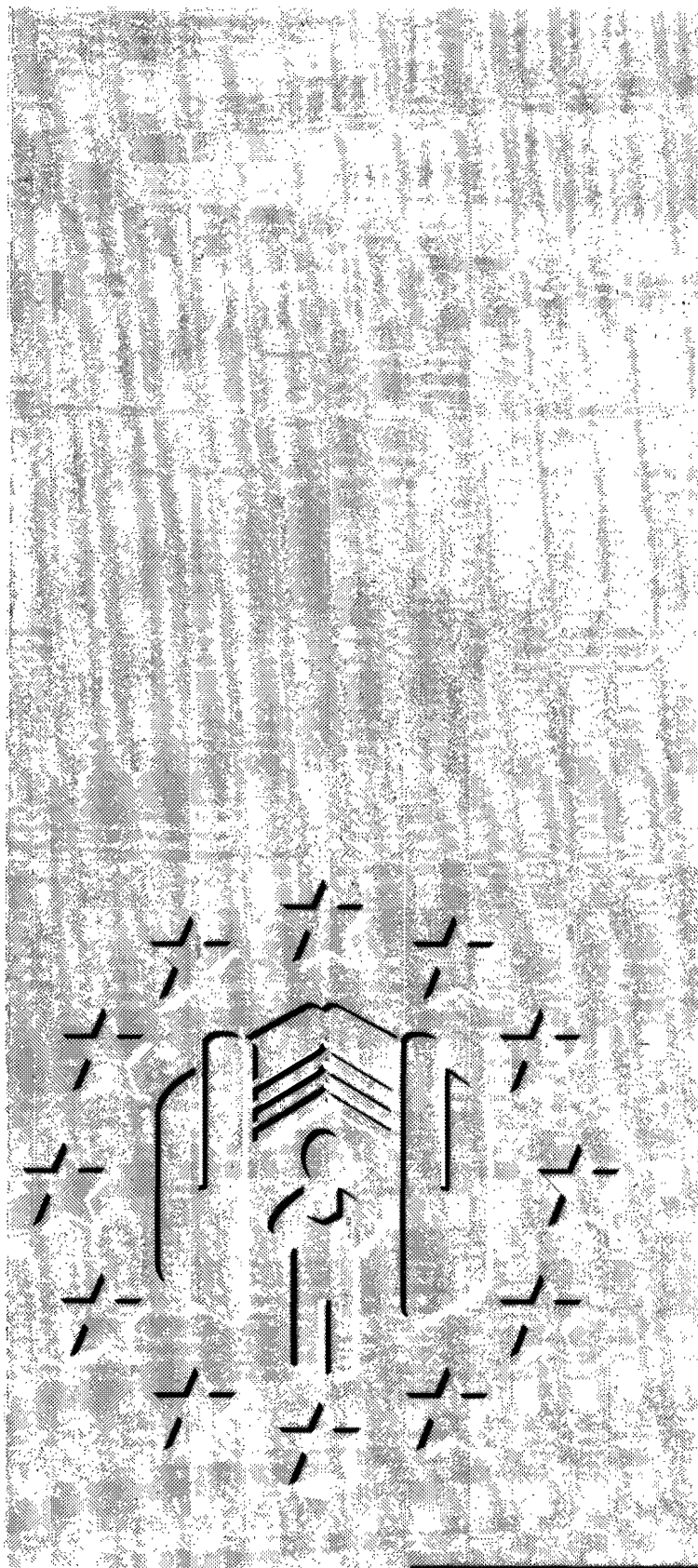




EUROPEAN COMMISSION

Information notices on diagnosis of occupational diseases



Health and safety

Information notices on diagnosis of occupational diseases

Comments and advice on this publication should be sent in writing to the following address:

Head of Occupational Health and Hygiene Unit
Public Health and Safety at Work Directorate
European Commission
Jean Monnet Building C4/89
L-2920 Luxembourg

The European Commission reserves the right to revise these information notices as the need arises and any comments received will be taken into consideration at that time.

Health and safety series

European Commission

health and safety

Information notices on diagnosis of occupational diseases

for the
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L-2920 Luxembourg

Directorate-General
Employment, Industrial Relations and Social Affairs

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Table of contents

Preface — Acknowledgements	9
Information for readers	11
Information notices on diagnosis of occupational diseases	11
DIAG 0001 (acrylonitrile monomer)	13
DIAG 0002 (arsenic and its inorganic compounds (except arsine))	14
DIAG 0003 (beryllium and its compounds)	16
DIAG 0004 (carbon monoxide)	18
DIAG 0005 (phosgene (carbon oxychloride))	20
DIAG 0006 (hydrocyanic acid (hydrogen cyanide))	21
DIAG 0007 (cyanides)	23
DIAG 0008 (isocyanates)	25
DIAG 0009 (cadmium and its compounds)	27
DIAG 0010 (chromium and its compounds)	29
DIAG 0011 (mercury and its inorganic compounds)	31
DIAG 0012 (manganese and its compounds)	33
DIAG 0013 (nitric acid)	35
DIAG 0014 (nitrogen oxides)	36
DIAG 0015 (ammonia)	37
DIAG 0016 (nickel and its compounds)	38
DIAG 0017 (phosphorus and its compounds)	39
DIAG 0018 (lead and its inorganic compounds)	41
DIAG 0019 (sulphuric acid and sulphur oxides)	43
DIAG 0020 (carbon disulphide)	45
DIAG 0021 (vanadium and its compounds)	47
DIAG 0022 (chlorine)	48
DIAG 0023 (bromine)	49
DIAG 0024 (iodine)	50
DIAG 0025 (fluorine and inorganic fluoride compounds)	51
DIAG 0026 (n-hexane)	53
DIAG 0027 (n-heptane)	55
DIAG 0028 (methylene chloride)	56
DIAG 0029 (trichloroethylene)	58
DIAG 0030 (tetrachloroethylene)	60
DIAG 0031 (vinyl chloride monomer)	62
DIAG 0032 (methyl bromide)	64
DIAG 0033 (butyl (butanol), methyl (methanol) and isopropyl (isopropanol) alcohols)	65
DIAG 0034 (ethylene glycol, diethylene glycol and 1,4-butanediol)	66
DIAG 0035 (nitro derivatives of glycols and glycerol)	67

DIAG 0036	(methyl ether, ethyl ether, isopropyl ether, vinyl ether, dichloroisopropyl ether, guaiacol)	69
DIAG 0037	(ethylene glycol monomethyl ether (2-methoxyethanol), ethylene glycol monoethyl ether (2-methoxyethanol))	70
DIAG 0038	(ketones, with special reference to methyl n-butyl ketone (MBK))	71
DIAG 0039	(organophosphorous esters)	73
DIAG 0040	(carbamates)	75
DIAG 0041	(methyl acrylate)	77
DIAG 0042	(formaldehyde)	78
DIAG 0043	(benzene)	79
DIAG 0044	(toluene)	81
DIAG 0045	(naphthalene and its derivatives (C _n H _{2n-12}))	82
DIAG 0046	(vinylbenzene, and divinylbenzene)	84
DIAG 0047	(halogenated derivatives of aromatic hydrocarbons)	86
DIAG 0048	(pentachlorophenol)	89
DIAG 0049	(halogenated derivatives of alkylarylsulphonates and alkylaryloxides)	91
DIAG 0050	(benzoquinone)	92
DIAG 0051	(aromatic amines)	93
DIAG 0052	(aliphatic amines and their halogenated derivatives)	95
DIAG 0053	(nitrated derivatives of aromatic hydrocarbons)	97
DIAG 0054	(nitro derivatives of phenols and the derivatives of hydroxybenzotrile)	101
DIAG 0055	(antimony and its inorganic compounds (except stibine))	102
DIAG 0056	(dithiocarbamates)	103
DIAG 0057	(methylmethacrylate)	104
DIAG 0058	(antimony hydride (stibine))	105
DIAG 0059	(organic acids)	106
DIAG 0060	(arsenic hydride (arsine))	108
DIAG 0061	(coal-miners' pneumoconiosis)	109
DIAG 0062	(<i>chronic toxic encephalopathy (CTE) caused by organic solvents</i>)	110
DIAG 0063	(naphthol and its chlorinated derivatives)	112
DIAG 0064	(nickel carbonyl)	113
DIAG 0065	(skin diseases and skin cancers caused by soot, tar, bitumen, pitch, anthracene or compounds thereof, mineral and other oils, crude paraffin, carbazole or compounds thereof, by-products of the distillation of coal)	114
DIAG 0066	(<i>occupationally caused cancers</i>)	116
DIAG 0067	(silicosis)	117
DIAG 0068	(asbestos)	119
DIAG 0069	(pneumoconiosis caused by silicates)	122
DIAG 0070	(inhalation of dusts and fibres from cotton, flax, hemp, jute and sisal)	124
DIAG 0071	(graphite dust (natural and artificial))	126
DIAG 0072	(inhalation of barium dust)	127
DIAG 0073	(dusts of hard metals)	129
DIAG 0074	(organic compounds of tin)	130
DIAG 0075	(inorganic tin dusts and fumes)	131
DIAG 0076	(wood dust)	132
DIAG 0077	(iron dust)	133
DIAG 0078	(infectious and parasitic diseases of occupational origin)	135

DIAG 0079 (infectious diseases transmitted by animals)	143
DIAG 0080 (noise)	148
DIAG 0081 (pressure exceeding atmospheric pressure (measured at sea level))	150
DIAG 0082 (pressure below that of ground level atmospheric pressure)	152
DIAG 0083 (mechanical vibration affecting the hands and arms)	154
DIAG 0084 (diseases of the periarticular bursae caused by mechanical pressure)	155
DIAG 0085 (non-ionizing radiation)	156
DIAG 0086 (nerve paralysis due to pressure)	160
DIAG 0087 (diseases caused by overstraining muscles and tendons)	161
<i>DIAG 0088 (occupationally caused asthma)</i>	163
<i>DIAG 0089 (occupationally caused allergic rhinitis and conjunctivitis)</i>	165
<i>DIAG 0090 (occupationally caused allergic contact dermatoses)</i>	166
<i>DIAG 0091 (occupationally caused irritation of the skin and mucous membranes)</i>	168
<i>DIAG 0092 (reproductive risks from occupational exposures)</i>	171
<i>DIAG 0093 (leucoderma (vitiligo))</i>	172
DIAG 0094 (hypersensitivity pneumonitis (extrinsic allergic alveolitis))	173
DIAG 0095 (meniscal diseases resulting from working over a prolonged period in a kneeling or crouching position)	174
DIAG 0096 (ionizing radiation)	175
Alphabetical key-word index	179
Cross-reference index	193

Annex

Commission recommendation (90/326/EEC) of 22 May 1990 to the Member States concerning the adoption of a European schedule of occupational diseases	199
Items of Annex I list of the Commission recommendation with cross-references to DIAG numbers	209

Preface

These information notices on diagnosis of occupational diseases have been prepared by an expert group convened by the European Commission to prepare medical information notices for the items listed in Annex I of the Commission recommendation concerning the adoption of a European schedule of occupational diseases (90/326/EEC) (OJ L 160, 26. 6. 1990, p. 39).

This work follows on from the report entitled 'Medical particulars on diseases recorded in the European schedule of occupational diseases' which was published in 1963 by the European Commission following the first recommendation in 1962.

The information notices provide information pertaining to the causal relationships between diseases and exposures in the workplace. The notices constitute a source of information for interested parties (physicians, hygienists, social partners, national authorities, etc.), because it is clear that the methods for reporting, recognizing and paying compensation for occupational diseases in the various Member States are still far from uniform.

The present notices are based on the published evidence obtained as a result of scientific investigations which have taken place over the last 30 years or more. These investigations contribute to the pool of knowledge on diseases, identifying competing causes including those which are occupational in nature. The expert group has applied accepted scientific criteria when evaluating and selecting sources of information. Although scientific evidence does not always exist for high-exposure situations, the possibility of establishing a causal link in a specific case of disease should not be excluded.

Because of developments in technology and in scientific and medical methods over time, earlier results have had to be appropriately interpreted to take this into account.

The expert group emphasizes the health risks of carrying out invasive diagnostic procedures, such as liver biopsy or bronchial provocation tests for the sole purpose of occupational disease recognition and, therefore, medical personnel should carefully take this fact into account in their decision making process.

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Information for readers

General

This publication consists of the Corpus (information notices) and three indexes (an alphabetical key-word index; a cross-reference index; a list of the items in Annex I of the Commission recommendation concerning the adoption of a European schedule of occupational diseases with cross-references to the information notices) and finally an annex containing the full text of the Commission recommendation mentioned above.

The Corpus contains the information notices on the diagnosis of occupational diseases which have been given individual sequential numbers (ref. DIAG: XXXX) to facilitate cross-referencing between the individual notices and to other language versions.

The reader will find that some information notices refer to several items of the European schedule of occupational diseases which have been grouped together for the purpose of this publication.

Also, to facilitate the task of the reader and to avoid unnecessary duplication in individual information notices, some information on more general topics has been extracted from individual notices and put together into what may be called 'horizontal notices' (in italic in the table of contents). References to horizontal notices appear in the individual notices.

The Corpus is followed by the alphabetical key-word index which is printed on blue paper.

Next follows the cross-reference index listing the DIAG numbers of the information notices (in DIAG number order), a list of relevant European schedule number(s) followed by a list of the information notices (DIAG numbers) to which reference has been made in individual notices.

Layout of information notices

Information notices rely on a systematic use of a number of standard terms.

The causal agent (definition of causal agent) is described in its common states and forms. The main occupational uses and sources of exposure listed are the most common ones offering the greatest risks of known exposure.

The effects are divided into two parts namely acute and chronic, and are then subdivided in local and systemic manifestations. These effects are described by signs and symptoms. For more detailed descriptions of diseases and specific methods of investigation the reader is recommended to refer to texts on occupational health.

A structured approach with specific concepts has been used to analyse the causal relationship between an exposure and a specific effect (disease):

Minimum intensity of exposure is given in the notices. This should be confirmed in the single case by medical history and, if possible, by hygiene assessment and measurement and, if available, the results of biological monitoring.

Minimum duration of exposure is indicated in the notices. This should be confirmed by anamnesis, and if possible, by professional description of work tasks.

Maximum latent period is the length of time after which no causal relationship can reasonably be established. This length of time is the period from the last exposure to the point of time at which an exposed person has demonstrated the initial signs or symptoms.

Induction period is the minimum length of time necessary to demonstrate a causal relationship. This length of time is the period from the beginning of exposure to the point of time at which an exposed person has demonstrated the initial signs or symptoms.

Readers should be aware that some effects (diseases) cannot be induced unless a high exposure has occurred during a certain time. A guide value indicated in the notices is consequently not necessarily identical with a permitted exposure level or an accepted biological absorption index, as these may have other endpoints (symptoms or diseases) as their basis.

* * *

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L-2920 Luxembourg

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Acrylonitrile monomer

Definition of causal agent

Acrylonitrile (vinyl cyanide) is a colourless, explosive and flammable liquid. It may polymerize spontaneously, particularly in the presence of oxygen or visible light.

Main occupational uses and sources of exposure:

Manufacture of synthetic fibres and plastic materials; chemical intermediate in the synthesis of antioxidants and paints.

