

## **Occupational skin ailments caused by scientifically recognised allergy-provoking or irritative substances not included under other headings**

### **Definition of causal agent**

Occupational skin diseases are represented by allergic and irritant contact dermatitis and also contact urticaria.

Allergic contact dermatitis (ACD) results from a T-cell-mediated immune response against haptens applied onto the skin. ACD is a disease, presenting as a pruritic eczema, characterized by erythema and vesicles, which develop within 24-48 h at the site of hapten penetration in sensitized individuals.

Irritant contact dermatitis (ICD) may be acute and it is commonly the result of a single exposure to an irritant. Chronic irritant dermatitis usually develops as a result of cumulative exposure to multiple irritants, resulting in disruption of the skin barrier function.

Contact urticaria is type -1 allergic response and the reaction is immediate, occurring within about 15 minutes after contact with the relevant substance.

### ***Main occupational uses and sources of exposure:***

The main agents are listed in the annex I, but there are a lot of substances or their mixtures which should be included in it i.e.: glyceryl monothioglycolate and derivatives, balsam Peru and others fragrances, chlorhexidine, glutaraldehyde, mercaptobenzothiazole and derivatives, colophony, Cl+Me-isothiazolinone and derivatives, plant products, urea, melamine formaldehyde resins and many others.

### ***Note: The following items are covered under this entry:***

- Occupationally caused allergic contact dermatoses
- Occupationally caused irritation of the skin and mucous membranes

And

- Methyl acrylate
- Dithiocarbamates
- Methylmethacrylate

### **Diagnostic criteria**

#### ***Symptoms:***

Allergic contact dermatitis is usually confined to the area of skin that comes in contact with the allergen, typically hands or face. It may present with pruritus redness, vesicles, scaling fissuring or secondary excoriation. In some cases the area of lesions is much larger than the area of contact.

In irritant contact dermatitis the symptoms can take many forms: redness, itching, crusting, swelling, blistering, oozing, dryness, scaliness, thickening of the skin. Most attacks are slight and confined to the hands and forearms, but can affect any part of the body that comes in contact with an irritating substance.

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Main symptoms of contact urticaria: red, itchy skin, inflamed skin, welts (in hives).

Anamnesis: The development of the skin lesions are in direct relationship to the work schedule. There is a recurrence of the disease on re-exposure to the same agent.

Immunological criteria: Allergic contact dermatitis is investigated by patch testing for all the suspected substances present at the workplace. The relevance of a positive reaction must be assessed.

There is no test for irritant contact dermatitis. The diagnosis is made by the history of exposure to known irritants and the exclusion of allergy on appropriate patch testing.

In cases of contact urticaria, prick tests and estimation of specific IgE antibodies in blood should be performed.

## Exposure criteria

See below sections on:

*Occupationally caused allergic contact dermatoses* and on

*Occupationally caused irritation of the skin and mucous membranes.*

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## Occupationally caused allergic contact dermatoses

### Definition of causal agent

The most common presentation for occupationally caused dermatoses are those of allergic contact dermatitis (synonym: allergic contact eczema), of contact urticaria and protein contact dermatitis.

Main causal agents are complex molecules with a molecular mass of less than 1000 Daltons, which are haptens or incomplete antigens, or proteins, which are complete antigens. Haptens are the most common cause of allergic contact dermatitis

A large number of substances may be responsible for occupationally caused allergic dermatoses. The main categories, with some examples are:

- I Low molecular mass substances  
Metals and/or their compounds (e.g. nickel and its compounds, hexavalent chromium compounds, water-soluble trivalent chromium compounds, cobalt compounds)  
Rubber and plastic chemicals (e.g. accelerators: resins, hardeners)  
Dyes and dye intermediates (e.g. paraphenylene-diamine)
- II Macromolecules  
Substances of animal or plant origin e.g. natural rubber latex
- III Photo-allergens  
Plants, fragrances

### Diagnostic criteria

An allergic skin disease may be dependent on:

- personal factors, including genetic factors,
- exogenous factors: chemical structure of the sensitizing agent, its concentration, the type of diluting agent or dispersant used (these may act as irritants through lipolytic action, modifying the pH of the skin and the skin defence system),
- site and extent of contact
- climatic conditions: e.g. temperature, humidity, sunlight (ultraviolet radiation).

