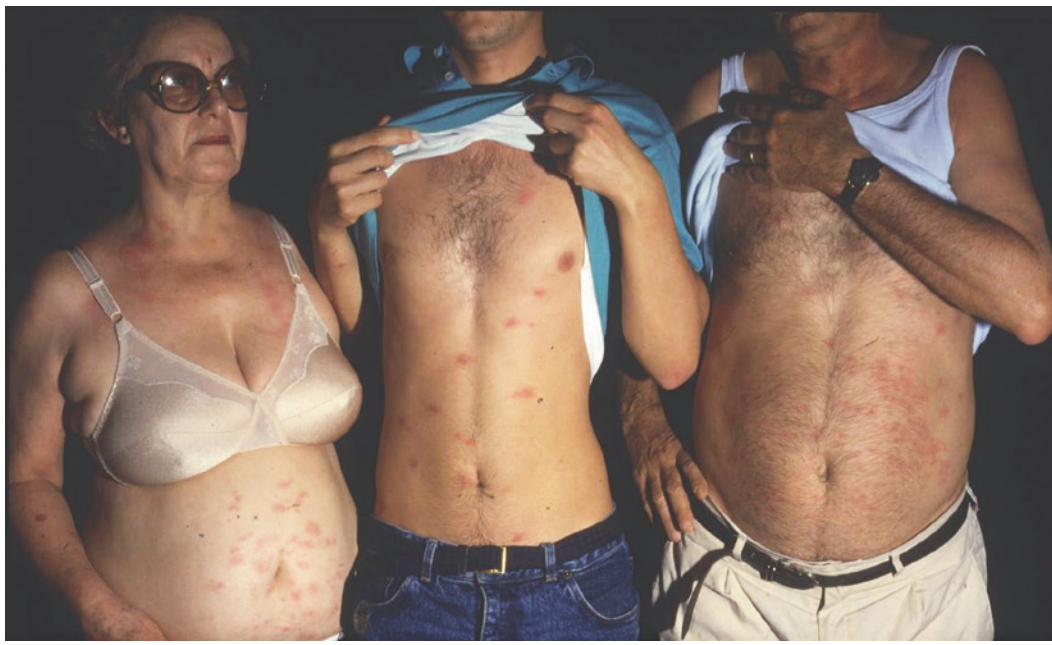

Fig. 11.37 Papulous airborne dermatitis due to the air-dispersed hairs of caterpillars in a family (Reproduced by Bonamonte and Coll [139])

place, and the need for crushing of the hairs to release the phatogenic substances. In vitro tests (IgE-immunoblotting) can be performed in patients with a positive prick test to confirm the allergenic nature of the cutaneous reaction.

Treatment shows scarce efficacy. Systemic antihistamines do not reveal any great utility. Topical steroids can accelerate resolution of the lesions, while systemic steroids may be administered in severe cases. Topical anti-itching products containing menthol or phenol can be helpful in relieving the pruritus. Topical potassium dobesilate 5% cream has recently been reported to provide some benefit [164].

11.7.2 Oak Caterpillar Dermatitis

The causal caterpillar is *T. processionea,* whose biological cycle differs from that of the pine species (larval life is considerably shorter in the former). The infestation occurs similarly to that of *T. pityocampa.* Holiday makers and forestry workers are at high risk. In this case, too, the substances responsible for the dermatitis are histamine-releasing proteins. The symptoms, diagnosis and treatment are the same as for the pine caterpillars form [165].

11.7.3 Moth Dermatitis

In some species of Lepidoptera, irritant setae are carried by the adults, for example moths of the genus *Hylesia* (Saturniidae family). They provoke various symptoms: urticarial lesions, papules of strophulous type surmounted by vesicles and eczematiform lesions. The complaint, that follows direct or more often airborne contact, resolves in about one week. In this case, too, ocular and respiratory involvement has been reported.

Owing to the particular reproduction cycle of this species, four epidemics per year are possible. The genus is notorious for causing outbreaks of "butterfly itch" or "moth dermatitis": the complaint is also known as "Guyane papillonite" or "Caripito itch" (from an epidemic form that broke out in the Caripito docks in Venezuela) in tropical South America (Argentina, Brazil, Peru) [166–173].

11.8 Chloracne

Together with acne due to coaltar products and petrolatum and its derivatives, chloracne, caused by halogenated aromatic hydrocarbons, is a variety of occupational acne (Table 11.16) [174–180].

Chloracne, a classic example of the impact of environmental pollution on human health, was first described in Germany by Von Bettman in 1887 [181] and then by Herxheimer in 1899 [182], who suggested the etiology to be chlorine exposure and also coined the name "chloracne" in view of its clinical similarity to acne vulgaris.

11.8.1 Etiology

The most potent acnegens are chloro- and bromo-substituted aromatic hydrocarbons. The culprits are most often chloronaphthalenes and bromonaphthalenes (used as electricity isolators), polychlorodiphenols (contained in closed electrical systems, transformers, and used in small quantities as plasticizers in cellulose, vinyl resins and rubber), some accidental contaminants of chlorphenolic herbicides (i.e. the dioxins tetrachlorodibenzodioxin and hexachlorodibenzodioxin and tetrachlorodibenzofuran), and some contaminants of herbicides, derivatives of 3,4-dichloroanyline (tetrachloroazoxybenzene, tetrachloroazobenzene) (Table 11.16).

All chloroacnegenic compounds share particular structural features including molecular planarity and 2 benzene rings with halogen atoms occupying at least 3 of the lateral ring positions. The position of the halogen substitutions is critical, since substitutions leading to molecular non-planarity greatly diminish the chloracnegenic activity [183]. Polychlorinated dibenzo-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) consist of 2 benzene rings bound by oxygen atoms. In PCDDs,

Table 11.16 Most common chloracnegens

Substances	Use
1. Polyhalogenated naphthalenes Polychloronaphthalenes Polybromonaphthalenes	Materials for electric and thermal isolation
2. Polyhalogenated biphenyls Polychlorobiphenyls Polybromobiphenyls	Closed electric circuits (transformers) Cellulose plasticizers Vinyl resins
3. Polyhalogenated dibenzofurans Polychlorodibenzofurans (Tetrachlorodibenzofuran) Polybromodibenzofurans (Tetrabromodibenzofuran)	Herbicides
4. Contaminants of polychlorophenyl compounds 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCCD) Hexachlorodibenzo-*p*-dioxin Tetrachlorodibenzofuran	Herbicides
5. Contaminants of 3,4-dichloroaniline 3,4,3',4'-Tetrachloroazoxybenzene 3,4,3',4'-Tetrachloroazobenzene	Herbicides

2 rings are joined by 2 oxygen bridges, and in PCDFs, by a carbon bond and an oxygen bridge. Chlorine atoms can be bound at 8 different places on the molecule, numbered from 1 at 8 (Fig. 11.38) [177]. Of the 210 dioxin and dibenzofuran congeners, only 17 are toxic. 2,3,7,8. Tetrachlorodibenzo-*para*-dioxin (TCDD), with 4 chlorine atoms, is the best known and most toxic dioxin [175] (Fig. 11.38).

Dioxins have no uses. The natural sources of dioxins are forest fires and volcanic activities. They are mostly formed and released as by-products of human activities, in particular of industrial processes and incomplete combustion processes like waste incineration. Other sources in the air are emissions from oil- or coal-fired power plants, and burning chlorinated compounds such as polychlorinated biphenyls (PCBs). Dioxins are released in waste waters from pulp and paper mills that employ chlorine or chlorinated substances in the bleaching process [177]. In any case, the most important sources of industrial emissions are waste incinerators, ferrous and nonferrous metal production and power generation, as well as heating, that contribute 45% of the total emissions. About another 40% of the total emissions are released by uncontrolled combustion processes [184].

Combustion-derived dioxins are linked to particles such as ashes, and small particles can be carried very far from the source of the emissions. They are hydrophobic and strongly lipophilic; their solubility in organic solvents increases with the chlorine content. Dioxins are not soluble in water, and in aquatic environments they mostly bind to any materials with a high organic content, such as microscopic plants and animals (plankton) eaten by larger animals. For this reason they circulate and accumulate at each step of the food chain (the biomagnification phenomenon) [177]. The toxicity of dioxins, their diffusion and production and the means for reducing and identifying them are reported in various specific works [175, 177, 178, 182–188].