Toxic effects

1. Local effects

Irritant effects

Acrylonitrile irritates the skin, eyes and respiratory tract.

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

Allergic effects

See document on occupationally caused allergic contact dermatoses.

2. Systemic effects

Acute poisoning

Syndrome similar to that of hydrocyanic acid poisoning:

headache, vertigo, weakness, nausea, vomiting, diarrhoea, oppressive feeling, tremor, irritability, convulsions, uncoordinated movements, paralysis, death.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by anamnesis and study of working conditions providing evidence of massive inhalation of acrylonitrile vapours or significant skin contact with liquid acrylonitrile.

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Pulmonary cancer

Since the causal relationship between prolonged or repeated exposure to acrylonitrile monomer and the occurrence of a pulmonary cancer has not been firmly established, and due to the multicausality of the occurrence of this type of cancer, the recognition of the occupational origin must lie on a thorough assessment based on rigorous scientific criteria taking into account all other possible etiologies.

Each case must therefore be considered separately.

See document on occupationally caused cancers.

Arsenic and its inorganic compounds (except arsine)

Definition of causal agent

Arsenic is a silver-grey metalloid which has a garlic odour. It oxidizes easily in damp air, the surface becoming covered with a layer of arsenic trioxide.

Inorganic compounds include arsine (AsH_3), arsenic trioxide (As_2O_3), cupric arsenite ($\text{Cu}(\text{AsO}_2)_2$), sodium arsenite (NaAsO_2), lead arsenate ($\text{Pb}_3(\text{AsO}_4)_2$), arsenic pentoxide (As_2O_5).

Sources of exposure and main occupational uses:

Manufacture and use of insecticides (now much less common), herbicides and fungicides; pigments industry; in alloys with other metals (e.g. Pb); Cu, Pb, Zn, Co refining (as present as an impurity); tanning; glassmaking; electronics industry; arsenic extraction from minerals, etc.

Toxic effects

1. Local effects

Irritant and corrosive effects

The mineral compounds of arsenic (particularly arsenic trioxide) are extremely irritant to the skin, eyes and respiratory tract.

They can cause contact dermatitis and sores, kerato-conjunctivitis and blepharitis.

Irritation of the respiratory mucous membranes may lead to ulceration or perforation of the septum (must occur within two weeks of exposure to be attributable to As).

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

2. Systemic effects

Skin lesions

Result of local systemic effects:

- palmar and plantar hyperkeratosis,
- melanoderma, depigmentation,
- arsenical warts.

Toxic polyneuropathy

Sensitive and motor.

Haematological disorders

Slight anaemia, leucopenia.

Peripheral circulation disorders

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged exposure to arsenic;
- and, if available,
 - biological monitoring:
guide value:
As (inorganic As and methylate metabolites) in urine
 - workplace air monitoring:
guide value:
atmospheric concentration of As > 0.05 mg/m³.

Minimum duration of exposure: Six months.

Maximum latent period: One year.

Malignant disorders

- Skin cancer
(Bowen's disease or primitive skin epithelioma)
- Pe Bronchial cancer and cancers of the upper respiratory tract

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged exposure to an atmosphere with a heavy arsenic dust or vapour content;
- and, if available,
 - biological monitoring
 - workplace air monitoring.

Minimum duration of exposure: One year.

Induction period: Five years.

See document on occupationally caused cancer.

Beryllium and its compounds

Definition of causal agent

Beryllium is a light, grey hard metal, with chemical properties between those of aluminium and magnesium. Its commonest ore is beryl (double silicate of aluminium and beryllium).

Main occupational uses and sources of exposure:

Beryllium extraction and metallurgy; nuclear industry (source of neutrons, nuclear reactors); space research (space shuttles, communications satellites, etc.); lithography for integrated circuits; manufacture of beryllium alloys; ceramics industry; precious metals industry. It is no longer used in fluorescent lamps.

Toxic effects

1. Local effects

Allergic effects

Beryllium can cause allergic contact dermatitis.

See document on occupationally caused allergic contact dermatoses.

Irritant effects

Beryllium causes irritation to the skin, eyes and respiratory tract.

Soluble salts can cause transient rhinitis and tracheo-bronchitis the severity of which depends on the intensity of exposure. Massive inhalation of less soluble salts, beryllium oxide fumes can cause immediate or delayed chemical pneumonitis or pulmonary oedema.

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

Specific effects

- Oedematous papulovesicular lesions;
- granulomatous ulcerations;
- sarcoid-like granulomas.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by anamnesis and study of working conditions providing evidence of exposure to beryllium compounds.

Minimum duration of exposure: May be very short (ulceration and subcutaneous granulomas develop if small beryllium crystals penetrate the skin).

Maximum latent period: One month.

2. Pulmonary effects

Granulomatous fibrosis

Radiology: opacities similar to that of pseudosarcoidosis.

Pulmonary function tests: restrictive and/or mixed obstructive/restrictive features.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to beryllium.

Minimum duration of exposure: Six months.

Maximum latent period: Five years.

Bronchial cancer

Since the causal relationship between prolonged or repeated exposure to beryllium and the occurrence of a bronchial cancer has not been firmly established, and due to the multicausality of the occurrence of this type of cancer, the recognition of the occupational origin must lie on a thorough assessment based on rigorous scientific criteria taking into account all other possible etiologies.

Each case must therefore be considered separately.

See document on occupationally caused cancers.

Carbon monoxide

Definition of causal agent

Carbon monoxide (CO) is, at ambient pressure and temperature, a colourless, odourless and non-irritant gas generated by incomplete combustion of organic material (coal, paper, wood, oil, gasoline, gas). It has a 200-fold greater affinity for haemoglobin than oxygen.

Main occupational uses and sources of exposure:

The largest sources are urban traffic, heating facilities, incineration and industrial processes. Occupations with potential exposure are numerous: garage personnel; firefighters; petroleum, metallurgical, gas and chemical industries workers. Cigarette smoking also contributes to carbon monoxide exposure.

Toxic effects

1. Acute and subacute effects

- 10% HbCO: shortness of breath on vigorous exertion, reduction of mental activity;
 20% HbCO: shortness of breath on moderate exertion, headache, throbbing temples;
 30% HbCO: headache, irritability, fatigue, dim vision, disturbed judgement, dizziness;
 40% HbCO: fainting on light exertion, severe headache, confusion, nausea, vomiting, tachypnea, tachycardia, collapse;
 >60% HbCO: convulsion, coma, cardiovascular collapse, respiratory failure, death.

Possibility of cardiovascular and neurological sequelae, the severity of which depends on the severity of the (sub)acute effects.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions revealing an important exposure to carbon monoxide,
- and, if available:
 - workplace air monitoring
 - biological monitoring:

carboxyhaemoglobin concentration in blood (sample taken at the time of removal from exposure before any treatment) or increase of carbon monoxide in exhaled breath.

The appearance of symptoms depends on the concentration of CO in the air, the duration of exposure, the degree of exertion, individual susceptibility, pre-existing cardiovascular or neurological diseases, etc. (The carboxyhaemoglobin in concentration value of heavy smokers may reach as much as 10%.)

Minimum duration of exposure: A few minutes to a few hours depending on the intensity in case of acute exposure, two weeks in case of subacute exposure.

Maximum latent period before onset of disease: The first symptoms should occur during the time of exposure and at the latest within 24 hours.

To be attributable to exposure to carbon monoxide, the cardiovascular or neurological sequelae should occur in the month following the acute exposure.

These could be considerably delayed in case of subacute exposure. Their assessment should be performed by an expert.

2. *Chronic effects*

Exacerbation of ischaemic heart disease

Prolonged exposure to carbon monoxide which gives rise to levels of carboxyhaemoglobinaemia in excess of 10% can exacerbate a pre-existing ischaemic heart disease.

Due to the multicausality of the occurrence of these pathologies, particularly tobacco smoking, the recognition of the occupational origin must be individually evaluated by experts.

Phosgene (carbon oxychloride)

Definition of causal agent

Phosgene (COCl_2) is a colourless gas at ambient pressure and temperature. Its vapours are heavier than air; it is a suffocating agent and smells of mouldy hay.

Main occupational uses and sources of exposure:

Phosgene is an intermediate in the production of isocyanates and of a large number of dyestuffs, polycarbonates and pharmaceuticals. Its chief toxicological importance lies in the fact that it is generated when a volatile chlorine compound comes into contact with flames or hot metal. This is why it is a potential hazard for firemen, dry cleaners and welders.

Toxic, irritant effects

Phosgene is particularly irritant to the ocular and respiratory mucous membranes. The liquid can cause skin burns.

Pulmonary oedema may develop (even in the absence of initial acute effects) after a latent period of six to 48 hours (or even longer) depending on the intensity of exposure.

If the victim survives there may be pulmonary sequelae.

Guide values:

risk of pulmonary damage: $> (0.8 \text{ mg/m}^3) 0.2 \text{ ppm}$

risk of severe pulmonary damage: $> (12 \text{ mg/m}^3) 3 \text{ ppm}$;

rapid death: $> (200 \text{ mg/m}^3) 50 \text{ ppm}$.

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

Hydrocyanic acid (hydrogen cyanide)

Definition of causal agent

Hydrogen cyanide is a colourless gas which liquifies at 26° C. It may thus be found in the workplace as either a gas or a liquid. It has the characteristic odour of bitter almonds but a third of the population cannot detect this smell. Hydrogen cyanide is highly flammable and explosive.

The toxicity of the gas lies in the cyanide radicle which is a powerful enzyme inhibitor (see also sections on cyanide) and acts as a chemical asphyxiant.

Main occupational uses and sources of exposure:

Used as a fumigant, rodenticide and insecticide; chemical intermediate in the manufacture of plastic and synthetic fibres; the gas may be generated in blast furnaces, coke ovens or in the combustion of polyurethane foam.

See also document on cyanides.

Toxic effects

1. Local irritant effects

Hydrogen cyanide gas is a mild irritant of the upper respiratory tract and mucous membranes.

Skin and eye irritation may follow from contact with the liquid. At high exposure (rare situation, usually limited to persons prevented from escaping) pulmonary oedema and laryngeal spasm may occur.

Guide values:

- exposure not to exceed: 10 ppm,
- irritation occurs at around 35 ppm,
- 100 ppm is barely tolerable for one hour.

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

2. Acute systemic effects

Clinical picture due to the affinity of the cyanide ions for hydroxocobalamin, cytochrome-oxidase and the respiratory pigments such as haemoglobin and methaemoglobin:

- headache, dizziness, nausea, vomiting
- bitter almonds taste
- tachypnoea, dyspnoea
- anxiety, stupor, loss of consciousness
- tachycardia, metabolic acidosis
- convulsions, coma, death.

Response:	Concentrations mg/m ³	ppm
Immediately fatal	300	270
Fatal after 10 minutes	200	180
Fatal after 30 minutes	150	135
Fatal after 30 to 60 minutes or later, or life threatening	120 to 150	110 to 120
Tolerated for 30 to 60 minutes without effect	50 to 60	45 to 54
Slight symptoms after several hours	20 to 40	18 to 36

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions providing evidence of a significant exposure to this substance (notice should be taken of skin absorption),
- and, if available:
 - biological monitoring:
thiocyanates, cyanide
 - workplace air monitoring:
for information: see above.

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

Maximum latent period: 24 hours.

Symptoms may take several weeks to resolve completely but the effects of hypoxia may be longer-lasting.

Cyanides

Definition of causal agent

The common cyanides used in industry are alkaline cyanide salts of sodium, calcium ('black cyanide') or potassium. They are white powders, flakes or granules with a faint almond odour.

These cyanides release hydrogen cyanide (HCN) on exposure to acid. These simple salts of hydrocyanic acid have a toxicity similar to hydrocyanic acid, due to the release of cyanide ions. They act as chemical asphyxiants.

Main occupational uses and sources of exposure:

Sodium and potassium cyanides are used in the extraction of gold and silver ores; electroplating; cleaning and heat treatment of metal; as raw materials in the manufacture of dyes, pigments, nylon and chelating agents. Cyanides are extensively used as laboratory agents. They are also used as insecticides and fumigants; calcium cyanide is used mainly as a fumigant.

See also document on hydrocyanic acid.

Toxic effects

1. Local effects

Irritant

Cyanides are irritant to the skin, eyes and respiratory tract.

They can cause epistaxis and ulceration of the nasal septum. Prolonged contact with aqueous cyanide solutions can cause caustic burns.

Chronic irritation of the skin is rare but may include itching, discolouration of the skin and ulceration.

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

2. Acute systemic effects

Clinical picture is due to the affinity of the cyanide ions for hydroxocobalamin, cytochrome-oxidase and the respiratory pigments such as haemoglobin and methaemoglobin:

headache, dizziness, nausea, vomiting;

bitter almonds taste;

tachypnoea, dyspnoea;

anxiety, stupor, loss of consciousness;

tachycardia, metabolic acidosis;

convulsions, coma, death.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions showing exposure to this substance (notice should be taken of skin absorption),
- and, if available:
 - biological monitoring:
thiocyanates, cyanides
 - workplace air monitoring.

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

Maximum latent period: 24 hours.

Isocyanates

Definition of causal agent

Monoisocyanates (methyl isocyanates) and diisocyanates (methylene diphenyl diisocyanate MDI, toluene diisocyanate TDI, etc.) are considered here.

Main occupational uses and sources of exposure:

Monoisocyanates are mainly used as synthesis agents in the chemical industry, while diisocyanates are used as hardeners in polyurethane varnishes and lacquers, in the manufacture of synthetic fibres, polyurethane foam, polyurethane-based adhesives, and paints containing organic isocyanates.

Toxic effects

1. Irritant and corrosive effects

Isocyanates irritate the skin and the ocular and respiratory mucous membranes.

Direct contact (or exposure to high concentrations) can lead to palpebral and corneal disorders with eye burns, photophobia, blepharospasm, conjunctival hyperhaemia and superficial corneal ulcerations.

Irritation of the airways may lead to an acute pulmonary oedema with bronchoconstriction and possible development of severe bronchiolitis, death from acute respiratory distress syndrome or fibrosis-type sequelae.

Guide values: (methyl isocyanate)

irritation of ocular mucous membrane: exposure > (470 µg/m); 0.2 ppm

palpebral and corneal disorders: exposure > (117.5 mg/m³) 50 ppm;

acute pulmonary oedema: exposure > (117.5 mg/m³) 50 ppm.

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

2. Immuno-allergic effects (Diisocyanates)

Allergic contact dermatitis

See document on occupationally caused allergic contact dermatoses.

Allergic rhinitis and conjunctivitis

See document on occupationally caused rhinitis and conjunctivitis.

Asthma

See document on occupationally caused asthma.

NB: The isocyanates provocation test is dangerous and should not be considered unless specialized medical facilities are available.

Hypersensitivity pneumonitis

See document on hypersensitivity pneumonitis.

3. *Chronic obstructive bronchopathy*

Expert evaluation is necessary to determine the causal link between exposure to isocyanates and the onset of chronic obstructive bronchopathy.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure to isocyanates confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions providing evidence of prolonged or repeated exposure to isocyanates;
- and, if available:
 - biological monitoring;
 - workplace air monitoring;
 - Guide value: atmospheric concentration TDI > (0.005 ppm) 0.036 mg/m³
 - MDI > (0.02 ppm) 0.047 mg/m³

Minimum duration of exposure: 10 years.