*Sites of the lesions:* linked with contact with the product in question. In some cases the area of lesions is larger than the area of contact.

*History:* occupational exposure to a substance known to trigger dermatoses. The development of the skin lesions are in direct relationship to the work schedule. There is recurrence of the disease on re-exposure to the same agent.

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## Immunological criteria

Patch tests should be carried out for all the suspected allergens present at the workplace. The interpretation of the results requires expertise in patch testing and dermatology. In cases of photo-sensitivity and contact urticaria, special test should be carried out (e.g. photo patch tests, prick test).

If positive, these tests together with appropriate sites of lesions and anamnesis provide adequate proof of the occupational origin of the disease, although such an origin cannot be wholly discounted if the tests are negative.

## Exposure criteria

*Minimum intensity of exposure:* There is a dose/effect relationship in the onset of allergic contact dermatitis, but in individual cases it usually is not possible to determine it retrospectively. Usually the exposure is greater for sensitization than for elicitation.

*Minimum duration of exposure:* In exceptional cases, a single contact is sufficient to cause sensitization (with dinitrochlorobenzene, dinitrofluorobenzene and methacrylates). Normally, several instances of exposure are required over periods which vary enormously in length. The sensitization period is generally 10 to 15 days from the first occupational contact, but usually much longer. After this period, any further exposure causes the lesions to appear rapidly. If sensitization occurs prior to occupational exposure the minimum exposure period may be shorter.

*Maximum latent period:* A few days.

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## Occupationally caused irritation of the skin and mucous membranes

### Definition of causal agent

Considered as causing irritation: non-corrosive substances and preparations which, through immediate, prolonged or repeated contact with the skin or mucous membranes, cause inflammation

Considered as corrosive: substances and preparations which, on contact with living tissues, cause severe damage.

A substance can cause irritation at low concentrations and be corrosive at higher concentrations.

Some physical agents are capable, in themselves, of producing an irritation reaction, such as, for example, dusts in contact with the mucous membranes of the eyes or respiratory tract or even by cutaneous friction.

Substances which meet the requirements to be classified according to the criteria in Annex IV of Council Directive 67/548/EEC as corrosives, irritants or sensitizers, may be identified by a risk phrase on the container as follows:

R 21: harmful to skin

R 34: causes burns,

R 35: causes severe burns,

R 36: causes irritation to the eyes,

R 37: causes irritation to the respiratory tract,

R 38: causes irritation to the skin,

R 41: risk of severe damage to the eyes.

R 43: may cause sensitization by skin contact.

### Skin irritation

#### *Diagnostic criteria:*

*Clinical effects:* the symptoms range from erythema (simple irritation) to third-degree chemical burns (corrosion) and, in the case of repeated exposure, to contact dermatitis.

Many factors can contribute to the occurrence and severity of the lesion, such as the degree of water and lipid solubility and liposolubility of the substance, its concentration, the duration of exposure, interaction with other substances, individual factors (e.g. resistance, sweating or dryness of the skin), and physical factors (e.g. occlusion, friction, laceration of the skin and ambient temperature and humidity).

There is also the possibility of dermatitis caused by irritation due to particles carried in the ambient air.

#### *Exposure to "strong irritants" and corrosive agents:*

— local reversible inflammatory reaction immediately following a single application,

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- in severe cases: caustic effect, chemical burns with necrosis and the possibility of sequelae (scarring).

For example: strong alkalis and acids.

*Exposure to "relatively mild irritants":*

These are substances which, under normal conditions of use, only cause irritation of superficial skin layers or substances causing defatting of the skin resulting in dermatitis after prolonged exposure.

The symptoms generally only appear after repeated or prolonged contact. Physical factors and multiple chemical exposure often play a role. For example: soaps and detergents.

*Repeated long-term exposure:*

Thickening and lichenification of the skin (with painful fissures) can occur after several days or weeks of continuous mild irritation, which can develop into chronic dermatitis.