In the 20th century there were at least 20 episodes of exposure to TCDD reported in the world at large, affecting industrial populations and more recently, also of non occupational type [174, 176, 177, 180]. Among the best known accidents, in the US already by the 1930s there had been observations of chloracne and various other symptoms in workers at factories producing pesticides, herbicides and other products with a high TCDD content. Among herbicides, the defoliant Agent Orange, used by the US army in the Vietman War from 1961 to 1971,

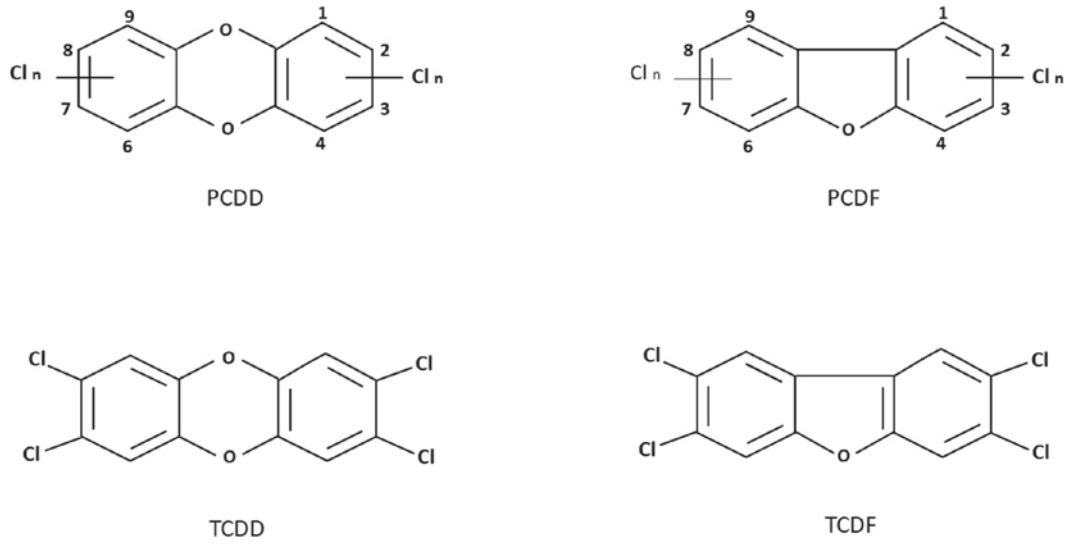

Fig. 11.38 Chemical structure of polychlorinated dibenzodioxins (PCDD) and dibenzofurans (PCDF). Chemical structure of 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF): two most potent chloracnegens

was notorious. Severe consequences, in the form of persistent chloracne lesions, were observed in 11.5% of Vietnam Veterans with a remote (17–22 years) history of exposure [189, 190]. In a study of 109 workers at a pentachlorophenol plant, the prevalence of chloracne was 73.4% of cases [191]. In another study of 3,538 workers with factory exposure to TCDD, 11% were found to have chloracne [192].

In July 1976, an explosion occurred in a 2,4,5-trichlorophenol reactor at the ICMESA chemical plant in Seveso (25 km north of Milan, Italy). In a vast residential area surrounding the town, 2 kg of TCCD were discharged into the atmosphere. Between September 1976 and February 1978, in 193 subjects, 170 of them (88%) under the age of 14 years, chloracne was diagnosed [193–196]. Another well known incident was the widespread ingestion of tainted rice cooking oil contaminated with PCBs in Yucheng in Taiwan: 17.5% of the exposed subjects developed chloracne [197].

The most notorious case of dioxin poisoning is that of the Ukrainian President Viktor Yushchenko during a dinner in Kiev on September 5, 2004 [198–201]. Serum levels were 108,000 pg/g lipid weight, so 50,000 times the average levels of TCDD in the general population [201]. Mr Yushchenko suffered severe health problems and chloracne.

Sporadic cases of chloracne have recently been reported in the literature. A 27-year-old man presented chloracne after he had been working for three months in a chemical laboratory where he had handled only *o*-dichlorobenzene [202]. Chloracne due to *o*-dichlorobenzene has also been reported in 9 factories producing chemicals based on monochlorobenzene, *o*-dichlorobenzene, and *p*-dichlorobenzene [203]. A further 8 cases were described in subjects all staying at the same holiday resort in the Appennines outside Bologna, Italy, and in a patient occupationally exposed to halogenated compounds [204].

11.8.2 Exposure Pathways and Pathogenic Mechanism

Human exposure to dioxins can occur due to environmental, occupational, or accidental pollution. Most such exposure is secondary to eating foods of animal origin or other products containing dioxin. According to the WHO, the major sources of dioxins in humans are meat,

fish and eggs [205]. Exposure can also be due to inhalation, drinking water, soil ingestion, and skin absorption. In the human organism, dioxins are partly metabolized and eliminated and partly stored in body fat. To be eliminated, dioxins must be converted to polar derivatives. The biological half-life differs in the various congeners; the TCDD half-life is between 5 and 10 years [206], or 7 and 11 years [207]. The elimination of dioxins depends on the dose (the elimination rate of TCDD is much greater at higher than lower levels) [178], age, gender (it is quicker in men and younger people), and quantity of body fat. According to the WHO, the standard tolerable daily intake of dioxins is at TEQ = (1 to 4) pg/kg-1 body weight per day or (10 to 30) pg/g-1 serum lipid [208]. However, even taking into account the variable individual sensitivity to dioxins, it seems to be difficult to diagnose chloracne on the sole basis of serum values. Analyses of various sporadic cases of chloracne, diagnosed on acceptable clinical and histological criteria, demonstrated, in fact, that the serum values were in the normal range [204]. This underlines the need for new biomarkers to evaluate contamination and make a more precise definition of the "no-effect level" [178].

The precise pathogenic cellular and molecular mechanisms underlying chloracne have not been entirely clarified, and are the object of various studies [175, 177–209]. TCDD induce a broad spectrum of effects at very low concentrations. The toxicity spectrum is known to be mediated by the binding and activation of the aryl hydrocarbon receptor (AHR), located in the cytoplasm of most cells, including all major cell types of the immunogenic system (B cells, T cells, dendritic cells, macrophages, granulocytes, and natural killer cells) [209, 210]. AHR forms a receptor complex with several proteins, including a 90-kD heat shock protein dimer [211]. Once bound by the ligand, the ligand-receptor complex translocates to the nucleus, where it binds cis elements of DNA known as xenobiotic- or dioxin-responsive elements [210]. The activation of AHR induces a variety of drug-metabolizing enzymes ("AHR battery"). Unlike most AHR ligands that induce their own metabolism, TCDD is resistant to these enzymes and its persistent occupancy of AHR is believed to be responsible for its strong toxicity [210]. The most common biomarker for AHR activation is the induction of cytochrome P450, of the enzyme superfamily that plays a critical role in the oxygenation of xenobiotics, including environmental and occupational pollutants such as dioxin [212, 213].

In the skin, different epithelial structures respond to TCDD in different ways: the epidermis and infundibulum undergo prominent hyperplasia; sebaceous glands and sweat glands lose their secretory activity and are replaced by keratinizing cells, while the lower portion of the follicle (hair bulb) undergoes a gradual involution [175]. Underlying these pathways are alterations of stem cell homeostasis induced by TCDD, resulting in hypoplasia of some skin epithelial structures and hyperplasia of others. The altered stem cell homeostasis thus brings about a shift from a pilosebaceous differentiation pattern to an epidermal one, as a result of an imbalance in early multipotent cells commitment [175]. This model of prefential differentiation towards an epidermal lineage and consequent diminution of the sebaceous lineage is consistent with the morphological skin alterations observed in patients [177, 214, 215] and in animal models with chloracne [216].

Hyperplasia of the infundibulum, with a switch of its content from semiliquid sebum to solid keratin, could explain the infundibulum dilatation and the development of comedones. The same mechanism could underlie the transformation of the eccrine sweat glands [175, 217].

The involvement of multipotent stem cells could also explain the delayed onset of chloracne after exposure to the causal chemicals, and its chronic course. In addition, the intervention of these same cells could explain the histologic differences between chloracne and acne vulgaris: the latter is associated with an exaggerated sebogenesis, while the former is characterized by the gradual transformation of sebocytes into keratinizing cells and consequent squamous metaplasia of the sebaceous glands [217].

11.8.3 Clinical Features

The skin is a key organ indicating exposure to various environmental poisons, and especially the group of dioxin chemicals. This "sentinel role" is likely linked to the fact that various poisons, absorbed either by cutaneous or systemic route, are metabolized in the skin.

Apart from the intensity and duration of the exposure, and the chloracnegenic power of the dioxins, the severity of chloracne also depends on individual susceptibility, that is highly variable. Developing fetuses and newborn babies are the most sensitive, especially those exposed to high levels of dioxins through mothers' milk. Experimental topical application of a mixture of hexa- and penta-chloronaphthalenes on the skin of healthy volunteers demonstrated that some subjects develop severe chloracne while others have no skin effects at all. Older females seem to show a weak response or none, even to chronic applications of high concentrations of chloracnegenics [179]. In some individuals, the onset of chloracne occurs within days, but in others it takes 2–3 months since the last known exposure. Younger men, especially if blonde, are the first to be affected. In some subjects the complaint is prevalently cystic, and in others comedonic, affecting all the pores [218].

Some studies have shown that in a certain proportion of cases, apart from chloroacne there are signs of systemic intoxication; it is interesting to note that only one patient with this sign failed to develop chloracne, so resistance in such cases seems to be rare [219, 220]. To elucidate the reasons for the highly variable susceptibility studies of genetic factors are needed [201].

The key clinical feature of chloracne is a non inflammatory alteration of the keratinization of the pilosebaceous unit [174, 221], leading to the formation of comedones, cysts, pustules and various symptoms, but rarely pruritus [222]. In any case, it is important to underline that there is no clinical sign specific only to chloracne [178].

The skin manifestations generally appear about two weeks after the harmful exposure, reach a peak after about 6–10 months and can persist for years due to the very slow decrease of TCDD in skin, unlike in serum [201]. Usually, chloracne starts as an acute marked erythema of the face sometimes associated with intense edema. After 15–20 days, the formation of fine comedones (blackheads and whiteheads), one of the most characteristic clinical features, is observed. The comedones involve almost every follicle of the exposed part, giving the skin a slate-gray appearance. In modest cases, these comedones are the only clinical sign. The comedones start to shed hairs, while sebaceous lobules are still active, although involuted, and continue to secrete sebum [214].