Maximum latent period: Five years.

Cadmium and its compounds

Definition of causal agent

Cadmium is a silver-white, malleable metal which is highly resistant to corrosion.

Its compounds include: cadmium acetate, cadmium sulphide, cadmium sulphoselenide, cadmium stearate, cadmium oxide, cadmium carbonate, cadmium sulphate, cadmium chloride, etc.

Main occupational uses and sources of exposure:

Used for electroplating other metals, mainly iron and steel; as pigments in paints and stabilizers in plastics.

Toxic effects

1. Acute effects

'Metal fume fever'

Pseudo-influenza type syndrome usually occurring shortly after exposure: irritation and dryness of the nose and throat, coughing, headache, weakness, shivering, fever, etc.

Acute broncho-pneumonia

In serious cases: severe bronchial and pulmonary irritation with the risk of chemical pneumonia, pulmonary oedema, shock and death.

Symptoms may not appear until a few hours later.

In the most severe cases, exposure may immediately prove fatal.

Repeated acute exposure may promote the development of pulmonary emphysema.

Possible hepatic and renal effects.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by anamnesis and study of working conditions providing evidence of intense inhalation of cadmium oxide fumes.

Minimum duration of exposure: From a few minutes to a few hours depending on the intensity of exposure.

Maximum latent period: The first symptoms appear at the latest 48 hours following exposure.

2. Chronic effects

Nephropathy

Mainly tubular lesions.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of repeated or prolonged exposure to cadmium;

— and, if available:

- biological monitoring (levels below which nephropathy is unlikely to be due to occupational exposure to cadmium)
guide values: CdU > 10 µg/g creatinine
CdB > 10 µg/L
- workplace air monitoring
guide values: atmospheric concentration > 2 µg/m³.

Minimum duration of exposure: One year.

Maximum latent period: The first signs of renal lesions may develop several years following exposure where the biological measurements confirm previous exposure.

Pulmonary lesions

Obstructive syndrome with or without emphysema.

Restrictive lesions have also been linked to exposure to cadmium.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of repeated or prolonged exposure to cadmium;
- and, if available:
 - biological monitoring (levels below which a pulmonary lesion is unlikely to be due to occupational exposure to cadmium)
guide values: CdU > 5 µg/g creatinine
CdB > 5 µg/L
 - workplace air monitoring
guide values: atmospheric concentration > 2 µg/m³

Minimum duration of exposure: 10 years.

Maximum latent period: Five years.

Lung cancer

An increased risk of lung cancer has been found among workers in foundries and battery manufacturing plants where exposure to cadmium has been confirmed. However, the causal relationship between lung cancer and prolonged exposure to cadmium or cadmium compounds has not been definitely established. An assessment by experts is therefore necessary.

See document on occupationally caused cancers.

Chromium and its compounds

Definition of causal agent

Chromium is a hard, greyish-white metal very resistant to wear and corrosion. It has three oxidation states II, III, VI.

Soluble chromium (VI) compounds: ammonium chromate, potassium chromate, sodium chromate; potassium dichromate, sodium dichromate; chromium trioxide (chromic anhydride or chromic acid);

Non-soluble or slightly soluble hexavalent chromium (VI) compounds: barium chromate, lead chromate, calcium chromate, strontium chromate, zinc chromate; mixed zinc chromate and potassium chromate;

Chromium (III) compounds: chromium acetate; chromium oxide; chromium orthophosphate; Cr pyrophosphate; Cr sulphate; Cr sulphide.

Main occupational uses and sources of exposure:

The manufacture of alloys (corrosion resistant); chromium electroplating; chromium tanning; manufacture of pigments (chrome yellow); manufacture of dichromates from iron chromate (applications in lithography, textile industry, printing, photography); chromic anhydride used as a pesticide in the treatment of wood; traces of chromium in cement, bleach.

Toxic effects

1. Local effects

Irritant and corrosive effects

Chromium (VI) (aerosol of chromic acid, chromate dusts, liquid chromate) irritates or even corrodes the skin and the mucous membranes of the eyes and respiratory tract (intense exposure to a chromic acid aerosol may give rise to pulmonary oedema).

The spraying of chromic acid can give rise to serious eye lesions.

Chrome ulcers (chrome 'holes')

Deep, round holes, clearly marked, usually at the base of the nails, the finger joints, the skin between the fingers, the back of the hand and the forearm (may also appear at other sites). The lesions are only slightly painful, if at all, but they take a long time to heal and scars are left.

Perforation of the nasal septum

May be the result of intense exposure for two weeks, or less intense exposure for several months. The ulcer is not usually painful and is sited approximately 1.5 to 2 cm from the lower anterior part of the nasal septum but may extend to the upper posterior part.

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

Allergic effects

Allergic dermatitis

See document on occupationally caused allergic contact dermatoses.

Asthma

See document on occupational caused asthma .

2. *Systemic effects*

Chronic obstructive bronchopneumopathy

Exposure to aerosols of compounds of chromium (VI) can cause lung disorders affecting ventilatory function.

Respiratory function: reduction in FEV₁ and maximal expiratory flow.

Possibility of complication in the form of an infection.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by

- anamnesis and a study of working conditions providing evidence of prolonged or repeated exposure to chromium,
- and, if available;
 - biological monitoring
 - workplace air monitoring.

Minimum duration of exposure: 10 years.

Maximum latent period: Five years.

Bronchial cancer

An increased risk of bronchogenic carcinoma has been found in association with a number of slightly soluble hexavalent chromium (VI) compounds: chromates of calcium, strontium and zinc chromates.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to insoluble chromium (VI) compounds.
- and, if available:
 - biological monitoring
 - workplace air monitoring:
 - guide value:
atmospheric chromium (VI) > 0.05 mg/m³.

Minimum duration of exposure: Six months.

Minimum induction period: Usually 10 to 20 years.

See document on occupationally caused cancer.

Mercury and its inorganic compounds

Definition of causal agent

Mercury is, at ambient temperature and pressure, a silver-grey liquid metal which slowly volatilizes. Its inorganic compounds are numerous and include oxides, sulphates, chlorides and nitrates.

Main occupational uses and sources of exposure:

Mercury metallurgical industry; manufacture, repairing of precision scientific apparatus (barometer, thermometer, manometer); electric and chemical industry; production of mercury compounds; preparation of medicines, amalgam.

Toxic effects

1. Local effects

Irritant effects

Mercury salts can cause irritation dermatitis.

Mercury vapours are irritating to the respiratory tract. In case of massive exposure they may lead to bronchiolitis, chemical pneumonia, acute pulmonary oedema and even renal tubular necrosis.

Irreversible pulmonary sequelae are possible after the acute manifestations.

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

Allergic effects

Allergic contact dermatitis

Metallic mercury and its salts can produce allergic reactions

See document on occupationally caused allergic contact dermatoses.

2. Systemic effects

(Sub)acute

Toxic encephalopathy

Toxic nephropathy

Renal tubular impairment.

Exposure criteria:

Minimum intensity of exposure:

Occupational exposure confirmed, and if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of (sub)acute exposure to mercury,

— and, if available:

- biological monitoring:
guide values:
Mercury in urine > 500 µg/g creatinine
Mercury in blood > 200 µg/L
- workplace air monitoring:
guide value:
atmospheric mercury > 1 mg/m³

Minimum duration of exposure: A few hours to a few days depending on the intensity of exposure.

Maximum latent period: One week.

Chronic

Toxic encephalopathy

Cerebellar syndrome

- (i) intentional tremor,
- (ii) ataxia, dysarthria.

Toxic polyneuropathy

- (i) sensory and motor nerve disturbances,
- (ii) Guillain-Barre syndrome.

Oral cavity disorders

- (i) gingivitis, stomatitis, excessive salivation, gingival pain,
- (ii) ulceration of the lips and the oral mucosa,
- (iii) dark mercurial line along the gingival margins, metallic taste, loss of teeth.

Toxic nephropathy

- (i) nephrotic syndrome,
- (ii) glomerulonephritis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, and if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of prolonged/repeated exposure to mercury;

— and, if available:

- biological monitoring:
guide values:
Mercury in urine > 50 µg/g creatinine
Mercury in blood > 20 µg/l
- workplace air monitoring:
guide value:
atmospheric mercury > 50 µg/m³.

Minimum duration of exposure: Six months.

Maximum latent period: One year.

Manganese and its compounds

Definition of causal agent

Manganese is a very hard, steel-gray metal. Its main compounds are the oxides of manganese, manganese (II) carbonate, manganese (II) chloride, manganese (II) sulphate, manganese (II) acetate, manganese borate, potassium permanganate and methylcyclopentadienyl manganese tricarbonyl (MMT).

Main occupational uses and sources of exposure:

Extraction and transport of ores; metallurgical industry: iron and steel industry, slags, alloys (copper, tin, nickel, antimony, aluminium, steel); welding; manufacture of dry cells; chemical industry: as an oxidizing agent, production of oxygen and chlorine; manufacture of organic derivatives of manganese; colorants (glass, ceramics) and feed additives (livestock); antiknock additive in petrol (MMT).

Systemic toxic effects

Acute bronchopneumonia

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of acute occupational exposure to manganese;
- and if available:
 - workplace air monitoring.

Minimum duration of exposure: From a few minutes to a few hours depending on the intensity of exposure.

Maximum latent period: 48 hours.

Toxic extrapyramidal syndrome

The initial phase of symptomatology comprises irritability and occasional psychotic features, emotional instability and psychomotor irritability. Extrapyramidal syndrome gradually appears during the second phase.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged/repeated exposure to manganese;

— and, if available:

- biological monitoring (qualitative)

- workplace air monitoring

guide values:

atmospheric concentration considerably higher than 5 mg/m³ (dusts)

1 mg/m³ (fumes).

Minimum duration of exposure: One year.

Maximum latent period: Cannot be determined.

Nitric acid

Definition of causal agent

Nitric acid (HNO_3) is a colourless or yellowish liquid with a suffocating smell.

Nitrous vapours (NO_x) are formed when nitric acid acts on metals or on organic matter (nitration of cotton or other cellulose-containing materials).

Main occupational uses and sources of exposure:

Nitric acid is widely used in industry, particularly in the production of metallic nitrates, oxalic, phthalic and sulphuric acids, nitrites and nitrous acids, trinitrophenol, trinitrotoluene, nitroglycerine, ethylene glycol dinitrates and dyes. It is also used in the production of jewellery, the pharmaceutical industry and a number of printing processes.

Local toxic effects

Irritant and corrosive effects

Nitric acid (liquid or the vapours of nitric acid and its derivatives, formed during chemical reactions involving the acid) causes major irritation of the skin and mucous membranes. A nitric acid aerosol is capable of causing intense irritation of the respiratory tract.

Guide value: atmospheric concentration > 4 ppm (10 mg/m³).

The inhalation of high concentrations of nitric acid vapours can cause acute pulmonary oedema which usually develops after a latent period of 6 to 24 or even 72 hours.

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

Nitrogen oxides

Definition of causal agent

Nitrogen oxides (NO_x) (synonym: nitric oxides).

Nitrogen mono-oxide (NO) (synonym: nitric acid): colourless, barely water-soluble gas, oxidizes readily to NO₂.

Nitrogen dioxide (NO₂): reddish-brown, barely soluble gas with sweet-sour odour. Condenses below 21° C. Heavier than air. Nitric acid (HNO₃) and nitric oxide (NO) form in the presence of water.

Dinitrogen monoxide (N₂O) (synonyms: nitrous oxide, laughing gas): colourless gas with a sweetish odour, heavier than air.

Nitrogen tetraoxide (N₂O₄): polymer of NO₂; occur together at the usual ambient temperatures.

Main occupational uses and sources of exposure:

Nitrogen dioxide: found industrially in arc and inert gas shielded welding in small unventilated rooms. By-product in the manufacture of dyes and explosives. May be evolved from silage.

Dinitrogen monoxide: used as anaesthetic gas.

Local effects

Nitric oxide and nitric tetraoxide are irritant to the mucous membranes of the eyes and the respiratory tract. In severe cases, pulmonary oedema occurs usually after a latent period (6 to 24 hours, up to 72 hours).

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

Systemic effects nitrous oxide is a central

Ammonia

Definition of causal agent

Ammonia is a colourless, suffocating, penetrating, acid-smelling gas at ambient temperature and pressure and weighs less than air. It may easily be liquified under pressure and it dissolves readily in water to form ammonium ions.

Main occupational uses and sources of exposure:

Manufacture of cleansing agents, pesticides, sodium carbonate, plastic materials, ammonia-containing fertilizers. Production of nitric acid, explosives. Refrigeration. Oil industry. Product of coal distillation (coking ovens, gasworks). Released in the putrefaction of bio-organic materials.

Toxic, irritant and corrosive effects

Ammonia may cause severe irritation of the skin, eyes and respiratory tract. Recovery without pulmonary sequelae is the rule but chronic bronchitis, bronchiectasis and obliterative bronchiolitis have been reported after short-term exposure to high levels of ammonia.

In the event of splashes to the eyes causing severe burns, there may be ocular sequelae (cataract, atrophy of the iris, corneal scars).

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

Nickel and its compounds

Definition of causal agent

Nickel is a lustrous, greyish white metal which is ductile, malleable and hard, with a fibrous structure.

Main occupational uses and sources of exposure:

Electrolytic nickel-plating; manufacture of nickel-cadmium batteries; coin and kitchen utensil manufacture; preparation of special steels (heat- and corrosion-resistant).

Toxic effects

Allergic contact dermatitis (nickel itch)

See document on occupationally caused allergic contact dermatoses.

Asthma

See document on occupationally caused asthma.

Cancer of the respiratory tract

Sinonasal cavities, ethmoid sinuses, trachea, bronchi, lung parenchyma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to nickel. It is still not possible to state with certainty which specific compounds are human carcinogens and which are not.

However, it seems clear that nickel-refining operations involve the risk of cancer for workers. This risk is particularly high for those employed at certain work stations, mainly those involving exposure to fairly insoluble compounds such as nickel sulphides and nickel oxides;

— and if available:

- biological monitoring (qualitative);
- workplace air monitoring.

Minimum duration of exposure: Six months.

Induction period: 20 years.

See document on occupationally caused cancers.

Phosphorus and its compounds

Definition of causal agent

Phosphorus exists in three forms namely, white (or yellow), red and black.

Red phosphorus is relatively non-toxic, whereas white phosphorus is very toxic.

Compounds of phosphorus relevant to occupational exposure include phosphine, phosphoric acid, phosphorus pentoxide, phosphorus pentachloride, phosphorus pentasulphide, phosphorus chloride and phosphorus oxychloride.

Phosphine gas can be produced from phosphoric acid on contact with metals or from heating phosphorus chloride.

Main occupational uses and sources of exposure:

White phosphorus is used in the manufacture of explosives, rodenticides and fertilizers and in the past was used in the manufacture of non-safety matches.

Red phosphorus is used in the manufacture of matches.

Black phosphorus is not used in industry.