Account should be taken of the possibility of splashes, and of immersion where occlusion increases the irritation (for instance: under rubber or plastic gloves or soaked clothes).

***Exposure criteria:***

*Minimum intensity of exposure:* Assessed by anamnesis revealing skin contact with a potentially irritating substance taking into account the process.

There is the possibility of the irritability of the skin persisting: a worker who has developed an irritation reaction to a product may, in some cases, develop greater susceptibility while, clinically, his skin appears to have recovered. The irritation reaction reappears far more rapidly if there is subsequent contact with the substance responsible.

*Minimum duration of exposure:* Usually, several months, but range from a few minutes to a few hours to several weeks, or even longer depending on the intensity of exposure.

*Maximum latent period:* The symptoms must appear during exposure or within 48 hours at the latest.

## **Irritation of the mucous membranes**

### **□ Irritation of the eyes**

***Diagnostic criteria:***

Clinical effects: the symptoms range from simple conjunctival irritation and tearing to severe corneal damage. Reactions can be diffuse and delayed.

***Exposure criteria:***

*Minimum intensity of exposure:* Assessed by anamnesis revealing occupational exposure of the eyes to a potential irritant.

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*Minimum duration of exposure:* Acute irritation: A few minutes to a few hours depending on the intensity of exposure.

Chronic irritation: Seven days.

*Maximum latent period:* The symptoms must appear during exposure or within 48 hours at the latest.

## □ Irritation of the respiratory tract

Irritation may be caused by dusts, fumes, vapours and aerosols.

As in the case of skin irritation, many factors can contribute to the appearance and severity of the lesions.

Some asthmatics or workers suffering from a disease of the respiratory tract, such as chronic bronchitis, may show increased sensitivity to the action of the irritants.

Particular sensitivity in some subjects who have no respiratory disease is possible.

Smoking or simultaneous exposure to different substances should be taken into account.

### ***Diagnostic criteria:***

Clinical effects: range from rhinitis and cough to laryngitis, bronchitis or even chemical pneumonia, pulmonary oedema and obliterating bronchiolitis.

Sequelae may occasionally include emphysema and fibrosis.

Bronchial hyper-reactivity syndrome:

Intense acute exposure to an irritant substance may cause an asthmatic response or bronchial hyperactivity in some workers.

The water solubility of the substance is an important factor in determining the site of action:

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|---------------------|---|
| very soluble:       | upper respiratory tract symptoms, within seconds: the irritant effects generally provide adequate warning preventing overexposure, e.g. ammonia, sulphur, dioxide;  |
| moderately soluble: | upper and lower respiratory tract symptoms, within minutes, e.g. chlorine, fluorine;  |
| slightly soluble:   | lower respiratory tract symptoms, insidious onset. The effects can be delayed (6 to 24 or even up to 72 hours), but are often (but not always) preceded by upper respiratory tract symptoms, e.g. ozone, phosgene, nitrogen oxides. |

### ***Exposure criteria:***

*Minimum intensity of exposure:* Variable, according to the potency of the substance.

*Minimum duration of exposure:* Acute irritation: A few minutes to a few hours depending on the intensity of the exposure.

Chronic irritation: Should be assessed by a competent person.

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*Maximum latent period:* The onset of symptoms should occur during exposure or within 72 hours at the latest. Delayed symptoms are possible with poorly soluble substances.

The first signs of bronchitis should appear during the period of employment causing exposure to the suspected substance.



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## Methyl acrylate

### Definition of causal agent

Methyl acrylate is a colourless, volatile, flammable liquid with an acrid odour. It polymerizes easily on standing, and the process is accelerated by heat, light and peroxides. It can react vigorously with oxidizing agents.

### *Main occupational uses and sources of exposure:*

Methyl acrylate is used primarily as a acrylonitrile comonomer in the preparation of acrylic and methacrylic fibres. These are used in clothes and furnishings. Methyl acrylate has also been used in the preparation of thermoplastic coatings, adhesives and sealants and amphoteric surfactants for shampoos and vitamin B1. It may also be used as a microencapsulation mixture component or for the polymerization of radioactive waste into block form. It can serve as a resin in the purification and decolouration of industrial effluents or aid in the timed release and disintegration of pesticides.