Initially, straw-colored cysts are less common than comedones, and mainly affect the face and neck. In more serious cases non inflammatory infundibular cysts predominate over comedones, being the peculiar lesions of advanced chloracne. Cysts with a central orifice or pores that may also not be obvious, range in size from 1 mm to 1 cm in diameter. Unlike with primary comedones, the pylar portion of infundibular cysts is almost always destroyed and few or no hairs remain within the cavity [175]. The cystic lesions are virtually sterile, but occasionally a secondary infection can occur [218].

Chloracne is not associated with cutaneous inflammation, but in severe cases, non-infectious folliculitis may occur: in this event the clinical picture can be comparable to that of a severe nodulo-cystic acne. The nodulo-cystic lesions are evident in particular on the back and legs [223]. At the palmoplantar level, hyperkeratotic lesions of sweat glands origin (acrosyringial plugging), similar to the plugging in comedones of follicular origin, can be seen [196, 215, 224, 225].

The distribution of chloracne lesions is highly characteristic. Comedones most often develop on the face and neck (in 90–100% of affected subjects) (Figs. 11.39, 11.40, and 11.41), and forearms (47%). At facial level, the sites most often affected are below the eye toward the outer side (the malar zone) and the post-auricular triangles. The ear lobes, suboccipital hairline and groin are often involved. There are fewer cysts on the cheeks, forehead and

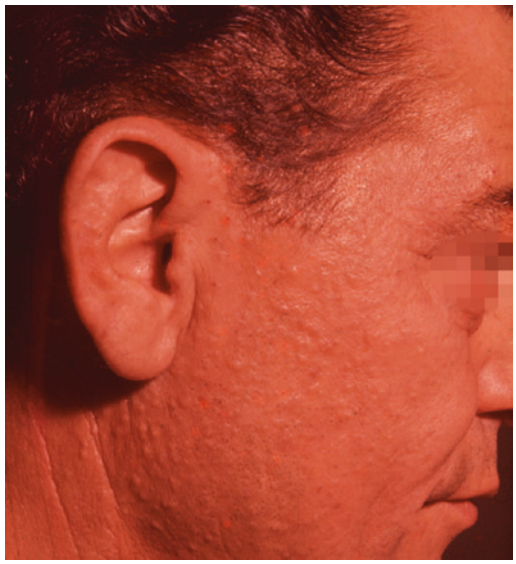

Fig. 11.39 Comedones of chloracne

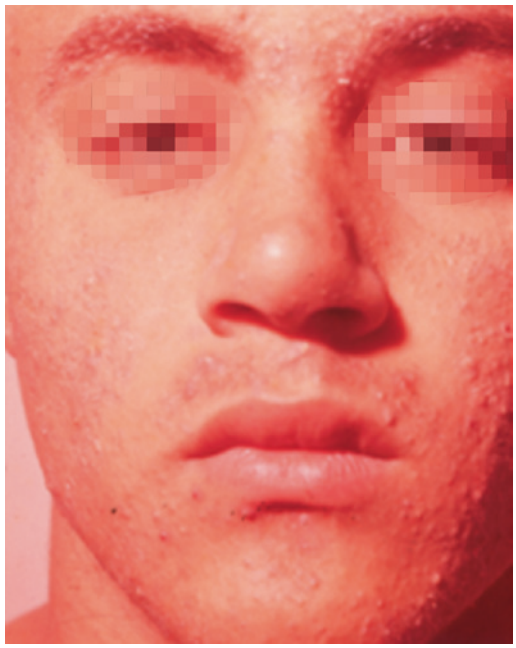

Fig. 11.40 Comedones of chloracne

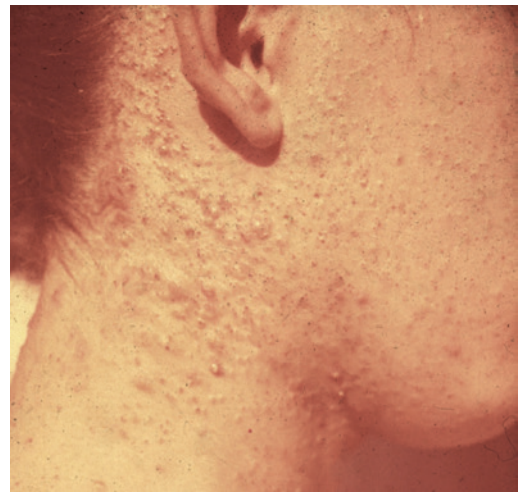

Fig. 11.41 Comedones and sterile pustules of chloracne

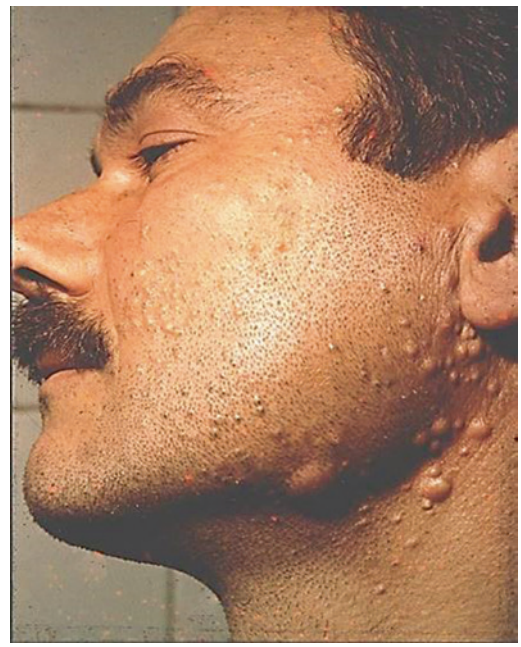

Fig. 11.42 Comedones and cysts of chloracne

sides of the neck (Fig. 11.42), while the nose, perioral zone and supraorbital regions are generally spared. The pustulous component is more evident on the neck. Comedones and cysts can also be present on the shoulders, back and chest (mid-portion), and sometimes on the outer surfaces of the forearms and anterior thighs. At the genital level, the penis is affected by comedones and the scrotum by cysts. The axillae can also be involved. Although all follicles can be affected, the vellus follicles are generally more sensitive than the scalp follicles [226].

Table 11.17 Clinical features of chloracne

Skin symptoms
Erythema and edema of face (acute signs)
Comedones (blackheads and whiteheads)
Slate-grey appearance of involved skin
Straw-colored cysts
Follicular hyperkeratosis
Pustules
Nodulocystic lesions
Skin thickening
Palmoplantar punctate keratoderma-like lesions
Absence of vellus follicles
Porphyria cutanea tarda
Skin xerosis
Decreased sebum secretion
Depressed scars (due to healing of nodulocystic lesions)
Systemic disturbances
Anorexia
Fatigue
Headache
Nausea
Vomiting
Conjunctivitis
Arthritis
Pancreatitis
Neuropathy
Impotence
Liver dysfunction
Hyperlipidemia
Anemia
Thyromegaly
Ophthalmitis
Impaired cell-mediated immunity
Teratogenicity
Porphyrinopathy
Diabetes
Hypertension
Atherosclerosis
Gastrointestinal, lymphatic, breast and hematopoietic cancers
Soft-tissue sarcoma

It is essential to understand that chloracne is not only a skin disease but in particular, a systemic intoxication disease. The skin symptoms are accompanied by systemic symptoms, some of which precede the skin involvement (Table 11.17) [201].

11.8.4 Histopathology

As already pointed out, there are no absolutely specific clinical signs for chloracne. Histology, instead, seems to provide a key sign that is both reproducible and pathognomonic, namely the disappearance of sebaceous glands [175, 178, 201, 204].

There are two major histologic findings, one being "structure loss" and the other "structure addition", with the preservation of other normal skin structures, and thereby compatible with hamartomas [179, 202]. The so-called "structure loss" was referred to the disappearance of the sebaceous glands, a crucial finding that was constantly evident in 252 histological slides studied. In human disease, there are no other examples of disappearance of the sebaceous glands. The term "chloracne" is therefore a misleading misnomer, since in acne there is hypertrophy of these same glands.

The "structure addition" is the presence of epidermal cysts, both superficial, with an open comedone-like aspect, and deeper in the derma. These cysts have specific characteristics: mantle-like columnar epithelial downgrowths, showing a high proliferative activity, and focal expression of CYP1A1 (the major dioxin-metabolizing CYP enzyme) in the epithelial walls. On the basis of these observations, made in a case of massive dioxin poisoning [200], the authors proposed that these cysts be called "metabolized acquired dioxin-induced skin hamartomas" [200, 201].

The crucial importance of these histological findings allowed a diagnosis of chloracne to be made in some cases, even if the serum dioxin titers were within normal range [204]. Apart from the absence of sebaceous glands, in this last study, too, follicular hyperkeratosis was present, with marked proximally infundibular dilatation giving the follicle a bottle-shaped aspect [214, 217–233] (Fig. 11.43). Some follicular orifices were filled by plugs of orthokeratotic hyperkeratosis. The follicular epithelium also showed hypergranulosis, sometimes true squamous metaplasia and numerous fine melanin granules in the stratum corneum [204].

It should be borne in mind that the first signs of histological changes appear already a few days after exposure to the chloracnegens [175].