Toxic effects

Phosphorus

1. Local effects

Irritant and corrosive effects

White phosphorus ignites spontaneously in air giving a garlic-like odour. The fumes cause irritation to the eyes (symptoms include photophobia and lacrimation) and respiratory tract and in severe cases can lead to pulmonary oedema. Solid phosphorus causes deep painful burns to the skin on contact. Repeated or prolonged inhalation of phosphorus fumes can lead to chronic bronchitis.

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

2. Systemic effects

Prolonged high level absorption of white phosphorus causes anaemia and necrosis of the maxilla with profuse salivation, loosening of the teeth and lesions on the oral mucosa.

Phosphorus compounds

1. Local effects

Irritant and corrosive effects

Phosphoric acid, phosphorus pentoxide, phosphorus pentachloride, phosphorus chloride and phosphorus oxychloride cause severe burns on skin contact. They also cause irritation to the eyes and respiratory tract.

Inhalation of phosphine gas, phosphorus pentoxide powder and phosphorus pentasulphide can cause delayed pulmonary oedema (maximum latent period: 72 hours). In time, liver and kidney function disorders may appear in some cases.

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

Lead and its inorganic compounds

Definition of causal agent

Lead is a blue-greyish, malleable and ductile metal. The inorganic salts of lead (II), lead sulphide and oxides of lead are in general not very soluble in water. Exceptions are lead nitrate, lead chlorate and, to a much lesser degree, lead chloride.

Main occupational uses and sources of exposure:

Lead and zinc mines; lead and zinc metallurgy; construction industry; ammunition manufacture; insecticides; accumulator plants; plumbing; pigments for paints, enamels, varnishes, plastic materials; noise, vibration and radiation protection screens; containers for corrosive liquids; oxyacetylene welding and cutting; cable and wire manufacturing; alloys with antimony and copper.

Toxic effects

1. Acute systemic effects

Effects on the gastrointestinal tract

Constipation, anorexia, abdominal discomfort or colic.

Toxic encephalopathy

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions showing significant exposure to lead;
- and if available:

- biological monitoring
 - blood: lead > 80 µg/mL (800 µg/L);
 - urinary S-amino laevulinic acid (ALA) > 20 mg/L.
- workplace air monitoring.

Minimum duration of exposure: From a few hours to a few days depending on intensity of exposure.

Maximum latent period: One week.

2. Chronic systemic effects

The toxic effects are classified as follows:

Haemopoietic system

Inhibition of haem synthesis as well as alteration in globin synthesis may induce anaemia of the hypochromic, normocytic or microcytic type; stippling of erythrocytes and reticulocytosis.

Gastrointestinal system

Constipation, anorexia, abdominal discomfort or colic.

Central and peripheral nervous systems

- Lead encephalopathy: effects and symptoms range from behavioural symptoms (vague subjective symptoms and reduction in mental and psychomotor performance) to dementia;
- Peripheral motor neuropathy;

Kidneys

Chronic lead nephropathy with aminoaciduria, glycosuria and phosphaturia.

Effects on reproduction

See document on reproductive risks from occupational exposures.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to lead;
- and, if available:
 - biological monitoring
 - blood lead > 60 µg/100 mL (600 µg/L)
 - free erythrocyte protoporphyrins > 300, µg/100 mL erythrocytes (3 mg/L erythrocytes)
 - urinary S-amino laevulinic acid (ALA) > 10 mg/g creatinine
 - workplace air monitoring:
 - guide value:
 - concentration in air > 0.15 mg/m³ .

NB: These measurements are given as guide values. Reduction in speed of conduction of the peripheral nerves, certain behavioural and psychomotoric problems and subjective disorders may be detected at lower levels: blood lead of 40 µg/100 mL (400 µg/L).

Minimum duration of exposure: One month. Chronic encephalopathy: six months.

Maximum latent period:

- gastrointestinal effects: one month,
- anaemia: three months,
- chronic neurological symptoms: one year,
- chronic renal insufficiency: 15 years.

Sulphuric acid and sulphur oxides

Definition of causal agent

Sulphuric acid (H_2SO_4) is a colourless or slightly brown, hygroscopic, oily liquid. Vaporization can begin from 30°C . Sulphur trioxide is emitted when heated.

Fuming sulphuric acid (synonym: oleum), a solution of sulphur trioxide in concentrated sulphuric acid, produces thick white fumes in the air.

Sulphur dioxide (SO_2) is a colourless pungent gas, heavier than air. It converts to sulphurous acid (H_2SO_3) in water.

Sulphur trioxide (SO_3) (synonym: sulphuric acid anhydride) is a solid crystalline substance which develops pungent-smelling fumes in the air and converts under thermic reaction with water to sulphuric acid (H_2SO_4).

Main occupational uses and sources of exposure:

Sulphuric acid is used as battery acid in accumulators, electroplating and in the chemical industry (production of fertilizer) as well as in laboratories.

Sulphur monoxide occurs as an intermediate product in various chemical processes and has no commercial use.

Sulphur dioxide occurs when sulphur is burnt (combustion of fossil fuel) and in the smelting process of metal ore. It is used as a coolant (in liquid form), for vulcanization of rubber, as a bleaching agent or for obtaining sulphuric acid.

Sulphur trioxide is an intermediate product in the manufacture of sulphuric acid and oleum and is used for sulphonation of organic acids.

Toxic effects

Acute

Irritant and corrosive effects

SO_2 is converted to sulphurous acid by moisture on sweating skin or on mucous membranes. H_2SO_4 is harmful not only as a liquid but also as acidic vapour and, because it has a great affinity to water, it corrodes the skin and the underlying tissue.

Although the following effects apply for both substances, SO_2 mainly produces irritant effects and H_2SO_4 produces the caustic effects.

These substances are highly irritant for the skin (burns), the eyes (possibility of kerato-conjunctivitis, deep corneal ulcerations, lid lesions) and the respiratory tract (in severe cases: bronchoconstriction, laryngospasm, pulmonary oedema with a latent period of variable length).

Exposure criteria:

Minimum intensity of exposure:

- occupational exposure confirmed, if possible assessed by anamnesis and study of exposure conditions, providing evidence of skin contact or inhalation;
- and, if available:
 - workplace air monitoring:
Guide values:
 - > (20 ppm) 52 mg/m³ SO₂: clear irritation symptoms,
 - > (400 ppm) 1 040 mg/m³ SO₂: death in a few minutes.

Minimum duration of exposure: Seconds to minutes.

Maximum latent period: The first manifestations should appear during exposure or within a few hours.

Chronic effects

Chronic irritation leads to drying and ulcerations of the skin (particularly the hands), chronic paronychia and perionychia, reddened glossy tongue, taste disturbances.

Chronic irritation of the respiratory tract can cause ulcerations of the nasal septum, nose-bleeding and possibly atrophic rhinitis and chronic obstructive ventilation disturbance.

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

Damage to dental enamel

The compounds effect particularly the incisors: loss of lustre, streaks, decalcification, yellow or brown flecks, increased sensitivity to temperature changes.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions showing evidence of prolonged/repeated exposure to these substances.

Minimum duration of exposure: A few months.

Maximum latent period: The first manifestations should appear during exposure.

Carbon disulphide

Definition of causal agent

Carbon disulphide (CS₂) is a colourless, volatile liquid with vapours denser than air.

It is very flammable and has a very high refractive index. In its pure state it has a sweet, pleasing and ethereal odour. Commercial forms and grades with a certain degree of dilution are foul-smelling.

Main occupational uses and sources of exposure:

Carbon disulphide is mainly used in the rubber industry and in the manufacture of viscose. It is also used as a solvent.

Toxic effects

1. Local effects

Irritant effects

Carbon disulphide causes irritation to the skin and the eyes.

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

2. Systemic effects

Acute effects

Neuropsychological manifestations

Excited state and mental confusion, narcosis, delirium, hallucinations, suicidal tendencies, psychosis, loss of consciousness, coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of considerable exposure to CS₂;

— and, if available:

- biological monitoring:

CS₂ in blood, (2-thiothiazolidine-4-carboxylic acid (TTCA)) metabolites in the urine, CS₂ in the exhaled air

- workplace air monitoring:

guide value:

atmospheric concentration > (600 mg/m³) 200 ppm.

Minimum duration of exposure: From a few minutes to a few hours depending on intensity of exposure.

Maximum latent period: 24 hours.

Chronic effects

The complex nature of the metabolic effects of exposure to carbon disulphide results in a unique set of toxic effects on the target organs. These effects may appear separately or together. They can be grouped,

somewhat arbitrarily, into effects on the central nervous system, the peripheral nervous system, the cardiovascular system and the reproductive system. Given the many causes of most of these effects, in order to determine whether an individual case can be recognized as an occupational disease or not, it must be examined in depth on the basis of strictly defined scientific criteria taking into account other possible causes.

Effects on the central nervous system

- Chronic toxic encephalopathy: fatigue, headache, drowsiness, irritability, memory loss.
See document on chronic toxic encephalopathy caused by organic solvents.
- Parkinsonism: damage to the extra-pyramidal system.
- Retrobulbar optical neuritis of neurological or vascular origin.

Toxic polyneuropathy

Polyneuropathy of the mixed sensory/motor type, predominantly affecting the lower limbs.

Cardiovascular effects

An increase in the incidence of the cardiovascular diseases in people exposed to CS₂.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions providing evidence of prolonged or repeated exposure to CS₂;
- and, if available:
 - biological monitoring of CS₂ in the blood, metabolites in the urine (2-thiothiazolidine-4-carboxylic acid (TTCA)), CS₂ in the exhaled air
 - workplace air monitoring:
guide value: atmospheric concentration > (31 mg/m³) 10 ppm.

Minimum duration of exposure: One year.

Chronic encephalopathy: 10 years.

Maximum latent period: Parkinsonism syndrome and effects on the peripheral nervous system: five years after the end of exposure. Other effects on the central nervous and cardiovascular systems: these assessments require an expert's report on a case-by-case basis.

Vanadium and its compounds

Definition of causal agent

Vanadium is a greyish white metal which resists corrosion. Its most common compounds are vanadium pentoxide (V_2O_5), vanadium dioxide (VO_2), vanadium trioxide (V_2O_3), sodium metavanadate ($NaVO_3$), vanadium tetrachloride, (VCl_4).

Main occupational uses and sources of exposure:

Metal manufacture; photography; manufacture of colouring substances; catalyst in the production of sulphuric acid and phthalic anhydride; in the manufacture of alloys for the production of special, highly elastic steels which are resistant to vibrations (ferrovanadium); alloys with other metals (Cu, Co, Ti, Cr); cleaning of boilers and flues in which vanadium-containing oils have been burnt.

Local toxic effects

Allergic contact dermatitis

See document on occupationally caused allergic contact dermatoses.

Asthma

See document on occupationally caused asthma.

Irritant effects:

Vanadium produces irritation of the eyes and the upper and lower respiratory tract. In more serious cases it can lead to highly obstructive bronchitis and bronchopneumonia.

Repeated or prolonged exposure may lead to chronic irritation of the upper respiratory tract (rhinitis, pharyngitis, chronic bronchitis, etc.)

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

Exposure criteria:

Maximum intensity of exposure: Occupational exposure confirmed, if possible assessed by:

- anamnesis and study of working conditions showing evidence of exposure to vanadium, vanadium exposure causes a characteristic green discolouration of the tongue;
- and, if available:
 - workplace air monitoring.
guide values: atmospheric vanadium $> 0.2 \text{ Mg/m}^3$

Minimum duration of exposure: A few hours to a few days depending on the intensity of exposure.

Maximum latent period: 48 hours.

Chlorine

Definition of causal agent

At ambient temperature and pressure chlorine is a greenish-yellow gas which is heavier than air and has a pungent, suffocating smell.

Main occupational uses and sources of exposure:

Chlorine is widely used in the chemical industry for the synthesis of derivatives such as: hydrochloric acid, hypochlorite, calcium and zinc chloride, organic chlorine compounds.

It is also used as a bleaching agent in the textiles and paper industries, and is a powerful disinfectant in water purification.

Toxic, irritant and corrosive effects

Chlorine may cause severe irritation of the skin, eyes and respiratory tract (pulmonary oedema). Recovery without pulmonary sequelae is usual, but some complications have been reported: bronchiolitis, pulmonary fibrosis, emphysema.

Direct contact with liquid chlorine produces severe ocular lesions and skin damage.

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

Note that 'chloracne' is a disease typically caused by halogenated derivatives of aromatic hydrocarbons and not by chlorine.

Bromine

Definition of causal agent

At ambient temperature and pressure, bromine is a dark reddish-brown low-boiling liquid yielding heavy, red, suffocating vapours that are heavier than air.

Main occupational uses and sources of exposure:

Used in the chemical, pharmaceutical and photographic industry. Bleaching agent and water disinfectant agent. Anti-explosive constituent in petrol. Gold-mining.

Toxic, irritant and corrosive effects

Bromine vapours may cause severe irritation of the skin, eyes and respiratory tract (pulmonary oedema). Direct skin contact with liquid or vapours can lead to painful chemical burns and destructive ulcers which take a long time to heal completely and often leave deep scars.
See document on occupationally caused irritation of the skin and mucous membranes.

Iodine

Definition of causal agent

At ambient temperature and pressure iodine is a solid in the form of dark grey crystals with a metallic lustre. Heating yields violet vapours.

Main occupational uses and sources of exposure:

Manufacture of iodine compounds, germicides, antiseptics. Used in photographic films.

(NB: Therapeutic use: thyroid dysfunction, topical disinfectant).

Toxic, irritant and corrosive effects

Iodine vapours may cause severe irritation of the eyes, respiratory tract and, to a lesser extent, the skin. Exposure of the eyes may lead to brown staining of the corneal epithelium and subsequent desquamation but recovery usually occurs without sequelae.

Iodine in crystalline form or in concentrated solution is a severe skin irritant: it produces thermal burns with brown staining which have a tendency to spread and take a long time to heal.

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

Comment:

The pharmacological use of iodine may lead to allergic dermatitis (possibly with systemic reaction) and to thyroid disorders; however, these disorders have not been encountered in the occupational setting.

Fluorine and inorganic fluoride compounds

Definition of causal agent

At ambient pressure and temperature, fluorine is a corrosive pale greenish-yellow gas with a bitter smell. It is highly reactive and combines with practically all other organic and inorganic substances with the exception of nitrogen and oxygen. It reacts with water to form hydrofluoric acid and possibly oxyfluoric acid.

Hydrofluoric acid (synonyms: fluorohydric acid, anhydrous hydrofluoric acid, hydrogen fluoride) is a highly volatile, colourless gas or liquid which is very soluble in water and which has a bitter smell.

Inorganic fluoride compounds include calcium, aluminium, sodium, magnesium, lead, tin, sulphur fluorides, nitrogen trifluoride, titanium tetrafluoride, antimony pentafluoride.

Main occupational uses and sources of exposure:

Fluorine: synthesis of organic and inorganic fluorine compounds; oxidizer in rocket fuel.

Hydrofluoric acid: production of organic and inorganic fluorine compounds; catalyst (particularly in paraffin alkylation in the petroleum industry); insecticide; arrest of fermentation in brewing; fluorination processes; removing sand from metallic castings; glass polishing; frosting and etching glass and enamel; decomposing enamel.