### Toxic effects

#### Irritant effects

Methyl acrylate is a lacrymating agent and irritates the mucous membranes. See above section on *Occupationally caused irritation of the skin and mucous membranes*.

#### Allergic contact dermatitis

Methyl acrylate causes sensitization of the skin. Cross reaction may occur with the following compounds: methyl vinyl ketone, 4-vinyl pyridine, trimethylol propane triacrylate and pentaerythritol triacrylate.

No cross reaction with acrylamide and methyl methacrylate is observed.

See above section on *Occupationally caused allergic contact dermatoses*.

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## Dithiocarbamates

### Definition of causal agent

Dithiocarbamates are disulphide carbamate analogues chemically derived from carbamic acid. They are hydrophiles and form heavy, water-soluble metallic complexes with metals such as, for example, manganese, zinc, iron, sodium. Some metallic dithiocarbamate compounds used as fungicides are insoluble in water but soluble in non polar solvents.

### *Main occupational uses and sources of exposure:*

Dithiocarbamates are mainly used in agriculture as fungicides and herbicides. Some dithiocarbamates are used in the chemical industry, as accelerators in the synthesis of plastics, or in vulcanization processes.

### Local toxic effects

#### Irritant effects

Dithiocarbamates may cause slight skin irritation.

See document on occupationally caused irritation of the skin and mucous membranes.

#### Allergic effects

Dithiocarbamates (notably manganese and zinc derivatives) can cause allergic contact dermatitis.

See above section on *Occupationally caused allergic contact dermatoses*.

### Chronic systemic effects

Dithiocarbamates, and in particular ethylenebisdithiocarbamates can exert, for very high exposures, a goitrogenic effect, due to the inhibition of the synthesis of thyroid hormones exerted by the main metabolite of these compounds, ethylenethiourea (ETU). As a consequence of the decrease of the synthesis of thyroid hormones, there is a compensative hypersecretion of thyroid stimulating hormone (TSH) which causes the goitrogenic effects. A goitrogenic effect has been observed in the past in heavily exposed workers, but it has never been reported in most recent periods.

The suspicion of a possible carcinogenicity for humans of ETU (thyroid cancer) in the conditions of exposure typical of the workplace has been ruled out by IARC.

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## Methylmethacrylate

### Definition of causal agent

Methylmethacrylate (MMA) is a clear, colourless, flammable liquid with an unpleasant, strong, acid odour. It is slightly soluble in water but very soluble in alcohol and ether. The odour threshold lies between 0.2 and 0.6 mg/m<sup>3</sup> in air. The chemical properties are defined by its highly reactive double binding. The monomer is readily polymerized by light, heat, oxygen, ionizing radiation and catalysts because of its ability to form a radical.

### *Main occupational uses and sources of exposure:*

Methylmethacrylate is primarily used in the manufacturing of polymethylmethacrylate (PMMA) to fabricate crystal-clear or coloured plastics, the so-called acrylic glasses, clear ceramic-like resins, and for acrylic moulding and extrusion powder.

The monomer and polymers have wide applicability in medical technology. MMA serves as a medical spray adhesive or non-irritant bandage solvent. It is also used to coat corneal contact lenses and to manufacture artificial nails. In orthopaedic surgery it is used as a bone cement for fixation of metal and plastic protheses.

### Toxic effects

#### □ Irritant effects

Methylmethacrylate can be irritating to the skin, eyes and mucous membranes.

See above section on *Occupationally caused irritation of the skin and mucous membranes*.

#### □ Allergic effects

— Allergic contact dermatitis

Methylmethacrylate can cause allergic dermatitis. In some cases, tenderness is observed, outlasting the duration of the eruption.

See above section on *Occupationally caused allergic contact dermatoses*.

— Allergic rhinitis and conjunctivitis

See Annex I entry nr. 304.07 on *Allergic rhinitis caused by the inhalation of substances consistently recognised as causing allergies and inherent to the type of the work*.

— Asthma

See Annex I entry nr. 304.06 on *Allergic asthmas caused by the inhalation of substances consistently recognised as causing allergies and inherent to the type of work*.