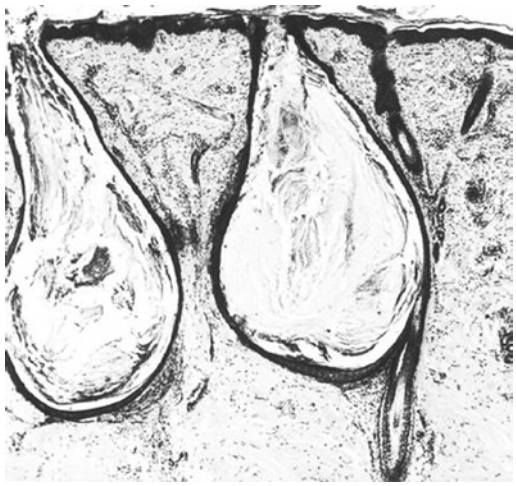

Fig. 11.43 Histopathology of chloracne: bottle-shaped infundibular dilatation (Hematoxylin-eosin,x 200)

11.8.5 Differential Diagnosis

Clinically, chloracne needs to be differentiated from other forms of occupational and non occupational acne.

Apart from chloracne, another form of occupational acne is *oil acne* or *oil folliculitis*, that presents with many comedones, follicular papules and pustules in sites of heavy oil exposure, namely the extensor surfaces of the arms and thighs and other sites of contact with oil-soaked clothing. There can also be furuncles. Modest pictures of occupational acne are caused by crude and cutting oils, coal-tar oils, pitch and creosote (Table 11.18). The backs of the hands, upper trunk and legs are less frequently affected. The lesions generally appear a few weeks after contact with the causal agents. The initial changes are marked by a dry, rough surface of the skin, with gradual atrophy of the hairs. Then the comedones appear, mostly large and open, as well as follicular papulous lesions the size of millet grains, that are red and congested at the periphery and yellowish-grey at the center. These may be followed by cystic lesions and, in particular on the face, backs of the hands and extensor surface of the forearms, by melanosis and diskeratosis. The observation of simple or spinulous follicular hyperkeratosis on exposed sites and the trunk, characterized by raised punctiforme follicles without signs of inflammation, is less common. The complaint is generally pruriginous [233].

Table 11.18 Occupational acne from oil and tar products

Petroleum and its derivates
Crude oils
Cutting oils
Coal-tar products
Coal-tar oils
Pitch
Creosote

The comedogenic action is linked to a dual mechanism: mechanical occlusion of the follicular ostium by oil and dirt, and hence the retention of glandular secretion causing stimulated keratinogenesis, and a direct irritant action of the hydrocarbons. Histology shows marked hyperkeratosis of the follicular ostium, hyperplasia of the follicular invagination epithelium, corneal pseudocysts, and a lymphomonocytic and histiocytic dermic infiltrate. Hypotrophy of the sebaceous glands is also evident. The evolution of oils-induced folliculitis ranges between weeks and months after the cessation of the harmful contact.

The differential diagnosis between chloracne and acne vulgaris is based on clinical aspects, namely the sites affected, age at onset and history of exposure [175] (Table 11.19). The sites of chloracne are distinctive: it can develop in any age group, including prepubertal children, but is not a predisposing factor for adolescent acne. Chloracne lesions rarely present inflammation whereas it is a common feature in acne vulgaris. In acne vulgaris the inflammation may be related to sebaceous lipids, their metabolites and by-products of the *Propionibacterium acnes,* that are known irritants [234]. *P. acnes* is the essential colonizer of acne vulgaris, whereas it is always absent in chloracne, whose lesions are sterile. In patients with chloracne the skin surface is not oily: the sebaceous glands show a reduced volume or are completely absent, and the production of sebum is dramatically reduced. Therefore, chloracne is associated with cutaneous xerosis. High sebum secretions are, instead,

Table 11.19 Differential characteristics of chloracne and acne vulgaris

	Chloracne	Acne vulgaris
Clinical features		
Age group	Any age group	Adolescence and early adulthood
Sites	Generalized, including retroauricolar and malar areas, axillae, groin, extremities; nose spared	Localized, including face (including nose), upper back and chest
Initial lesions	Miriad comedones	Limited comedones, papules, pustules, cysts
Inflammation	Very rare (as secondary effect of cyst rupture)	Inflammatory lesions are common
Sebum production	Decreased	Increased
Pathogenic factor		
Microflora	No bacteria	*Propionibacterium acnes* *Propionibacterium granulosum*
Histopathology		
Sebaceous gland	Atrophic, gradual replacement with keratinocytes	Hypertrophic
Sweat gland	Palmoplantar hyperkeratotic lesions, acrosyringial plugging	Uninvolved
Hair follicles	Hyperplasia of infundibulum and significant thickening of upper follicle	Thinning of infundibular epithelial wall

a must in acne vulgaris, and correlated with the severity of the complaint. Sebaceous secretion is androgen-dependent, while chloracne patients appear to have suppressed androgenic effects and hence sebogenesis.

Various drugs (including corticosteroids, anabolic steroids and synthetic androgens, anticonvulsivants, antiepileptics, isoniazid, bromides and iodides) can induce acneiform eruptions. Clinically, the picture is monomorphic with inflammatory papules and pustules, with little evidence of comedones, in contrast with the heterogeneous morphology normally observed in acne vulgaris. The face and upper trunk are most often involved. The interval between taking the drug and the acneiform eruption and pathogenic mechanism depend on the causal agent. Corticosteroids, that may provoke an acneiform reaction regardless of their route of administration, induce cornification in the upper part of the pilosebaceous duct, without acting on the number of surface bacteria. Androgens and anabolic steroids can increase the production of sebum and the surface population of *P. acnes*. This type of acne is most commonly observed in athletes and body builders, especially young men who make ample use of anabolic steroids. Finally, iodides and bromides are one of the most common causes of follicular acne, whose onset occurs rapidly after starting the drug.

11.8.6 Chloracne Persistence

The natural history of chloracne is highly variable. In general, it starts after 2–4 weeks from the initial harmful exposure; in cases with intensive exposure, the symptoms can appear after only a few days [227]. In cases of less severe intoxication, a slow, spontaneous improvement may quickly be evident [228]; however, in general, assuming there is no further exposure, the skin lesions take 2–3 years to resolve [222, 225]. Sometimes the disease can persist even 15 years after the cessation of exposure [218]. In workers accidentally exposed to by-products of 2,4,5-trichlorophenoxyacetic acid, the mean duration was 26 years; some subjects remained disfigured after more than 30 years from the accident [229]. In a group of Vietnamese Veterans with a remote history (17–22 years) of exposure to a herbicide (Agent Orange) the chloracne persisted in 11.5% of the cases [230]. Similarly, 20 years after the Seveso accident, TCDD plasma levels were still elevated (>10 ppt) in 78 (26.6%) of the 293 subjects recruited, and particularly in females, in subjects who had eaten home-grown animals, and in older subjects, those with a higher body mass index and those resident near the accident site. Plasma dioxin was strongly associated with chloracne. After 20 years, the health conditions of chloracne cases were similar to those of controls from the same geographic area [193].

The reasons why chloracne turns into a chronic disease are not known. It is possible that because chloracnegens are highly lipophilic they remain in the fatty tissues for long periods. However, it is also true that the duration and extension of the disorder are not necessarily correlated with the concentration and the half-life of the chloracnegens in the body. Chloracne lesions have also been reported to recur despite the total absence of further contact with the causal agent [231, 232]; a satisfactory explanation of this phenomenon has not yet been found.

The severity of chloracne depends on the intensity and duration of the exposure, on the chloracnegenic potency of the chemicals and on individual susceptibility.

It must also be noted that classic chloracne lesions can be observed in workers' relatives who have never been exposed to chloracnegens. The lesions are likely caused by contact with work clothes or tools brought home, or by direct bodily contact [232], demonstrating that even trace amounts of chloracnegens can cause disease.