Fluorides: electrolyte in aluminium manufacture; flux in smelting nickel, copper, gold, silver; catalyst for organic reactions; fluoridation agent for drinking water; bleaching agent; pesticides, rodenticides; fermentation inhibitor; cleaning graphite, metals, windows, glassware; preparation of fertilizer from phosphate rock by addition of sulphuric acid.

Toxic effects

I. Fluorine and hydrogen fluoride

Local effects

Irritant and corrosive effects

Fluorine and hydrofluoric acid are particularly irritating to the skin, eyes and respiratory tract (possibility of bronchospasm, laryngospasm and acute pneumonitis, pulmonary oedema in the event of massive exposure).

Nose-bleeding and sinus trouble may develop on low chronic exposure to these compounds.

Cutaneous contact may lead to extremely painful burns. The chemical burns cause deep tissue destruction and may not become symptomatic until several hours after contact, depending on the dilution. Possibility of developing systemic symptoms following skin absorption from burn sites.

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

II. Inorganic fluoride compounds

1. Local effects

Irritant effects

Some inorganic fluoride compounds are irritating to the skin, eyes and respiratory tract.

Nose-bleeding and sinus trouble may develop on low chronic exposure to fluorides.

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

2. Systemic effects

Skeletal fluorosis

Excessive absorption of fluorides may result in an osteosclerosis that is recognizable by X-ray (first signs of changes in density appearing in the lumbar spine and pelvis). Usually some ossification of ligaments occur.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of excessive prolonged or repeated exposure to inorganic fluoride dusts or vapours,

— and, if available:

- biological monitoring:

significant increase in the urinary level of fluoride during the working day. For workers employed in exposed working areas: urine fluoride should be less than 4 mg/L, when taken on Monday mornings. Workers should be interviewed on oral intake of fluoride-rich food (examples: tea, mineral water, toothpaste, fluoride-rich drinking water).

Workers not presently exposed but having verified deposits (fluorosis) have no elevated urine fluoride values unless other sources cause excretion.

- workplace air monitoring:

guide value:

atmospheric concentration well above 2.5 mg/m³ of fluorine ions.

Minimum duration of exposure: One year.

Maximum latent period: One year.

n-hexane

Definition of causal agent

n-hexane is a colourless, highly volatile, liquid aliphatic hydrocarbon with a distinctive smell.

Sources of exposure and main occupational uses:

Essentially used as a solvent (especially in glue).

Toxic effects

1. Local effects

Irritant effects

n-hexane causes irritation of the skin, eyes and respiratory tract.

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

2. Systemic effects

Narcotic syndrome

Headache, vertigo, nausea, drowsiness, weakness, confusion, loss of consciousness, sometimes coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions providing evidence of acute n-hexane intoxication by inhalation or skin contact;
 - and, if available:
 - biological monitoring
 - workplace air monitoring:
- guide values:
atmospheric concentration $> (3.5\text{g/m}^3) 1\ 000$ ppm.

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Sensorimotor polyneuropathy

Signs and symptoms

Clinical picture showing distal sensorimotor polyneuropathy, predominant in the lower limbs:

distal paraesthesia, various sensory anomalies (touch, vibration, etc.), cramp-like pains;

muscle weakness, paresis of the limbs (predominant in the lower limbs), paralysis, muscle atrophy, quadriplegia, paralysis of the respiratory muscles.

Electrophysiological examination shows axonal disorders.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions providing evidence of prolonged/repeated exposure to n-hexane. Assessment must also take account of skin absorption;

— and, if available:

- biological monitoring:

 - guide values:

 - urine: 2-hexanol, 2,5-hexanedione (>5 mg/g creatinine at end of shift) (2,5-hexanedione is also a metabolite of methyl-n-butylketone)

 - blood: n-hexane (> 150 µg/L during exposure)

 - exhaled air: n-hexane (> 40 ppm during exposure)

- workplace air monitoring:

 - guide values:

 - atmospheric concentration: > (176 mg/m³) 50 ppm.

These concepts need to be reassessed if there is a possibility of potentiation by other organic solvents of the ketone type (especially methyl-n-butylketone).

Minimum duration of exposure: One month.

Maximum latent period: Six months.

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

n-Heptane

Definition of causal agent

N-heptane ($\text{CH}_3\text{-(CH}_2\text{)}_5\text{-CH}_3$) (synonyms: methyl hexane, dipropyl methane, hexyl methane, n-heptyl hydride) is a colourless, highly inflammable liquid which is fairly insoluble in water but readily soluble in alcohol, petrol and chloroform.

Main occupational uses and sources of exposure:

It is a constituent in various special benzines and fuels (up to 40 %). It is mainly used in the rubber industry (for tyre manufacture).

Pure n-heptane (> 90 %) is only used for laboratory analysis.

Toxic effects

1. Local effects

Irritant effects

Liquid n-heptane is irritant to the skin and mucous membranes.

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

2. Systemic effects

Narcotic syndrome

Headaches, dizziness, nausea, drowsiness, weakness, confusion, unconsciousness, possibly coma.

Exposure criteria:

Minimal intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and analysis of the working conditions showing evidence of an acute exposure to n-heptane (take into account possibility of skin absorption),

— and, if available:

- workplace air monitoring:
guide values:

Atmospheric concentration well above (2 000 mg/m³) 900 ppm at 5000 ppm, light central nervous system symptoms occur after 4 to 7 minutes.

Minimum duration of exposure: From a few minutes to a few hours depending on the intensity of exposure.

Maximum latent period: 24 hours.

Methylene chloride

Definition of causal agent

Methylene chloride CH_2Cl_2 (dichloromethane or methylene dichloride) is a colourless, volatile, water-soluble liquid. It has a sweetish odour detectable by most individuals above 200 to 300 ppm, although adaptation to the odour can occur. At 2 300 ppm the odour is strong and intensely irritating.

Methylene chloride is metabolized in part to carbon monoxide. In presence of fire, methylene chloride may result in phosgene production.

The toxicity of methylene chloride is related to the toxicity of the other similar solvents and of carbon monoxide.

Main occupational uses and sources of exposure:

Degreasing agent used as paint and varnish remover; propellant for aerosol sprays; solvent for plastic and blowing agent for foams.

Toxic effects

1. Local effects

Irritant effects

Methylene chloride is irritant to the skin, eyes and respiratory tract (pulmonary oedema, coma).

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

2. Systemic effects

Acute

Narcotic syndrome

Headache, nausea, vertigo, drowsiness, weakness, confusion, loss of consciousness, sometimes coma.

Possibility of cardiovascular and neurological sequelae, the intensity of which depends on the severity of the exposure.

Exposure criteria:

Minimal intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions showing significant exposure to methylene chloride,
- and, if available:
 - biological monitoring: exposure confirmed by measurement of dichloromethane in blood and carboxyhaemoglobinaemia guide values:

an increase of 5 % or more in carboxyhaemoglobin (in non-smokers) within an hour of exposure, or a similar increase of carbon monoxide in exhaled breath within two hours of exposure.

- workplace air monitoring:

guide values:

at exposures to 2 300 ppm over 5 minutes or for longer exposures above 300 ppm, dizziness results.

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

Maximum latent period: The first symptoms should occur during the exposure and at the latest within 24 hours.

Chronic

Chronic toxic encephalopathy

CNS effects similar to those for acute exposure can also occur with repeated, prolonged exposure.

See document on chronic toxic encephalopathy caused by organic solvents.

Exacerbation of ischaemic heart disease

Prolonged exposure which gives rise to levels of carboxyhaemoglobinaemia in excess of 10% can exacerbate a pre-existing ischaemic heart disease.

Due to the multicausality of the occurrence of these pathologies, particularly tobacco smoking, the recognition of the occupational origin must be individually evaluated by experts.

To be attributable to the exposure to methylene chloride, the cardiovascular or neurological sequelae should occur in the month following the acute exposure. These could be considerably delayed in case of subacute exposure. Their assessment should be performed by an expert.

Trichloroethylene

Definition of the causal agent

Trichloroethylene ($\text{CHCl}=\text{CCl}_2$) (synonyms: trichloroethene, chlorylene, TRI) is a non-inflammable fluid with a chloroform-like odour. It is not readily soluble in water but soluble in organic solvents. Vapour/air mixtures are explosive. Decomposition occurs on exposure to heat, with formation of dichloro-acetylene, hydrochloric acid fumes, carbon monoxide and phosgene (see the documents concerning these substances).

The principal metabolites of trichloroethylene are trichloroethanol and trichloroacetic acid.

Sources of exposure and main occupational uses:

Trichloroethylene is used as a solvent and extracting agent and as an insecticide. It is also a component of certain stain removers.

Toxic effects

1. Local effects

Irritant effects

Trichloroethylene can cause irritation of the skin and mucous membranes.

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

2. Systemic effects

Acute

Narcotic syndromes

Headache, dizziness, nausea, drowsiness, weakness, confusion, loss of consciousness, possibly leading to coma.

NB: In patients undergoing treatment, trichloroethylene can also cause cardiac arrhythmia as a result of depression of the threshold of sensitivity to catecholamines.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of acute exposure to trichloroethylene,
- and, if available:
 - biological monitoring
 - trichloroethanol in blood > 5 mg/L (end of shift sample)
 - trichloroacetic acid in urine > 100 mg/L

-
- workplace air monitoring
(108 mg/m³) 20 ppm: perceptible odour,
(594 mg/m³) 110 ppm: increase in reaction time may occur,
(6,9 g/m³) 1 280 ppm: state of prenarcois after six minutes,
(13,5 g/m³) 2 500 ppm: rapid full narcois.

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

Chronic

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

Damage to cranial nerves

Hypoaesthesia, paraesthesia, of the trigeminal nerve.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to trichloroethylene (taking account of the possibility of cutaneous absorption),

— and, if available:

- biological monitoring:
guide values:
trichloroethanol in blood: > 5 mg/L
trichloroacetic acid in urine: > 100 mg/L
- workplace air monitoring:
guide value:
atmospheric concentration well above (270 mg/m³) 50 ppm.

Minimum duration of exposure: Chronic toxic encephalopathy: 10 years.

Damage to trigeminal nerve: Several years.

Maximum latent period: Chronic toxic encephalopathy: The first signs of nervous system disturbance should occur in the year following cessation of exposure.

Damage to the trigeminal nerve: Immediate.

Tetrachloroethylene

Definition of causal agent

Tetrachloroethylene ($\text{CCl}_2=\text{CCl}_2$) (synonyms: tetrachlorethene, perchlorethylene) is a colourless, volatile, non-flammable solvent which smells like ether. It is only slightly soluble in water but is soluble in organic solvents. It breaks down when exposed to heat, into carbon monoxide, phosgene and hydrochloric acid fumes (see document on these substances). Of the dose absorbed, 80 to 95% is excreted unaltered via the lungs. A small amount undergoes biological transformation into trichloroacetic acid (< 3%). Tetrachloroethylene has a long half-life because of deposition in body fat.

Main sources of exposure and occupational uses:

It is widely used for dry cleaning, the treatment of textiles and metal degreasing.

Toxic effects

1. Local effects

Irritant effects

Tetrachloroethylene can irritate the skin and mucous membranes.

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

2. Systemic effects

Narcotic syndrome

Headache, dizziness, nausea, drowsiness, weakness, confusion, fainting, possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of acute exposure to tetrachloroethylene,

— and, if available:

- biological monitoring:
blood tetrachloroethylene level > 1 mg/L measured prior to the next work shift
- workplace air monitoring:
guide values:
(680 mg/m³) 100 ppm: slight smell; dizziness, headache after seven hours exposure
(34g/m³) 5 000 ppm: strong smell; symptoms after six minutes exposure.

Minimum duration of exposure: From several minutes to several hours depending on intensity of exposure.

Maximum latent period: 24 hours.

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure taking the possibility of cutaneous absorption into account,

— and, if available:

- biological monitoring:
blood tetrachloroethylene content
- workplace air monitoring:
guide value:
concentration in the atmosphere well above (345 mg/m³) 50 ppm.

Minimum duration of exposure: 10 years.

Maximum latent period: The first signs of mental disorder will appear during the year following the end of exposure.

Vinyl chloride monomer

Definition of causal agent

At normal temperature and pressure, vinyl chloride is a gaseous monomer.

Main occupational uses and sources of exposure:

Mainly used in the production of polyvinyl chloride.

Toxic effects

Irritant effects

Vinyl chloride monomer may be irritant to the skin (irritant dermatitis), the eyes (keratoconjunctivitis) and the upper respiratory tract.

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

Narcotic syndrome

Headache, dizziness, nausea, somnolence, weakness, confusion, unconsciousness, may lead to coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions showing evidence of intense exposure to vinyl chloride monomer at atmospheric concentration > 800 ppm (2.08 g/m³)

— and, if available:

- workplace air monitoring:

guide value: atmospheric concentration $> (2.08$ g/m³) 800 ppm.

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

Raynaud's phenomenon in the hands and feet

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;

— and, if available:

- workplace air monitoring:

guide value: atmospheric concentration $> (130$ mg/m³) 50 ppm.

Minimum duration of exposure: One year.

Maximum latency period: Three years.

Acro-osteolysis in the terminal phalanges of the hands and feet

May accompany angioneurotic disorders. Confirmed by X-ray (loss of structure from bones)

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
- and, if available:
 - workplace air monitoring:
guide value: atmospheric concentration > (130 mg/m³) 50 ppm.

Minimum duration of exposure: One year.

Maximum latent period: Three years.

Distal skin disorders

Scleroderma-like syndrome with smooth, shiny skin, possibly accompanied by general symptoms (arthralgia, myalgia).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
- and, if available:
 - workplace air monitoring:
guide value: atmospheric concentration > (130 mg/m³) 50 ppm.

Minimum duration of exposure: One year.

Maximum latent period: Three years.

Liver fibrosis with portal hypertension

Portal hypertension syndrome.

Fibrosis confirmed by histology or indirectly by echography.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
- and, if available:
 - workplace air monitoring:
guide value: atmospheric concentration > (130 mg/m³) 50 ppm.

Minimum duration of exposure: Two years.

Maximum latent period: 30 years.

Minimum induction period: Five years.

Angiosarcoma

Angiosarcoma of the liver.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
- and, if available:
 - workplace air monitoring:
guide value: atmospheric concentration > (130 mg/m³) 50 ppm.

Minimum duration of exposure: 10 years.

Minimum induction period: 10 years.

See document on occupationally caused cancers.

Methyl bromide

Definition of causal agent

At ambient temperature and pressure, methyl bromide is a colourless and normally odourless gas which is heavier than air. At high concentrations its smell resembles that of chlorine.

Main professional uses and sources of exposure:

Used as insecticide and nematocide via fumigation (greenhouse floors), rodenticide, refrigerant, methylation agent in the chemical industry.

Toxic effects

1. Local effects

Irritant effects

Methyl bromide is highly irritating to the ocular and respiratory mucous membranes (pulmonary oedema may develop after a latency period of 6 to 24 or even 48 hours). It causes erythema, blisters and swellings.

As a liquid, methyl bromide is also highly irritant to the mucous membranes and causes severe skin burns.

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

2. Systemic effects

Acute neurological syndrome

Signs and symptoms:

Headache, vertigo, sleepiness, blurred vision, nausea, vomiting, anorexia.

Dysarthria, ataxia, muscular incoordination, twitching, fasciculations, myoclonia, trembling, convulsions.

Healing may be very slow and there may be sequelae (motor impairment, cortical deafness, optic neuritis).

Exposure criteria:

Minimum intensity of exposure:

Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing acute poisoning by methyl bromide via inhalation or skin contact;
- and, if available:
 - biological monitoring:
 - blood: bromide (qualitative dose);
 - workplace air monitoring

Minimum duration of exposure: From some minutes to some hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Butyl (butanol), methyl (methanol) and isopropyl (isopropanol) alcohols

Definition of causal agent

The butyl, methyl and isopropyl alcohols are aliphatic hydrocarbons in which one hydrogen atom is replaced by a hydroxyl group.

Butyl alcohol (butanol) exists in four isomeric forms: 1-butanol, 2-butanol, isobutanol and tertiary butanol.

Main occupational uses and sources of exposure:

The three alcohols are used as solvents and detergents in industry.

The uses of the isomers of butanol differ, as only 2-butanol may be used in perfumes and tertiary butanol as a hydrophilic agent. Methyl alcohol is widely used as a denaturing agent for ethanol, marketed for technical use.

Local toxic effects

Irritant effects

These substances cause irritation to the skin, eyes and respiratory tract (consider of splashes and immersion in as a means of skin contact).

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

Ethylene glycol, diethylene glycol and 1,4-butanediol

Definition of causal agent

Glycols are aliphatic hydrocarbons which possess two hydroxyl groups.

Ethylene glycol ($\text{HOCH}_2\text{-CH}_2\text{OH}$) or ethanediol, diethylene glycol ($(\text{HOCH}_2\text{CH}_2)^{20}$) and 1,4 butanediol ($\text{OH}(\text{CH}_2)_4\text{OH}$) are liquids with a fairly low vapour pressure.

There is therefore likely to be a risk of inhalation only at high temperatures or where aerosols are formed. Under normal working conditions the levels absorbed through the skin are also low. Glycols are therefore unlikely to cause harmful systemic effects under normal working conditions.

Main occupational uses and sources of exposure:

Ethylene glycol and diethylene glycol are widely used in industry. Ethylene glycol is often used in antifreeze or liquid coolants, while diethylene glycol is often used in brake fluids and lubricants. Some butanediols are used in cosmetics.

Local toxic effects

Irritant effects

These substances may cause slight irritation of the skin and mucous membranes.

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

Nitro derivatives of glycols and glycerol

Definition of causal agents

The nitro derivatives of glycols and glycerol are volatile liquids at ambient pressure and temperature.

Main occupational uses and sources of exposure

Used as explosives (nitroglycerine, ethylene glycol dinitrate, propylene glycol dinitrate), as therapeutic agents, vasodilators (nitroglycerine) and as a marine engine fuel (propylene glycol dinitrate). Occupational exposure can occur both in production and handling of these products.

Toxic effects

1. Local effects

Irritant effects

These substances may irritate the skin.

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

NB: Repeated contact with the hands may cause:

- eruptions on the palms and between the fingers, and
- in some cases, subungual ulceration (probably as a result of vasospasm).

2. Systemic effects

Acute

Vasodilation and methaemoglobinaemia

Headaches, flushing, nausea, vomiting, abdominal pain, sweating, dizziness, palpitation, hypotension, confusion, delirium.

The symptoms are generally aggravated by simultaneous intake of alcohol.

Prolonged or repeated exposure brings tolerance in respect of headaches, which can disappear within around 48 hours.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing significant exposure to these substances, taking into account the fact that the substances are absorbed by the skin;
- and, if available:
 - biological monitoring shows presence of the substance and degree of methaemoglobinaemia;
 - workplace air monitoring guide values: ethylene glycol dinitrate causes hypotension and severe headaches within 1 to 3 minutes, at a concentration in air of (1.2 mg/m³) 0.2 ppm

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 48 hours.

**Chronic
Cardiovascular disorders**

- attacks of angina, sudden death which may occur in the absence of pre-existing heart disease.
A delayed reaction generally occurs within 24 to 72 hours following exposure and may be provoked even by very light activities.
Hypotension and signs of hyperexcitability may be observed during exposure.
- Raynaud's phenomenon.

Exposure criteria

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions, showing
inhalation of large quantities of these volatile substances and/or poor work practices resulting in significant cutaneous contact;
- and, if available:
 - biological monitoring;
 - workplace air monitoring.

Minimum duration of exposure: Raynaud phenomenon: five to 10 years depending on intensity of exposure. Attacks of angina, sudden death, hypotension: minimum duration of exposure is probably less than five years.

Maximum latent period: Four days.

Methyl ether, ethyl ether, isopropyl ether, vinyl ether, dichloroisopropyl ether, guaiacol

Definition of causal agent

With the exception of methyl ether, which is gaseous, all ethers are colourless, volatile liquids. They form explosive peroxides in air and/or daylight.

Main occupational uses and sources of exposure:

Ethers are used as organic solvents. Methyl ether, ethyl ether and vinyl ether are mainly used as anaesthetic agents. Methyl ether is also used as a refrigerant, an aerosol dispersant and a rocket propellant. Ethyl ether and dichloroisopropyl ether are industrial solvents for fats, oils, resins and waxes. Isopropyl ether is a commercial paint and varnish stripper, rubber adhesive, component of aircraft fuel, and is used to extract nicotine from tobacco. Guaiacol is used in printing inks and in surface coatings. It is also used as a therapeutic agent (expectorant).

Toxic effects

1. Local effects

Irritant effects

Prolonged or repeated skin contact may result in irritant dermatitis. Dermatitis is less likely from guaiacol and has not been reported for dichloroisopropyl ether.

High concentrations of ether may also cause irritation of the ocular mucous membranes and respiratory tract. Diethyl ether is less irritating to the eyes and throat than to the nose.

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

2. Systemic effects

Narcotic syndrome

Headache, vertigo, nausea, drowsiness, weakness, confusion, unconsciousness, possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by anamnesis and study of working conditions showing intense exposure to the substances, taking into account the possibility of cutaneous absorption of guaiacol and dichloroisopropyl ether (as opposed to diethyl ether).

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Chronic toxic encephalopathy

Possible development of chronic toxic encephalopathy as a result of exposure to significant quantities over a long period.

See document on chronic toxic encephalopathy caused by organic solvents.

**Ethylene glycol
monomethyl ether
(2-methoxyethanol),
ethylene glycol monoethyl
ether (2-methoxyethanol)**

Definition of causal agent

Glycol ethers derive from the combination of a glycol and one or two alcohols. They are volatile liquids.

Main occupational uses and sources of exposure:

These compounds are used chiefly as solvents and co-solvents (lacquers, resins, pigments, etc.), in the micro-electronics industry (manufacture of semiconductors), as constituents of hydraulic fluids and in the manufacture of radiography film and cellophane.

Local toxic effects

Irritant effects

Direct contact or exposure to the fumes at high concentrations can cause conjunctival irritation.

Guide value:

atmospheric concentration > 50 ppm.

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

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing major skin contact or massive inhalation of a ketone;
- and, if available:
 - workplace air monitoring:
disorders of the central nervous system may become evident at concentrations of:
 - > (methyl isobutyl ketone) (328 mg/m³) 80 ppm;
 - > (methyl butyl ketone) (600 mg/m³) 150 ppm;
 - > (acetone) (476 mg/m³) 200 ppm.

Minimum duration of exposure: Depending on the dose and type of ketone, may range from a few minutes to several hours.

Example for duration of less than one hour:

atmospheric concentration of acetone > (about 28 g/m³) 12 000 ppm;

atmospheric concentration of MIBK > (about 2 g/m³) 500 ppm.

Maximum latent period: 24 hours.

Possibility of toxic hepatitis resulting from the synergic effects of certain chlorinated solvents (CCl₄, chloroform) and certain ketones (acetone).

Polyneuropathy

Pathology similar to that caused by n-hexane.

See document on n-hexane.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions showing evidence of exposure to MBK (methyl butyl ketone). To a considerably lesser extent, other ketones may have similar effects due to synergism of MBK with other substances (such as methyl ethyl ketone) which have the same metabolites, or due to the presence of impurities of MBK and similar substances.

Assessment should take into account the different absorption pathways (respiratory, cutaneous, gastrointestinal);

- and, if available:

- biological monitoring
guide values:

methyl-n-butyl ketone: > 5 mg 2,5-hexanedione/g creatinine in urine.

NB: 2,5-hexanedione is also a metabolite of n-hexane.

- workplace air monitoring
guide values:

methyl-n-butyl ketone: > (20 mg/m³) 5 ppm.

Minimum duration of exposure: Six months.

Maximum latent period: One month.

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

Organophosphorous esters

Definition of causal agent

Organophosphorous insecticides are derivatives of ester, amides or thiols of phosphoric, phosphonic, phosphorothioic or phosphonothioic acids.

They have identical effects, namely the inhibition of acetylcholinesterase.

Main occupational uses and sources of exposure:

Used as pesticides.

Toxic effects

1. Acute systemic effects

Clinical picture similar to that caused by carbamate poisoning. Inhibition of acetylcholinesterase is prolonged, while it is only transitory in the case of carbamate poisoning.

Miscellaneous disorders:

profuse sweating, lacrimation, disturbed vision,
muscular fasciculations, asthenia.

Digestive disorders:

increased salivation, nausea, vomiting, diarrhoea, abdominal cramps.

Respiratory disorders:

bronchial hypersecretion, tightness of chest, bronchioconstriction, dyspnoea, pulmonary oedema.

Cardiovascular disorders:

arrhythmia, hypotension, shock.

Neurological disorders:

headache, dizziness, agitation, anxiety, mental confusion,
tremors, convulsions, coma, delayed polyneuritis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions showing significant exposure to the substances; taking into account the possibility of cutaneous absorption; the time and sequence of appearance of symptoms and signs are a function of the chemical agent, the dose and the absorption pathway;
- and, if available:
 - biological monitoring:
 - significant reduction in cholinesterase activity (at least 30% as compared with the base level);
 - identification of the relevant substances or their metabolites in biological liquids;
 - workplace air monitoring.

Minimum duration of exposure: From a few minutes to several hours, depending on the intensity of exposure.

Maximum latent period: Three days.

2. Chronic systemic effects

Peripheral neuropathy

Certain substances (phosphate triesters) may cause peripheral sensory and motor neuropathy in the lower limbs.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions, providing evidence of prolonged or repeated exposure to these substances taking into account the possibility of cutaneous absorption;
- and, if available:
 - biological monitoring
measurement of cholinesterase activity;
identification of the relevant substance or its metabolites in biological liquids;
 - workplace air monitoring.

Minimum duration of exposure: Several years, depending on the intensity of exposure.

Maximum latent period: Indeterminate.

Carbamates

Definition of causal agent

Carbamates are nitrogen substituted urethanes. The salts and esters of substituted carbamic acid are more stable than carbamic acid. This enhanced stability is the indispensable basis for the synthesis of many derivatives that are used as pesticides. Indeed the toxic effects given below relate only to pesticides.

Used as pesticides, they are subdivided into three main classes: the methyl substituted insecticides, the aromatic hydrocarbon substituted herbicides and the benzimidazole substituted fungicides.

Main occupational uses and sources of exposure:

Carbamates are used in agriculture, sometimes as biocides for industrial or other commercial applications, and in household products; they may also be used in public health vector control.

Toxic effects

Clinical picture similar to organophosphorous ester poisoning and is due to acetylcholinesterase inhibition. Inhibition of acetylcholinesterase is transitory, while it is prolonged in the case of organophosphorous ester poisoning.

Miscellaneous disorders:

profuse sweating, lacrimation, disturbed vision, muscular fasciculations, asthenia.

Digestive disorders:

increased salivation, nausea, vomiting, diarrhoea, abdominal cramps.

Respiratory disorders:

bronchial hypersecretion, tightness of chest, bronchoconstriction, dyspnoea, pulmonary oedema.

Cardiovascular disorders:

arrhythmia, hypotension, shock.

Neurological disorders:

headache, dizziness, agitation, anxiety, mental confusion, tremors, convulsions, coma, delayed polyneuritis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions showing significant exposure to the substances, taking into account the possibility of cutaneous absorption;
- the time and sequence of appearance of symptoms and signs are a function of the chemical agent, the dose and the absorption pathway. Symptoms are less persistent than in the case of organophosphorous ester poisoning;

— and, if available:

- biological monitoring
 - significant reduction in cholinesterase activity (at least 30% as compared with the base level) (measured within six hours of exposure);
 - identification of the relevant substances or their metabolites in biological liquids;
- workplace air monitoring.

Minimum duration of exposure: From a few minutes to several hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

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 co-monomer 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 micro-encapsulation 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 document 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 document on occupationally caused allergic contact dermatoses.

Formaldehyde

Definition of causal agent

Formaldehyde (methanal, formic aldehyde) is a colourless gas, flammable at ambient temperature. Workplace exposure is usually associated with a 30 to 50% (by weight) aqueous solution (formalin).

Main occupational uses and sources of exposure:

Exposure to formaldehyde occurs during its production; the synthesis of formol-based plastics; the manufacture of chemical substances; disinfection; in the textiles industry (dressing of hides and fabrics). It is also released during the combustion of a number of organic materials (incinerators, car exhaust fumes, etc.), and from chipboard made using formaldehyde-based resins.

Toxic effects

1. Local effects

Irritant effects

Formaldehyde is extremely irritant to the skin (skin ulceration can occur), eyes and respiratory tract (acute pulmonary oedema follows intense exposure).

Guide values:

irritation of the eyes: (0.1 ppm) 0.12 mg/m³;

irritation of the respiratory tract: (0.5 ppm) 0.6 mg/m³.

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

Allergic effects

Formaldehyde is only rarely responsible for allergic effects.

However, because of its irritant effects, it is likely to aggravate any asthma pre-existing already present.

See documents on occupationally caused asthma and occupationally caused allergic contact dermatoses.

2. Systemic effects

Nasal cancer

The causal relationship between prolonged or repeated exposure to formaldehyde and the occurrence of nasal cancer has not been firmly established, and due to the multiple aetiology of this type of cancer, the recognition of the occupational origin must lie on a thorough assessment taking into account all other possible aetiologies.

Each case must therefore be considered separately.

See document on occupationally caused cancers.

Benzene

Definition of causal agent

Benzene is a volatile, colourless, liquid, aromatic hydrocarbon whose vapours are heavier than air.

Main occupational uses and sources of exposure:

In the past, benzene was widely used as a solvent (glues, paints, varnishes, lacquers, scouring of metal parts, dry cleaning, printing inks, etc.). Currently, such uses are strictly regulated. It is still present in car fuel (1 to 5% in petrol). It is used in the synthesis of a great variety of chemical products (nitrobenzene, chlorobenzene, phenol, etc.). Exposure is also possible during the production of benzene via coal tar distillation or from petroleum or when cleaning of tanks in which benzene has been stored.

Toxic effects

1. Local effects

Irritant effects

Benzene irritates the skin, eyes and respiratory tract.