References

1. Dooms-Goossens A, Debusschère KM, Gevers DM, et al. Contact dermatitis caused by airborne agents. A review and case reports. J Am Acad Dermatol. 1986;15:1.
2. Lachapelle JM. Industrial airborne irritant or allergic contact dermatitis. Contact Dermatitis. 1986;14:137.
3. Dooms-Goossens A, Deleu H. Airborne contact dermatitis: an update. Contact Dermatitis. 1991;25:211.
4. Angelini G, Vena GA. Airborne contact dermatitis. Clin Dermatol. 1992;10:123.
5. Lachapelle JM, Frimat P, Tennstedt D, et al. Dermatoses aéroportées. In: Lachapelle JM, Frimat P, Tennstedt D, et al., editors. Dermatologie professionnelle et de l'environement. Paris: Masson; 1992. p. 141.
6. Tennstedt D, Leroy B, Lachapelle JM. Dermatoses de contact aéroportées d'origine allergique. Ann Dermatol Vénéreol. 1994;121:850.
7. Björkner BE. Industrial airborne dermatoses. Dermatol Clin. 1994;12:501.
8. Angelini G, Vena GA. Dermatosi aerotrasmesse. In: Angelini G, Vena GA. editors. Dermatologia professionale e ambientale, vol I. Brescia: ISED; 1997. p 107.
9. Lotti T, Menchini G, Teofoli P. The challenge of airborne dermatitis. Clin Dermatol. 1998;16:27.
10. Lachapelle JM. Occupational airborne skin diseases. In: Kanerva L, Elsner P, Wahlberg JE, et al., editors. Handbook of occupational dermatology. Berlin: Springer; 2000. p. 193.
11. Huygens S, Goossens A. An update on airborne contact dermatitis. Contact Dermatitis. 2001;44:1.
12. Handa S, De D, Mahajan R. Airborne contact dermatitis—current perspectives in etiopathogenesis and management. Indian J Dermatol. 2011;56:700.
13. Pirilä V. Thiokol as a frequent cause of dermatitis. Allergy. 1950;3:329.
14. Pirilä V, Noro I, Iaamanen A. Air pollution and allergy. Acta Allergol. 1963;18:113.
15. Stam-Westerveld EB, Coenraads PJ, van der Valk PG, et al. Rubbing test responses of the skin to man-made mineral fibres of different diameters. Contact Dermatitis. 1994;31:1.
16. Schloemer JA, Zirwas MJ, Burkhart CG. Airborne contact dermatitis: common causes in the USA. Int J Dermatol. 2015;54:271.
17. Cashman MW, Reutemann PA, Ehrlich A. Contact dermatitis in the United States: epidemiology, economic impact, and workplace prevention. Dermatol Clin. 2012;30:87.
18. Rycroft RJG, Smith WD. Low humidity and occupational dermatoses. Contact Dermatitis. 1980;6:488.
19. Dooms-Goossens A, Boyden B, Ceuterick A, et al. Dimethylthiourea, an unexpected hazard for textile workers. Contact Dermatitis. 1979;5:367.
20. Mensing H, Kimming W, Hausen BM. Airborne contact dermatitis. Hautarzt. 1985;36:398.
21. Pecegueiro M, Brandão FM. Airborne contact dermatitis to plants. Contact Dermatitis. 1985;13:277.
22. Sharma SC, Kaur S. Airborne contact dermatitis from Compositae plants in northern India. Contact Dermatitis. 1989;21:1.
23. Hostetler SG, Kaffenberger B, Hostetler T, et al. The role of airborne proteins in atopic dermatitis. J Clin Aesthet Dermatol. 2010;3:22.
24. Nilsen A. Facial rash in visual display unit operators. Contact Dermatitis. 1982;8:25.
25. Santos R, Goossens A. An update on airborne contact dermatitis: 2001–2006. Contact Dermatitis. 2007;57:353.
26. Schaefer H, Redelmeier TE. Skin barrier. Basel: Karger; 1996. p. 56.
27. Lademann J, Otberg N, Richter H, et al. Investigation of follicular penetration of topically applied substances. Skin Pharmacol Appl Skin Physiol. 2001;14(Suppl 1):17.
28. Schaefer H, Lademann J. The role of follicular penetration. A differential view. Skin Pharmacol Appl Skin Physiol. 2001;14(Suppl 1):23.
29. Otberg N, Richter H, Schaefer H, et al. Variations of hair follicle size and distribution in different body sites. J Invest Dermatol. 2004;122:14.

30. Lademann J, Schaefer H, Otberg N, et al. Penetration von Mikropartikeln in die menschliche Haut. Hautarzt. 2004;55:1117.
31. Lademann J, Otberg N, Jacobi U. Follicular penetration and targeting. J Invest Dermatol Symp Proc. 2005;10:301.
32. Clemmensen OJ, Menné T, Kaaber K, et al. Exposure of nickel and the relevance of nickel sensitivity among hospital cleaners. Contact Dermatitis. 1981;7:14.
33. Clemmensen OJ, Jorgensen J, J Joins O, et al. Exposure to chromium from hospital cleaning. Derm Beruf Umwelt. 1983;31:54.
34. Angelini G, Vena GA. Allergia da contatto al nichel. Considerazioni su vecchie e nuove acquisizioni. Boll Dermatol Allergol Profes. 1989;4:5.
35. Handfield-Jones S, Boyle J, Harmann RRM. Contact allergy caused by metal sprays. Contact Dermatitis. 1987;16:44.
36. Arlette J, Mitchell JC. Compositae dermatitis: current aspects. Contact Dermatitis. 1981;7:129.
37. Vena GA, Foti C, Grandolfo M, et al. Mercury exanthem. Contact Dermatitis. 1994;31:214.
38. Sharma VK, Sethuraman G. *Parthenium* dermatitis. Dermatitis. 2007;18:183.
39. Sharma VK, Sahoo B. Prurigo nodularis-like lesions in *Parthenium* dermatitis. Contact Dermatitis. 2000;42:235.
40. Lindskov R. Contact urticaria to formaldehyde. Contact Dermatitis. 1982;8:333.
41. Fisher AA. Contact dermatitis in medical and surgical personnel. In: Maibach HI, Gellin GA, editors. Occupational and industrial dermatology. Chicago: Year Book Medical; 1982. p. 223.
42. Bhutani LK, Rao DS. Photocontact dermatitis caused by *Parthenium hysterophorus*. Dermatologica. 1978;157:206.
43. Burge SM, Powell SM. Contact urticaria to phosphorus sesquisulphide. Contact Dermatitis. 1983;9:424.
44. Angelini G, Vena GA, Foti C, et al. Contact allergy associated with airbone contact allergy from phosphorus sesquisulfide. Am J Contact Dermatitis. 1994;5:84.
45. Konzen JL. Fiberglass and the skin. In: Maibach HI, Gellin GA, editors. Occupational and industrial dermatology. Chicago: Year Book Medical; 1982. p. 229.
46. Sertoli A, Giorgini S, Farli M. Fiberglass dermatitis. Clin Dermatol. 1992;10:167.
47. Meneghini CL. Fiberglass dermatitis. Contact Dermatitis. 1977;3:218.
48. Björnberg A, Löwhagen GB. Patch testing with mineral wool (rockwool). Acta Dermatol Venereol. 1977;57:257.
49. Tarvainen K, Estlander T, Jolanki R, et al. Occupational dermatitis caused by man-made mineral fibers. Am J Contact Dermatitis. 1994;5:22.
50. Rom W, Moshell A, Greaves W, et al. A study of dermatitis in trona miners and millers. J Occup Med. 1983;25:295.
51. Lachapelle JM, Mahmoud G, Vanherle R. Anhydrite dermatitis in coal mines. An airborne irritant reaction assessed by laser Doppler flowmetry. Contact Dermatitis. 1984;11:188.
52. Lachapelle JM. Occupational airborne irritant contact dermatitis to slag. Contact Dermatitis. 1984;10:315.
53. Nethercott JR. Airborne irritant contact dermatitis due to sewage sludge. J Occup Med. 1981;23:771.
54. Lachapelle JM. Occupational airborne irritant contact reaction to the dust of a food additive. Contact Dermatitis. 1984;10:250.
55. Williams DT, Otson R, Bothwell PD. Formaldehyde levels in the air of houses containing urea-formaldehyde foam insulation. Can J Public Health. 1981;72:331.
56. Schmutz JL, Rigon JL, Mougeolle, et al. Cutaneous accidents caused by self-defense sprays. Ann Dermatol Vénéreol. 1987;114:1211.
57. Shmunes E, Taylor JS. Industrial contact dermatitis. Effect of the riot control agent orthochlorobenzylidene malononitrile. Arch Dermatol. 1973;107:212.
58. Holland P, White RG. The cutaneous reactions produced by o-chlorobenzyl-idenemalononitrile and chloroacetophenone when applied directly to the skin of human subjects. Br J Dermatol. 1972;86:150.
59. Penneys NS, Israel RM, Indgin SM. Contact dermatitis due to 1-chloroacetophenone and chemical mace. N Engl J Med. 1969;281:413.
60. Maibach HI, Marzulli FN. Allergic sensitization potential of riot control lacrimants: Human Draize test. Contact Dermatitis Newsl. 1971;5:209.
61. Calnan CD. Chloracetophenone (CN) dermatitis. Contact Dermatitis. 1979;5:195.
62. Dejobert Y, Piette F, Bergoend F, et al. Contact dermatitis to self defence spray. Boll Dermatol Allergol Profes. 1987;5:71.
63. Angelini G, Vena GA, Foti C, et al. Dermatite da contatto con gas iprite. Boll Dermatol Allergol Profes. 1990;5:71.
64. Vena GA, Foti C, Grandolfo M, et al. Contact irritation associated with airborne contact irritation from mustard gas. Contact Dermatitis. 1994;31:130.
65. Momeni AZ, Enshaeih S, Meghdadi M. Skin manifestations of mustard gas. A clinical study of 535 patients exposed to mustard gas. Arch Dermatol. 1992;128:775.
66. Sartorelli E, Giubileo M, Bartalini E. Study of asthma-forming chronic bronchitis with pulmonary emphysema as a complication of occupational poisoning with yperite. Med Lav. 1957;48:336.
67. Gaffuri E, Felisi A. Chronic occupational pulmonary lesions due to yperite. Med Lav. 1957;48:539.
68. Bonamonte D, Verni P, Romita P, et al. Aquatic skin diseases from chemical and physical causes. In: Bonamonte D, Angelini G, editors. Aquatic dermatology. Biotic, chemical and physical agents. Berlin: Springer; 2016. p. 227.

69. Hjorth N. Food poisoning from cod-roe contaminated by mustard gas; a report with five case histories. Acta Med Scand. 1953;147:237.
70. Mongelli-Sciannameo N. Collective accident due to dichlorodiethyl sulfide in a group of fishermen. Rass Med Ind Ig Lav. 1960;29:441.
71. Bonamonte D, Angelini G. Aquatic dermatology. Biotic, chemical and physical agents. Berlin: Springer; 2016.
72. Calnan CD. Carbon and carbonless copy paper. Acta Derm Venereol. 1979;(Suppl 85)59:27.
73. Marks JG Jr, Trautlein JJ, Zwillich CW, et al. Contact urticaria and airway obstruction from carbonless copy paper. JAMA. 1989;252:1038.
74. Menné T, Asnaes G, Hjorth N. Skin and mucous membrane problems from "no carbon required" paper. Contact Dermatitis. 1981;7:72.
75. Rietschel RL, Fowler JF Jr. Dermatitis due to gases and propellants. In: Rietschel RL, Fowler JF Jr, editors. Fisher's contact dermatitis. Philadelphia: Lippincott Williams and Wilkins; 2001. p. 481.
76. van Ketel WG. Allergic contact dermatitis from propellants in deodorant sprays in combination with allergy to ethyl chloride. Contact Dermatitis. 1976;2:115.
77. Bircher AJ, Hampl K, Hirsbrunner P, et al. Allergic contact dermatitis from ethyl chloride and sensitization to dichlorodifluoromethane (CFC 12). Contact Dermatitis. 1994;31:41.
78. Wester RC, Hartway T, Serranzana S, et al. Human skin in vitro percutaneous absorption of gaseous ethylene oxide from fabric. Food Chem Toxicol. 1997;35:513.
79. Biro L, Fisher AA, Price E. Ethylene oxide burns. A hospital outbreak involving 19 women. Arch Dermatol. 1974;110:924.
80. Fisher AA. Postoperative ethylene oxide dermatitis. Cutis. 1973;12:177.
81. Romaguera C, Vilaplana J. Airborne occupational contact dermatitis from ethylene oxide. Contact Dermatitis. 1993;39:85.
82. Taylor JS. Dermatologic hazards from ethylene oxide. Cutis. 1977;19:189.
83. Angelini G, Rigano L, Foti C, et al. Occupational sensitization to epoxy resin and reactive diluents in marble workers. Contact Dermatitis. 1996;35:11.
84. Dahlquist I, Fregert S. Allergic contact dermatitis from volatile epoxy hardeners and reactive diluents. Contact Dermatitis. 1979;5:406.
85. Lundov MD, Mosbech H, Thyssen JP. Two cases of airborne allergic contact dermatitis caused by methylisothiazolinone in paint. Contact Dermatitis. 2011;65:176.
86. Swinnen I, Goossens A. An update on airborne contact dermatitis: 2007–2011. Contact Dermatitis. 2013;8:232.
87. Poison ivy, oak, and sumac. https://www.aad.org/public/diseases/itchy-skin/poison-ivy-oak-and-sumac.
88. Hausen BM, Oestmann G. The incidence of occupationally-induced allergic skin diseases in a large flower market. Derm Beruf Umwelt. 1988;36:117.
89. Ducombs G, Schmidt RJ. Plants and plant products. In: Rycroft RJG, Menné T, Frosch PJ, et al., editors. Textbook of contact dermatitis. Berlin: Springer; 2001. p. 883.
90. Holst R, Kirby J, Magnusson B. Sensitization to tropical woods giving erythema multiforme-like eruptions. Contact Dermatitis. 1976;2:295.
91. Hjorth N, Roed-Petersen J, Thomsen K. Airborne contact dermatitis from Compositae oleoresins simulating photodermatitis. Br J Dermatol. 1976;95:613.
92. Foussereau J, Muller JC, Benezra C. Contact allergy to Frullania and *Laurus nobilis:* cross-sensitization and chemical structure of the allergens. Contact Dermatitis. 1975;1:223.
93. Thune PO, Solberg YJ. Photosensitivity and allergy to aromatic lichen acids, Compositae oleoresins and other plant substances. Contact Dermatitis. 1980;6:64.
94. Problems with Pesticides. Tocsics Action Center: http//www.tocsicsaction.org/problems-and-solutions/pesticides.
95. Lisi P. Pesticides in occupational contact dermatitis. Clin Dermatol. 1992;10:175.
96. Lidén C. Pesticides. In: Rycroft RJG, Menné T, Frosch PJ, et al., editors. Textbook of contact dermatitis. Berlin: Springer; 2001. p. 767.
97. Mamuskiatti W, Abrasm K, Hogan DJ, et al. Pesticide-related dermatoses in agricultural workers. In: Kanerva L, Elsner P, Wahlberg IE, et al., editors. Handbook of occupational dermatology. Berlin: Springer; 2000. p. 781.
98. World Health Organization and United Nations Environmental Programm (WHO/UNEP). Public health impact of pesticides used in agriculture. Geneve: WHO; 1980.
99. Cronin E. Pesticides. In: Cronin E, editor. Contact dermatitis. Edimburgh: Churchill Livingstone; 1980. p. 391.
100. Hogan DJ, Graftan LH. Pesticides and other agricultural chemicals. In: Adams RM, editor. Occupational skin disease, 3rd ed. Philadelphia: Saunders;1999. p. 597.
101. Gordon M, Richter ED. Hazards associated with aerial spraying of organophosphate insecticides in Israel. Rev Environ Health. 1991;9:229.
102. Lagaspi JA, Zenz C. Occupational health aspects of pesticides. Clinical and hygienic principles. In: Zenz C, Dickerson OB, Hovarth EP, ediors. Occupational medicine, 3rd ed. Saint Louis: Mosby; 1994; p. 617.
103. Matsushita T, Nomura S, Wakatsuki T. Epidemiology of contact dermatitis from pesticides in Japan. Contact Dermatitis. 1980;6:255.
104. Paulsen E. Occupational dermatitis in Danish gardeners and greenhouse workers. Contact Dermatitis. 1998;38:14.
105. Bonamonte D, Foti C, Cassano N, et al. Contact dermatitis from organo-phosphorus pesticides. Contact Dermatitis. 2001;44:179.

106. Cellini A, Offidani A. An epidemiological study on cutaneous diseases of agricultural workers authorized to use pesticides. Dermatology. 1994;189:129.
107. Lisi P, Caraffini S, Assalve D. A test series for pesticide dermatitis. Contact Dermatitis. 1986;15:266.
108. Meneghini CL, Angelini G. Le dermatiti da contatto. Roma: Lombardo Ed.; 1982.
109. Bonamonte D, Vestita M, Filoni A, et al. Tobacco-induced contact dermatitis. Eur J Dermatol. 2016;26:223.
110. Steele MC, Ive FA. Recurrent facial eczema in females due to "strike anywhere" matches. Br J Dermatol. 1982;106:477.
111. Bonamonte D, Filoni A, Verni P, et al. Dermatitis caused by algae and Bryozoans. In: Bonamonte D, Angelini G, editors. Acquatic dermatology. Biotic, chemical and physical agents. Berlin: Springer; 2016. p. 127.
112. Fraser JH, Lyell A. Dogger Bank itch. Lancet. 1963;1:61.
113. Newhouse ML. Dogger itch: survey of trawlermen. Br Med J. 1966;1:142.
114. Pathenanaban ON, Porter JS, White IR. Dogger Bank itch in the eastern English Channel: a newly described geographical distribution of an old problem. Clin Exp Dermatol. 2005;30:622.
115. Audebert C, Lamoureux P. Professional eczema of trawlermen by contact with bryozoaires in the "baie de Seine". Ann Dermatol Vénéreol. 1978;105:187.
116. Jeanmougin M, Janier M, Prigent F, et al. Eczema de contact avec photosensibilité à *Alcyonidium gelatinosum*. Ann Dermatol Vénéreol. 1983;110:725.
117. Angelini G, Vena GA, Grandolfo M, et al. Iatrogenic contact dermatitis and eczematous reactions. Clin Dermatol. 1993;11:467.
118. Lachapelle JM. Les dermites de contact aéroportées. Bull Actual Thér. 1985;30:299.
119. Thune P. Contact allergy due to lichens in patients with a history of photosensitivity. Contact Dermatitis. 1977;3:267.
120. Bonamonte D, Foti C, Lionetti N, et al. Photoallergic contact dermatitis to 8-methoxypsoralen in *Ficus carica*. Contact Dermatitis. 2010;62:34.
121. Tennstedt D, Lachapelle JM. Allergy to latex. Now Dermatol (Strasburg). 1998;17:397.
122. Handfield-Jones SE. Latex allergy in health-care workers in an English district general hospital. Br J Dermatol. 1998;138:273.
123. Tarvainen K, Jolanki R, Estlander T, et al. Immunologic contact urticaria due to airborne methylhexahydrophthalic and methyltetrahydrophthalic anhydrides. Contact Dermatitis. 1995;32:204.
124. Dooms-Goossens A, Deveylder H, Duron C, et al. Airborne contact urticaria due to cinchona. Contact Dermatitis. 1986;15:258.
125. Bonamonte D, Filoni A, Vestita M, et al. Role of environmental risk factors in the pathogenesis and clinical outcome of atopic dermatitis. Biomed Research Int. 2019. https://doi.org/10.1155/2019/2450605.
126. Clark RA, Adinoff AD. Aeroallergen contact can exacerbate atopic dermatitis: patch tests as a diagnostic tool. J Am Acad Dermatol. 1989;21:863.
127. Beck HI, Korsgaard J. Atopic dermatitis and house dust mites. Br J Dermatol. 1989;120:245.
128. Champion RH. Atopic sensitivity to algae and lichens. Br J Dermatol. 1971;85:551.
129. Tupker RA, De Monchy JG, Coenraads PJ, et al. Induction of atopic dermatitis by inhalation of house dust mite. J Allergy Clin Immunol. 1966;97:1064.
130. Jürgens M, Wollenberg A, Hanau D, et al. Activation of human epidermal Langerhans cells by engagement of the high affinity receptor for IgE, Fc epsilon RI. J Immunol. 1995;155:5184.
131. Jacob SE, Breithaupt AD. An important difference between "exposed" and "photodistributed" underscores the importance of identifying common reactions. J Clin Aesthet Dermatol. 2009;2:44.
132. Bonamonte D, Foti C, Carpentieri A, et al. Dermatite allergica da contatto in età pediatrica. Ann Ital Dermatol Allergol. 2010;64:1.
133. Romita P, Foti C, Stingeni L, et al. Contact allergy in children with atopic dermatitis: a retrospective study. Endocr Metab Immune Disord Drug Targets. 2019. https://doi.org/10.2174/1871530319666190211123342.
134. Marks R, Dawber RPR. Skin surface biopsy: an improved technique for the examination of the horny layer. Br J Dermatol. 1971;84:117.
135. Lidén C, Lundgren L, Skare L, et al. A new whole-body exposure chamber for human skin and lung challenge experiments—the generation of wheat flour aerosols. Ann Occup Hyg. 1988;42:541.
136. Bergand J-M. La chenille processionnaire du pin *(Thaumetopoea pityocampa* Schiff*)* et l'homme. These no. 41, Université de Bordeaux; 1978.
137. Ducombs G, Lamy J-J, Bergand JM, et al. La chenille processiomaire *(Thaumetopoea pityocampa* Schiff, Lépidoptères) e l'homme. Ann It Dermatol Vénéreol. 1979;106:769.
138. Leigheb G. Dermatoses caused by arthropods. In: Giannetti A, Del Forno C, editors. Textbook of dermatology and sexually transmitted diseases. Padova: Piccin Nuova Libraria; 2013. p. 747.
139. Bonamonte D, Profeta G, Foti C, et al. Humans and pine caterpillar *(Thaumetopoea pityocampa* Schiff). Ann Ital Dermatol Allergol. 2007;61:91.
140. Bonamonte D, Foti C, Vestita M, et al. Skin reactions to pine processionary caterpillar *Thaumetopoea pityocampa* Schiff. Sci World J. 2013. http://dx.doi.org/101155/2013/867431.
141. Battisti A, Stastny M, Netherer S, et al. Expansion of geographic range in the pine processionary moth caused by increased winter temperatures. Ecolog Appl. 2005;15:2084.
142. Vega JM, Moneo I, Ortiz JCG, et al. Prevalence of cutaneous reactions to the pine processionary moth *(Thaumetopoea pityocampa)* in an adult population. Contact Dermatitis. 2011;64:220.