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

2. Systemic effects

Narcotic effects

Headaches, dizziness, nausea, drowsiness, weakness, confusion, unconsciousness, possibly coma.

Exposure criteria:

- Minimum intensity of exposure:* Occupational exposure confirmed, if possible assessed, by:
- anamnesis and study of working conditions showing evidence of acute benzene poisoning;
 - and, if available:
 - biological monitoring;
 - workplace air monitoring.

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Non-carcinogenic haematological effects

Hypoplasia: thrombocytopenia and/or leukopenia, and/ or anaemia

Hyperplasia: thrombocytosis, and/or leukocytosis, and/or erythrocytosis

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of exposure to benzene;

— and, if available:

- biological monitoring:
 - blood: benzene
 - expired air: benzene
 - urine: phenol, mucoic acid;
- workplace air monitoring:
 - guide value:
atmospheric concentration > (32 mg/m³) 10 ppm.

Minimum duration of exposure: A few days are sufficient to cause depression of the bone marrow when exposure takes place at high atmospheric concentrations (160 mg/m³) (>50 ppm). One month for other haematological phenomena.

Maximum latent period: One year for medullary hyperplasia. One month for medullary depression.

Leukaemia

Although the most common forms are acute myeloblastic leukaemia, current knowledge suggests that other forms of leukaemia may also be induced by benzene. See document on carcinogenic substances.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of exposure to benzene;

— and, if available:

- biological monitoring:
 - blood: benzene
 - expired air: benzene
 - urine: phenol, muconic acid
- workplace air monitoring:
 - guide value:
atmospheric concentration > (3.2 mg/m³) 1 ppm.

Minimum duration of exposure: Six months unless there are antecedents of medullary aplasia.

Maximum latent period: Does not apply.

Induction period: Five years.

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

Toluene

Definition of causal agent

Toluene is a volatile, easily flammable liquid at ambient temperature and pressure.

Main occupational uses and sources of exposure:

Mainly used in the production of benzoic acid, benzaldehyde, explosives and many other organic compounds; as a solvent for paints, lacquers, adhesives, etc; petrol additive; extraction agent.

Toxic effects

1. Local effects

Irritant effects

Toluene irritates the skin, eyes and respiratory tract.

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

2. Systemic effects

Narcotic syndrome

Headache, dizziness, nausea, drowsiness, weakness, confusion, unconsciousness, possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of working conditions showing evidence of acute toluene poisoning,
— and, if available:

- biological monitoring: Blood toluene at the end of shift and/or urinary hippuric acid;
 - workplace air monitoring
- guide value: atmospheric concentration $> (750 \text{ mg/m}^3) 200 \text{ ppm}$.

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

Chronic toxic encephalopathy

See document on chronic toxic encephalopathy caused by organic solvents.

Naphthalene and its derivatives (C_nH_{2n-12})

Definition of causal agent

Naphthalene is a solid substance with a fairly high vapour pressure. Naphthalene and its derivatives are by-products of industrial coke and gas production; alkyl-naphthalenes are in the fraction with a distillation point between 204° and 288°C.

Naphthalene is used in the chemical industry as the starting product in the synthesis of a number of products such as wood preservatives, and in the manufacture of moth-proofing products. Some alkyl-naphthalenes are present in carbonless copy paper.

Toxic effects

1. Local effects

Irritant effects

These products irritate the skin, eyes and respiratory tract.

In some cases, contact with the eyes can lead to punctiform keratitis and, in particularly serious cases, corneal ulceration.

The irritant effect of alkyl-naphthalenes varies: some substances in the naphthalene family have marked effects, whereas others, such as methylnaphthalene, have no irritant effects.

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

2. Systemic effects

Acute

Non-specific effects

Headache, dizziness, nausea, vomiting, trembling and, in severe cases, convulsions; haemolytic anaemia (particularly in subjects with a congenital glucose-6-phosphate dehydrogenase deficiency).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of particularly intense exposure to naphthalene,
- and, if available:
 - workplace air monitoring.

Minimum duration of exposure: A few minutes to a few hours, depending on level of exposure.

Maximum latent period: 15 days.

Chronic

Chloracne

This occurs from exposure to chloronapthalenes.

Small, pale yellow cysts and comedones.

In very severe cases, inflammatory lesions with larger cysts, abscesses, follicular hyperkeratosis.

Main sites: face (nose generally excluded), neck, shoulders, chest, back, scrotum. This condition is extremely persistent and may last for decades, even after exposure has ceased.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged/repeated exposure to chloronapthalenes (usually penta- and hexachloronapthalene derivatives). Skin contact is most often the cause of this condition, but inhalation and ingestion may also be responsible.

Minimum duration of exposure: A few weeks to a few months depending on level of exposure.

Maximum latent period: Six months.

Vinylbenzene, and divinylbenzene

Definition of causal agent

Vinylbenzene (styrene) is a colourless or yellowish liquid with a characteristic smell. Divinylbenzene (diethenylbenzene or vinylstyrene) exists as ortho-, meta- and para-isomers.

Main occupational uses and sources of exposure:

Occupational exposure to vinylbenzene occurs during synthesis and manufacture of polymers (polystyrene), copolymers (acrylonitrile-butadiene-styrene or ABS) and polyester resins. It is also used as a solvent and as an additive in aircraft fuel.

Divinylbenzene is used as a basis for the production of polymers, as a monomer in the manufacture of insecticides and as an ion-exchange resin in water purification and in dentistry.

Toxic effects

1. Local effects

Irritant effects

Styrene causes irritation to the skin and mucous membranes.
for information:

- (600 ppm) 2.6 g/m³: intense irritation
- (800 ppm) 3.4 g/m³: immediate acute symptoms.

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

2. Systemic effects

Acute

Narcotic syndrome

Headache, dizziness, nausea, drowsiness, weakness, confusion, loss of consciousness and possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of intense exposure to (di)vinylbenzene (taking account of the possibility of cutaneous absorption);

— and if available:

- biological monitoring: styrene: mandelic and phenylglyoxylic acids in the urine, styrene in the blood and in the exhaled air
- workplace air monitoring:

guide value:

atmospheric concentration well above 100 ppm styrene (426 mg/m³).

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

3. Chronic effects

Chronic toxic encephalopathy

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to (di)vinylbenzene (taking account of the possibility of cutaneous absorption);

— and, if available:

- biological monitoring: styrene: mandelic and phenylglyoxylic acid in the urine, styrene in the blood and in the exhaled air
- workplace air monitoring:
guide value: atmospheric concentration > (213 mg/m³) 50 ppm (in a cumulative dose over 10 years).

Minimum duration of exposure: 10 years.

Maximum latent period: The first symptoms of mental deterioration should be seen within one year following the end of exposure.

See document on chronic toxic encephalopathy caused by organic solvents.

Halogenated derivatives of aromatic hydrocarbons

Definition of the causal agent

The benzene nucleus is the basic chemical entity of this group of substances which can be divided into three subgroups:

(i) benzene derivatives in which one or more hydrogen atoms have been replaced by one or more halogen atoms.

Main substances: chlorinated benzene: mono-, di-, tri-, hexachlorobenzene; brominated benzene: monobromobenzene; chlorinated toluene: mono-, trichlorotoluene;

(ii) biphenyls and polyphenyls in which one or more hydrogen atoms have been replaced by one or more halogen atoms.

Main substances: polychlorobiphenyls, polybromobiphenyls;

(iii) polynuclear compounds composed of two or more fused benzene rings in which one or more hydrogen atoms have been replaced by one or more halogen atoms.

Main substances: chlorinated naphthalene: hexachloronaphthalene.

Main occupational uses and sources of exposure:

(i) Chloro-, bromobenzenes, chlorotoluene: mainly used as solvents, pesticides, herbicides, fungicides and chemical intermediates;

(ii) Polychloro-, polybromobiphenyls: dielectric fluids in condensers and transformers, lubricant, plasticizers, synthetic rubber, fireproofing material and carbonless copy paper;

(iii) Chloronaphthalenes: manufacture of electric condensers, insulation of electric cables and wires, additives for extreme pressure lubricants.

Toxic effects

Halogenated derivatives of benzene

1. Local effects

Irritant effects

These substances can be irritant for the skin, eyes and respiratory tract.

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

2. Systemic effects

Narcotic syndrome

Headache, vertigo, nausea, drowsiness, weakness, confusion, unconsciousness, possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of an intense exposure to monochlorobenzene or monobromobenzene. The possibility of skin absorption should be considered.

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

Maximum latent period: 24 hours.

Halogenated derivatives of biphenyls (PCB, PBB)

1. Local effects

Irritant effects

These substances can be irritant for the skin.

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

2. Systemic effects

Chloracne

Small straw-coloured cysts and comedones.

More severe cases: inflammatory lesions with larger cysts, abscesses, follicular hyperkeratosis.

The lesions typically involve the face (nose generally spared), then the neck, shoulders, chest, back and scrotum.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of acute or repeated/prolonged exposure to these substances; generally occurs after skin contact but also inhalation and ingestion.

Minimum duration of exposure: A few weeks to a few months depending on the intensity of exposure.

Maximum latent period: Six months.

Toxic hepatitis

Generally reversible functional impairment, rarely more severe disturbances.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of repeated/prolonged exposure to PCB, PBB (the possibility of skin absorption should be taken into account),

— and, if available:

- biological monitoring:
for information: PCB, PBB in blood.

Minimum duration of exposure: A few months.

Maximum latent period: Six months.

Halogenated derivatives of naphthalene

1. Local effects

Irritant effects

These substances can be irritant for the skin, eyes and respiratory tract.

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

2. Systemic effects

Toxic hepatitis

Liver impairment ranging from functional and reversible disorders to acute liver atrophy.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of repeated/prolonged exposure to hexachloronaphthalene (the possibility of skin absorption should be taken into account).

Minimum duration of exposure: A few months.

Maximum latent period: Six months.

Chloracne

Small straw-coloured cysts and comedones.

More severe cases: inflammatory lesions with larger cysts, abscesses, follicular hyperkeratosis.

The lesions typically involve the face (nose generally spared), then the neck, shoulders, chest, back and scrotum.

The disease is extremely persistent and in some cases may last for decades after cessation of exposure.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of acute or repeated/prolonged exposure to hexachloronaphthalene. Generally occurs after skin contact but also inhalation and ingestion.

Minimum duration of exposure: A few weeks to a few months depending on the intensity of the exposure.

Maximum latent period: Six months.

Pentachlorophenol

Definition of causal agent

Pentachlorophenol (C₆Cl₅OH) (synonym: PCP) is a solid, odourless substance consisting of needle-like crystals. It is almost insoluble in water and is soluble in alcohol, ether, acetone, benzene and alkali solutions. It exhibits weak acidic and strong lipophilic reactions and is slightly biodegradable. Technical-grade PCP contains impurities in the form of various chlorinated phenols and dibenzo-p-dioxins, but no 2,3,7,8-tetrachlorodibenzo-p-dioxin. It acts by decoupling reactions in the oxidative phosphorylation process, which explains its systemic effects.

Sources of exposure and main occupational uses:

PCP is used as a wood, textile and leather preservative, as a fungicide and as a disinfectant.

Toxic effects

1. Local effects

Irritant effects

PCP irritates the eyes and the upper respiratory tract.

Guide values:

0.003 mg/m³: no reaction,

1 mg/m³: painful irritation of the nasal mucous membranes,

NB: 2.4 mg/m³: no discomfort to persons accustomed to the substance.

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

2. Systemic effects

Acute effect: hyperthermic syndrome

Excessive sweating, rapid weight loss and dehydration in severe cases: loss of consciousness, convulsions, death by heart failure, respiratory arrest, pulmonary oedema.

Subacute effect: digestive syndrome

Abdominal pain, vomiting, diarrhoea.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of intense exposure to PCP (high risk of absorption through skin),

— and, if available:

- biological monitoring:
guide value:
the first signs of poisoning become apparent at 3 to 10 mg PCP/L urine or 40 to 80 mg/L blood.

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

Maximum latent period: Acute syndrome: Two days. Subacute syndrome: Seven days.

Chloracne

Probably caused by impurities in PCP rather than PCP itself.

Small, pale yellow cysts and comedones.

In very severe cases: inflammatory lesions with larger cysts, abscesses, follicular hyperkeratosis.

Main sites: face, less frequently neck, shoulders, chest, back and scrotum.

Exposure criteria:

Minimum intensity and duration of exposure:

Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of acute exposure to or prolonged or repeated contact with the substance.

Skin contact is probably most often the cause of this condition, but inhalation and ingestion may also be responsible;

— and, if available:

- biological monitoring:
guide value:
pentachlorophenol in urine
- workplace air monitoring.

Minimum duration of exposure: A few weeks to a few months depending on the intensity of exposure.

Maximum latent period: Six months.

Halogenated derivatives of alkylarylsulphonates and alkylaryloxides

Definition of causal agent

Alkylarylsulphonates: the basic compound is benzenesulphonic acid with an alkyl group attached to the other end of the benzene ring. With metal hydroxides their corresponding metal salts are synthesized. Further halogenation produces the halogenated derivatives. Examples: chlorinated polypropylene benzene sulphonate, chlorinated hexane benzene sulphonate.

Alkylaryloxides: halogenated derivatives of alkylaryl(R-O-Ar) oxides or halogenated ethers of alkyl and aryl. The most important group are the halogenated derivatives of anisol (or methylphenylether): 2-chloroanisol, 2,4-dichloroanisol, tri-, tetra-, pentachloroanisol; brominated, iodized, fluorinated derivatives of anisol. There are no available data on human toxicity implicating this type of substance.

Main occupational uses and sources of exposure:

Alkylarylsulphonates: some sulphonates are important household items and some are used medically as bactericides and antiseptics, as such, or as part of mixtures.

Alkylaryloxides: use limited to synthesis in organic chemistry. The most used substance is 2-chloroanisol which is a methoxyphenyl agent.

Toxic effects

Local effects

Irritant effects

The halogenated derivatives of alkylarylsulphonates can induce eye irritation, and in some cases defatting of the skin.

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

Allergic contact dermatitis

Some halogenated derivatives of alkylarylsulphonates can induce allergic contact dermatitis.

See document on occupationally caused allergic contact dermatoses.

Benzoquinone

Definition of causal agent

Benzoquinone is an oxidizing agent. It is a volatile, flammable solid which forms yellow crystals. The compound sublimes as soon as heat is applied, forming toxic gases. It has a penetrating odour resembling that of chlorine.

Main occupational uses and sources of exposure:

Benzoquinone is used chiefly as an intermediate in the manufacture of hydroquinone, dyes and fungicides. It is also used in photography, in tanning hides, in making gelatine insoluble and in strengthening animal fibres.

Its wide use is due to its ability to transform certain nitrogen compounds into a variety of coloured substances.

Toxic local effects

Irritant effects

Irritates the respiratory and ocular mucous membranes (causing conjunctival irritation and, in some cases, oedema and severe corneal ulceration).

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

Leucoderma

See document on leucoderma (vitiligo).