143. Vega JM, Moneo I, Armentia A, et al. Anaphylaxis to a pine caterpillar. Allergy. 1997;52:1244.
144. Vega J, Vega JM, Moneo I, et al. Occupational immunologic contact urticaria from pine processionary caterpillar *(Thaumetopoea pityocampa):* experience in 30 cases. Contact Dermatitis. 2004;50:60.
145. Moschen M, Policaro RD, Savastano G. Unusual bullous dermatitis due to pine caterpillars. Arch Ital Dermatol Venereol Sessuol. 1969;33:474.
146. Henwood BP, MacDonald DM. Caterpillar dermatitis. Clin Exp Dermatol. 1983;8:77.
147. Vega ML, Vega J, Vega JM, et al. Cutaneous reactions to pine processionary caterpillar (*Thaumetopoea pityocampa*) in pediatric population. Pediatr Allergy Immunol. 2003;14:482.
148. Vega JM, Moneo I, Armentia A, et al. Allergy to the pine processionary caterpillar (*Thaumetopoea pityocampa*). Clin Exp Allergy. 1999;29:1418.
149. Vega JM, Moneo I, Armentia A, et al. Pine processionary caterpillar as a new cause of immunologic contact urticaria. Contact Dermatitis. 2000;43:129.
150. Haluska FG, Puliafito CA, Henriquez A, et al. Experimental gypsy moth *(Lymantria dispar)* ophthalmia nodosa. Arch Ophthalmol. 1983;101:799.
151. Watson PG, Sevel D. Ophthalmia nodosa. Br J Ophthalmol. 1966;50:209.
152. Hosler EW. Caterpillars and moths: Part I: dermatologic manifestations of encounters with Lepidoptera. J Am Acad Dermatol. 2010;62:1.
153. Hosler EW. Caterpillars and moths: Part II: dermatologic manifestations of encounters with Lepidoptera. J Am Acad Dermatol. 2010;62:13.
154. Santos-Magadán S, González de Olano D, Bartolomé-Zavala B, et al. Adverse reactions to the processionary caterpillar: irritant or allergic reactions? Contact Dermatitis. 2009;60:109.
155. Lundberg U, Salazar V, Tovar M, et al. Isolation and partial characterization of proteins with vasodegenerative and proinflammatory properties from the egg-nests of *Hylesia metabus* (Lepidoptera, Saturniidae). J Med Entomol. 2007;44:440.
156. Lamy M, Pastureaud MH, Novak F. Thaumetopoein: an urticating protein from the hairs and integument of the pine processionary caterpillar (*Thaumetopoea pityocampa* Schiff, Lepidoptera, Thaumetopoeidae). Toxicon. 1986;24:347.
157. Werno J, Lamy M, Vincendeau P. Caterpillar hairs as allergens. Lancet. 1993;342:936.
158. Rebollo S, Moneo I, Vega JM, et al. Pine processionary caterpillar allergenicity increases during larval development. Int Arch Allergy Immunol. 2002;128:310.
159. Rodriguez-Mahillo AI, Gonzalez-Muñoz M, Vega JM, et al. Setae from the pine processionary moth *(Thaumetopoea pityocampa)* contain several relevant allergens. Contact Dermatitis. 2012;67:367.
160. Burton OT, Zaccone P. The potential role of chitin in allergic reactions. Trends Immunol. 2007;28:419.
161. Fagrell B, Jörneskog G, Salomonsson AC, et al. Skin reactions induced by experimental exposure to setae from larvae of the northern pine processionary moth *(Thaumetopoea pinivora)*. Contact Dermatitis. 2008;59:290.
162. Carruthers R. Caterpillar dermatitis. Br Med J. 1967;2:765.
163. De Jong MIM, Hoedemaeker PJ, Jongebloed WL, et al. Investigative studies of the dermatitis caused by the larva of the brown-tail moth *(Euproctis chrysorrhoea* Linn*).* II. Histopathology of skin lesions and scanning electron microscopy of their causative setae. Arch Dermatol Res. 1976;21:177.
164. Cuevas P, Angulo J, Giménez-Gallego G. Topical treatment of contact dermatitis by pine processionary caterpillar. BMJ Case Rep. 2011;11:2011.
165. Hesler LS, Logan TM, Benenson MW, et al. Acute dermatitis from oak processionary caterpillars in a U.S. military community in Germany. Mil Med. 1999;164:767.
166. Ducombs G, Lamy M, Michel M, et al. La papillonite de Guyane Française. Etude clinique et épidémiologique. Ann Dermatol Vénéreol. 1983;110:809.
167. Dinehart SM, Archer ME, Wolf JE, et al. Caripito itch: dermatitis from contact with *Hylesia* moths. J Am Acad Dermatol. 1985;13:743.
168. Burnett JW, Calton GJ, Morgan RJ. Caterpillar and moth dermatitis. Cutis. 1986;37:320.
169. Von Krogh G, Maibach HI. The contact urticaria syndrome. In: Marzulli FN, Maibach HJ, editors. Dermatotoxicology. Hemisphere, Washington; 1983. p. 301.
170. Hill WR, Rubenstein AD, Kovacs J Jr. Dermatitis resulting from contact with moths (genus *Hylesia)*; report of cases. J Am Med Assoc. 1948;138:737.
171. Pesce H, Delgado A. Poisoning from adults moths and caterpillars. In: Bucherl W, Buckley EE, editors. Venomous animals and their venoms, vol. III. Venomous Invertebrates: Academic Press, New York; 1971. p. 119.
172. Dinehart SM, Jorizzo JL, Soter NA, et al. Evidence for histamine in the urticating hairs of *Hylesia* moths. J Invest Dermatol. 1987;88:691.
173. Southcott RV. Lepidopterism in the Australian region. Rec Adelaide Children's Hosp. 1978;2:87.
174. Tindall JP. Chloracne and chloracnegens. J Am Acad Dermatol. 1985;13:539.
175. Panteleyev AA, Bickers DR. Dioxin-induced chloracne—reconstructing the cellular and molecular mechanisms of a classic environmental disease. Exp Dermatol. 2006;15:705.
176. Ju Q, Zouboulis C, Xia L. Environmental pollution and acne: chloracne. Dermato Endocrinol. 2009;1:125.
177. Marinković N, Pašalić D, Ferenčak G, et al. Dioxins and human toxicity. Arh Hig Rada Toksikol. 2010;61:445.
178. Saurat JH, Sorg O. Chloracne, a misnomer and its implications. Dermatology. 2010;221:23.

179. Suskind RR. Chloracne, "the hallmark of dioxin intoxication". Scand J Work Environ Health. 1985;11:165.
180. Taylor JS. Environmental chloracne: update and overview. Ann N Y Acad Sci. 1979;320:295.
181. Bornemann W. Über die Histologie der Chloracne. Arch Dermatol Res. 1982;62:75.
182. Herxheimer K. Über Chloracne. Munch Med Whochenschc. 1899;46:278.
183. English JS, Dawe RS, Ferguson J. Environmental effects and skin disease. Br Med Bull. 2003;68:129.
184. Ren Z, Zheng M. Impacts of human activities on dioxins emissions at national scale. Chemosphere. 2009;76:853.
185. Shibamoto T, Yasuhara A, Katami T. Dioxin formation from waste incineration. Rev Environ Contam Toxicol. 2007;190:1.
186. Inoue K, Yasuda K, Kawamoto K. Atmospheric pollutants discharged from municipal solid waste incineration and gasification-melting facilities in Japan. Waste Manag Res. 2009;27:617.
187. Ni Y, Zhang H, Fan S, et al. Emissions of PCDD/Fs from municipal solid waste incinerators in China. Chemosphere. 2009;75:1153.
188. Zhu J, Hirai Y, Sakai S. Potential source and emission analysis of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans in China. Chemosphere. 2008;73(Suppl 1):872.
189. Institute of Medicine (US). Committee to review the health effects in Vietnam Veterans of exposure to herbicides. Other health effects. In: Veterans and Agent Orange: health effects of herbicides used in Vietnam. New York: National Academic Press; 1994. p. 672.
190. Le TN, Johansson A. Impact of chemical warfare with agent orange on women's reproductive lives in Vietnam: a pilot study. Reprod Health Matters. 2001;9:156.
191. Cheng WN, Coenraads PJ, Hao ZH, et al. A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. Am J Ind Med. 1993;24:81.
192. Piacitelli L, Marlow D, Fingerhut M, et al. A retrospective job exposure matrix for estimating exposure to 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin. Am J Ind Med. 2000;38:28.
193. Baccarelli A, Pesatori AC, Consonni D, et al. Health status and plasma dioxin levels in chloracne cases 20 years after the Seveso, Italy accident. Br J Dermatol. 2005;152:459.
194. Bertani PA, Di Domenico A. Health consequences of the Seveso, Italy, accident, In: Schecher A, Gasiewicz TA, editors. Dioxins and health, 2nd ed. New York: Wiley-Interscience; 2003. p. 827.
195. Pesatori AC, Consonni D, Bachetti S, et al. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso accident". Ind Health. 2003;41:127.
196. Caputo R, Monti M, Ermacora E, et al. Cutaneous manifestations of tetrachlorodibenzo-*p*-dioxin in children and adolescents. Follow-up 10 years after the Seveso, Italy, accident. J Am Acad Dermatol. 1988;19:812.
197. Guo YL, Yu ML, Hsu CC, et al. Chloracne, goiter, arthritis, and anemia after polychlorinated biphenyl poisoning: 14-year follow-up of the Taiwan Yucheng cohort. Environ Health Perspect. 1999;107:715.
198. Chivers CJ. A dinner in Ukraine made for Agata Christie. The New York Times, December 20;2004.
199. Sterling JB, Hanke CW. Dioxin toxicity and chloracne in the Ukraine. J Drugs Dermatol. 2005;4:148.
200. Sorg O, Zennegg M, Schmid P, et al. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) poisoning in Viktor Yushchenko: identification and measurement of TCDD metabolites. Lancet. 2009;374:1179.
201. Saurat JH, Kaya G, Saxer-Sekulic N, et al. The cutaneous lesions of dioxin exposure: lessons from the poisoning of Viktor Yushchenko. Toxicol Sci. 2012;125:310.
202. Violante FS, Milani S, Malenchini G, et al. Chloracne due to o-dichlorobenzene in a laboratory worker. Contact Dermatitis. 2005;52:108.
203. Rosas Vazquez E, Campos Macias P, Ochoa Tirodo JG, et al. Chloracne in the 1990s. Int J Dermatol. 1996;35:643.
204. Passarini B, Infusino SD, Kasapi E. Chloracne: still cause for concern. Dermatology. 2010;221:63.
205. World Health Organitation (WHO). Dioxins and their effects on human health. 12 November 2010. http://www.who.intmediacentre/factshcets/ts225/en/index.html.
206. Olson JR. Pharmacokinetics of dioxin and related chemicals. In: Schecter A, editor. Dioxins and health. New York: Plenum Press; 1994. p. 163.
207. Pirkle JL, Wolfe WH, Patterson DG, et al. Estimates of the half-life of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in Vietnam Veterans of Operation Ranch Hand. J Toxicol Environ Health. 1989;27:165.
208. Wold Health Organitation (WHO). Executive summary. Assessment of health risks of dioxins: re-evaluation of the tolerable daily intake (TDI). Geneva: WHO; 1998.
209. Marshall NB, Kerkvliet NJ. Dioxin and immunoregulation: emerging role of aryl hydrocarbon receptor in the generation of regulatory cells. Ann N Y Acad Sci. 2009;1183:25.
210. Lawrence BP, Kerkuliet NJ. Immunomodulation by TCDD and related polyhalogenated aromatic hydrocarbons. In: Imebkec R, House R, Kimber J, editors. Immunotoxicology and immunopharmacology. Boca Raton: CRC Press; 2007. p. 239.
211. Wilhelmsson A, Cuthill S, Denis M, et al. The specific DNA binding activity of the dioxin receptor is modulated by the 90 kd heat shock protein. EMBO J. 1990;9:69.
212. Ma Q. Induction of CYP1A1. The AHR/DRE paradigm: transcription, receptor regulation, and expanding biological roles. Curr Drug Metab. 2001;2:149.

213. Whitlock JP. Induction of cytochrome P4501A1. Ann Rev Pharmacol Toxicol. 1999;39:103.
214. Pastor MA, Carrasco L, Izquierdo MJ, et al. Chloracne: histopathologic findings in one case. J Cutan Pathol. 2002;29:193.
215. Geusau A, Jurecka W, Nahavandi H, et al. Punctate keratoderma-like lesions on the palms and soles in a patient with chloracne: a new clinical manifestation of dioxin intoxication? Br J Dermatol. 2000;143:1067.
216. Panteleyev AA, Thiel R, Wanner R, et al. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCCD) affects keratin 1 and keratin 17 gene expression and differentially induces keratinization in hairless mouse skin. J Invest Dermatol. 1997;108:330.
217. Panteleyev AA, Thiel R, Rosenbach T, et al. Acne chlorina and acne vulgaris—casual likeness or casual homology? Arch Dermatol Res. 2000;292:577.
218. May G. Chloracne from the accidental production of tetrachlorodibenzodioxin. Br J Ind Med. 1973;30:276.
219. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med. 1982;3:179.
220. Pazderova-Vejlupková J, Lukás E, Němcova M, et al. The development and prognosis of chronic intoxication by tetrachlordibenzo-*p*-dioxin in men. Arch Environ Health. 1981;36:5.
221. Zugerman C. Chloracne. Clinical manifestations and etiology. Dermatol Clin. 1990;8:209.
222. Jensen NE. Chloracne: three cases. Proc R Soc Med. 1972;65:687.
223. Crow KD. Chloracne. Semin Dermatol. 1982;1:305.
224. Poskitt LB, Duffill MB, Rademaker M. Chloracne, palmoplantar keratoderma and localized scleroderma in a weed sprayer. Clin Exp Dermatol. 1994;19:264.
225. Kuratsune M, Yoshimura T, Matsuzaka J, et al. Yusho, a poisoning caused by rice oil contaminated with polychlorinated biphenyls. HSMHA Health Rep. 1971;86:1083.
226. Hambrick GW Jr. The effect of substituted naphthalenes on the pilosebaceous apparatus of rabbit and man. J Invest Dermatol. 1957;28:89.
227. Taylor JS. Chloracne—a continuing problem. Cutis. 1974;13:585.
228. McDonagh AJ, Gawkrodger DJ, Walker AE. Chloracne—study of an outbreak with new clinical observations. Clin Exp Dermatol. 1993;18:523.
229. Moses M, Lilis R, Crow KD, et al. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: comparison of findings with and without chloracne. Am J Ind Med. 1984;5:161.
230. Panteleyev AA, Roumak VS, Stepanova LV, et al. Clinical and ultrastructural characterization of human skin after exposure to dioxin-contaminated defoliants. Proceedings Joint Russian-Vietnam Tropical Centre, Moscow; 1991. p. 300.
231. Bauer H, Schulz KH, Spregelberg U. Occupational poisonings in the production of chlorphenol compounds. Arch Gewerbepathol Gewerbehyg. 1961;18:538.
232. Taylor JS, Wuthrich RC, Lloyd KM, et al. Chloracne from manufacture of a new herbicide. Arch Dermatol. 1977;113:616.
233. Foti C. Dermatosi da agenti chimici. In: Angelini G, Vena GA, editors. Dermatologia professionale e ambientale, Vol I. Brescia: ISED; 1997. p. 85.
234. Leyden JJ. New understandings of the pathogenesis of acne. J Am Acad Dermatol. 1995;32:S15.