Ocular detriment

Chronic exposure may cause gradual brownish discolouration of the conjunctiva and cornea confined to the palpebral fissure. Small opacities and structural corneal changes result in loss of visual acuity. The pigmentary changes are reversible, but the more slowly developing structural changes in the cornea may progress.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of exposure conditions providing evidence of prolonged or repeated exposure to benzoquinone;
- and if available:
 - workplace air monitoring.

Minimum duration of exposure: Two years.

Maximum latent period: One year.

Aromatic amines

Definition of causal agent

Aromatic amines are chemical compounds derived from aromatic hydrocarbons by the replacement of at least one hydrogen atom by an amino group (-NH₂).

Most common compounds: aniline, aminophenol, 4-aminodiphenyl, toluidine, 4,4-diaminodiphenylmethane (MDA), benzidine, phenylenediamine.

Main occupational uses and sources of exposure:

Synthesis of dyes and pigments; used as intermediates in the manufacture of isocyanates; accelerators and anti-oxidants in the rubber industry; pharmaceutical industry. The production and use of the following aromatic amines have been banned in the EU, according to Council Directive 88/364/EEC: 2-naphthylamine, 4-aminobiphenyl, benzidine and 4-nitrodiphenyl and their salts.

Toxic effects

Aromatic amines do not form a homogeneous group; despite their polymorphous clinical nature the effects can be divided into the following categories:

1. Local effects

Irritant effects

Aromatic amines can irritate the skin, eyes and upper respiratory tract.

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

Immunoallergic effects

Some aromatic amines induce hypersensitivity in the skin and respiratory tract, e.g. para (meta) phenylenediamine, nitroanilines.

See document on occupationally caused allergic contact dermatoses.

See document on occupationally caused asthma.

2. Systemic effects

Acute

Haematological disorders

Methaemoglobinaemia

cyanosis: methaemoglobinaemia > 10%,

hypoxia: methaemoglobinaemia > 20 to 25%,

more serious cases: low blood pressure, headache, disturbed mental capacity, disorders of the central nervous system.

Haemolytic anaemia

presence of Heinz bodies in red cells.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of repeated acute or intense exposure to aromatic amines known to have a toxic effect on the red corpuscles, such as: phenyl hydroxylamine, p-nitroaniline, aniline (taking into account the possibility of absorption via the skin),
- and, if available:
 - biological monitoring
 - workplace air monitoring.

Minimum duration of exposure: From a few minutes to a few hours according to the intensity of exposure.

Maximum latent period: Four days.

Chronic

Toxic hepatitis

Most occupational over-exposures lead to transient liver function difficulties. Disorders of the liver ranging from reversible functional disorders to severe atrophy. Jaundice occurred in cases of ingestion of MDA.

Cancer of the bladder

There is a risk of cancer of the bladder after prolonged exposure to certain aromatic amines. A link has been established with 2-naphthylamine, 4-aminodiphenyl, benzidine, o-toluidine.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged/repeated exposure to the above mentioned aromatic amines (taking into account the possibility of absorption via the skin),
- and, if available:
 - biological monitoring
 - workplace air monitoring.

Minimum duration of exposure: One year.

Minimum induction period: 10 years.

See document on occupationally caused cancers.

Aliphatic amines and their halogenated derivatives

Definition of causal agent

Aliphatic amines are derivatives of ammonia in which one or more hydrogen atoms are replaced by one, two, or three alkyl or alkanol radicals. The more commonly used amines are gases or fairly volatile liquids.

For example: Monoamines: I methylamine
 II dimethylamine, diethylamine
 III trimethylamine, triethylamine

Polyamines: diamine
 ethylenediamine, tetra-hexamethylene diamine
 triamine
 diethylenetriamine

Alkanolamine: ethanolamine
 triethanolamine, dimethylethanolamine

Halogenated derivatives: chloramine

Main occupational uses and sources of exposure:

Chemical intermediates in the synthesis of pharmaceutical products, pigments, ion exchange resins, emulsifiers and detergents used in the plastics industry (catalysers, hardeners) and textiles, leather and photography industries. Several amines (ethanolamines) are used in lubricating oils, or as solvents. Some types of flux in welding rods contain aliphatic amines.

Toxic effects

1. Allergic

Allergic contact dermatitis

Main allergenic substances: ethylenediamine, tetra-hexamethylenediamine, chloramine (urticaria).

See document on occupationally caused allergic contact dermatitoses.

Asthma

Main allergenic substances: dimethylethanolamine, ethylenediamine, diethylenetriamine.

See document on occupationally caused asthma.

Allergic conjunctivitis and rhinitis

Main allergenic substances: see above.

See document on occupationally caused rhinitis and conjunctivitis.

2. Irritant and corrosive effects

Aliphatic amines are bases and form strongly alkaline solutions. They are (in gas, liquid or vapour form) highly irritant for the skin and mucous membranes.

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

Corneal oedema

Aliphatic amines may cause corneal oedema with vesicles which produce a visual impression of fog or 'halos' around lights.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by anamnesis and clinical examination showing evidence of irritation to the eyes and exposure to aliphatic amines.

Minimum duration of exposure: Brief.

Maximum latent period: 48 hours.

Nitrated derivatives of aromatic hydrocarbons

Definition of causal agent

The term 'aromatic nitrocompounds' covers a group of compounds in which at least one hydrogen atom of the benzene ring has been replaced by a nitro-group (NO₂).

Some of them, like the nitrated derivatives of phenol, have been considered in a separate document.

Only the other most widely used compounds are considered here.

Nitro-, dinitrobenzene: one/two hydrogen atoms of the benzene ring have been replaced by one/two nitro-groups.

Dinitrobenzene exists in three isomers: ortho-meta-, para- Dinitro-, trinitrotoluene: two/three hydrogen atoms of the toluene ring have been replaced by two/three NO₂ groups. The main constituents of technical dinitrotoluene (DNT) are 2,4-DNT and 2,6-DNT.

Main occupational uses and sources of exposure:

They are used as solvents, in the production of dyes, pigments, explosives, cosmetics, pesticides, plastics and pharmaceuticals. They are also used in the chemical, textile and paper industries and in chemical laboratories.

Nitrobenzene: used in the production of aniline; as a solvent for some paints; in the manufacture of chemical products; in shoes and floor polishes; and in leather dressings. Dinitrobenzene: mainly used in the synthesis of dyestuffs, explosives and celluloid production.

Dinitrotoluene: mainly used in the synthesis of organic compounds and dyes and in explosives production.

T-nitrotoluene: mainly used as an explosive.

4-nitrodiphenyl: This compound has been banned from production and use in the European Union according to Council Directive 88/364/EEC.

Toxic effects

Nitrobenzene

1. Local effects

Irritant effects

Nitrobenzene can be irritant to the skin and mucous membranes.

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

Allergic contact dermatitis

Nitrobenzene may produce allergic dermatitis, this is nevertheless uncommon.

See document on occupationally caused allergic contact dermatoses.

2. Systemic effects

Acute

Haematological disorders

— Methaemoglobinaemia

cyanosis at methaemoglobin levels > 10%,

hypoxia at methaemoglobin levels > 20 to 25%,

at a later stage: hypotension, headache, nausea, impairment of mental ability, central nervous system impairment.

— Haemolytic anaemia presence of Heinz bodies in red cells.

Exposure criteria:

Minimum intensity of exposure:

occupational exposure confirmed, and if possible assessed, by:

— the anamnesis and study of working conditions showing evidence of acute or intense repeated exposure to this substance. (the possibility of skin absorption should be taken into account)

— and, if available:

- biological monitoring
dose-dependent levels of methaemoglobin
- workplace air monitoring.

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

Maximum latent period: Four days.

Dinitrobenzene

1. Local effects

Irritant effects

Dinitrobenzene can be irritant to the skin and respiratory tract.

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

2. Systemic effects

Acute

Haematological disorders

— Methaemoglobinemia

cyanosis at methaemoglobin levels > 10%,

hypoxia at methaemoglobin levels > 20 to 25%,

at a later stage: hypotension, headache, nausea, impairment of mental ability, central nervous system impairment.

— Haemolytic anaemia presence of Heinz bodies in red cells.

Exposure criteria:

Minimum intensity of exposure:

occupational exposure confirmed, and if possible assessed, by:

— the anamnesis and study of working conditions showing evidence of acute or intense repeated exposure to this substance. (the possibility of skin absorption should be taken into account)

— and, if available:

- biological monitoring
dose-dependent levels of methaemoglobin.
- workplace air monitoring.

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

Maximum latent period: Four days.

Dinitrotoluene

1. Local effects

Irritant effects

Local irritative effects are uncommon.

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

2. Systemic effects

Acute

Haematological disorders

— **Methaemoglobinemia**

cyanosis at methaemoglobin levels > 10%,

hypoxia at methaemoglobin levels > 20 to 25%,

at a later stage: hypotension, headache, nausea, impairment of mental ability, central nervous system impairment.

Exposure criteria:

Minimum intensity of exposure:

occupational exposure confirmed, and if possible assessed, by:

- anamnesis and study of the working conditions showing evidence of acute or intense repeated exposure to this substance. (the possibility of skin absorption should be taken into account)
- and, if available:
 - biological monitoring
dose-dependent levels of methaemoglobin.
 - workplace air monitoring.

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

Maximum latent period: Four days.

Trinitrotoluene (TNT)

1. Local effects

Irritant effects

Trinitrotoluene may be irritant to the mucous membranes: eyes, nose, throat.

Acute dermatitis is uncommon, however prolonged or repeated exposure may cause a dermatitis characterized by papular eruption, oedema and desquamation. Sometimes orange staining of the hands arms and face occurs.

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

Allergic contact dermatitis

Trinitrotoluene may cause allergic contact dermatitis. This is however rare.
See document on occupationally caused allergic contact dermatoses.

2. Systemic effects

Acute

Haematological disorders

— Methaemoglobinemia

cyanosis at methaemoglobin levels > 10%,

hypoxia at methaemoglobin levels > 20 to 25%,

at a later stage: hypotension, headache, nausea, impairment of mental ability, central nervous system impairment.

Acute hepatitis

Cases of jaundice have been reported in those exposed to large amounts of trinitrotoluene. Deaths from toxic hepatitis have occurred.

Exposure criteria:

Minimum intensity of exposure:

occupational exposure confirmed, and if possible assessed, by:

— anamnesis and study of working conditions showing evidence of acute exposure a repeated exposure to TNT. The possibility of skin absorption should be taken into account

— and, if available:

- workplace air monitoring.

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

Maximum latent period: Four days.

Acute hepatitis: seven days

Chronic

Aplastic anaemia

Aplastic anaemia with purpura haemorrhages have been reported in workers exposed to TNT in munitions plants.

Minimum intensity of exposure:

occupational exposure confirmed, and if possible assessed, by:

— anamnesis and study of working conditions showing evidence of acute exposure a repeated exposure to TNT. The possibility of skin absorption should be taken into account

— and, if available:

- workplace air monitoring.

Minimum duration of exposure: A few months.

Maximum latent period: Six months.

4-Nitro diphenal

See document on aromatic amines.

Nitro derivatives of phenols and the derivatives of hydroxybenzotrile

Definition of causal agent

These substances are dinitro-derivatives of phenol (dinitrophenol, dinitro orthocresol, dinoseb and their salts) and the halogenated derivatives of hydroxybenzotrile (ioxynil, bromoxynil). All trigger oxidative phosphorylation reactions and this explains their systemic effects.

Main occupational uses and sources of exposure:

Mainly used as herbicides.

Toxic effects

1. Local effects

Irritant effects

The substances irritate the skin and ocular and respiratory mucous membranes.

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

2. Systemic effects

Acute effect

Hyperthermia with profuse sweating, rapid weight loss.

Subacute effect

Gastrointestinal symptoms:

abdominal pains, vomiting, diarrhoea and in some cases toxic hepatitis.

Exposure criteria:

Minimum intensity of exposure: Severe occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions showing significant exposure to these substances

Possibility of skin absorption.

In certain cases: yellowing of the skin.

— and, if available:

● biological monitoring.

identification of the substance or its metabolites in biological blood and urine.

● workplace air monitoring.

Minimum duration of exposure: A few minutes to a few hours, depending on intensity of exposure.

Maximum latent period:

Acute effects: Two days

Subacute effects: Seven days.

Antimony and its inorganic compounds (except stibine)

Definition of causal agent

Antimony in crystalline form is a silver-white element. It exists in both inorganic and organic complexes. Included as inorganic compounds are: antimony tri-pentoxide, antimony tri-pentasulfide, antimony trichloride, antimony potassium tartrate, sodium antimony dimercaptosuccinate.

Main occupational uses and sources of exposure:

Antimony extraction and refining; alloys (lead, copper, tin); electronic, textile, glass, ceramic industry (pigment, dye); rubber industry; matches.

Some derivatives are used in the treatment of parasitic diseases.

Toxic effects

Irritant effects

Antimony and its inorganic compounds are irritating to the skin, eyes and respiratory tract. Intense exposure to vapours may induce acute pulmonary oedema.

Skin contact with antimony or antimony salts can cause papular and pustular eruptions. These eruptions are transient and mainly affect skin areas exposed to heat and those where sweating occurs.

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

Stibiosis

Long-term exposure to antimony dust may induce a benign (overload) pneumoconiosis which is often asymptomatic and in this case diagnosed by a Chest X-ray. Lung function is normal.

Exposure criteria:

Minimum duration of exposure: Occupational exposure confirmed, and if possible assessed, by:

- anamnesis and study of the working conditions showing evidence of prolonged/repeated exposure to antimony dust;
- and, if available:
 - workplace air monitoring:
 - guide value:
 - Sb atmospheric concentration well above 0.5 mg/m³.

Minimum duration of exposure: Six months.

Maximum latent period: None.

Dithiocarbamates

Definition of causal agent

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

Main occupational uses and sources of exposure:

They are mainly used in agriculture as insecticides, herbicides and fungicides. They are also used as pesticides in industrial and other commercial applications, and in the manufacture of household goods. Some dithiocarbamates are used in the public health field for vector control.

Local toxic effects

Irritant effects

Dithiocarbamates may cause slight skin irritation.

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

Allergic effect

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

See document on occupationally caused allergic contact dermatoses.

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/m³ 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 prostheses.

Toxic effects

Irritant effects

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

See document 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 document on occupationally caused allergic contact dermatoses.

— Allergic rhinitis and conjunctivitis

See document occupationally caused allergic rhinitis and conjunctivitis.

— Asthma

See document on occupationally caused asthma.

Antimony hydride (stibine)

Definition of causal agent

Stibine is a colourless gas.

Main occupational uses and sources of exposure:

Stibine is formed when nascent hydrogen comes into contact with metallic antimony, when some antimony compounds come into contact with acid or in the case of electrolytic processing (as when charging a battery).

Stibine (antimony hydride) is used as a fumigating agent.

Toxic effects

Acute systemic effects

Haemolytic syndrome

Headache, asthenia, dizziness, gastro-intestinal symptoms, cardiovascular effects, jaundice, acute renal failure.

Exposure criteria:

Minimum duration of exposure: Occupational exposure confirmed, and if possible assessed, by:

- anamnesis and study of the working conditions showing evidence of acute exposure to stibine (SbH_3),
- and, if available:
 - workplace air monitoring.

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

Maximum latent period: 48 hours.

Organic acids

Definition of causal agent

Carboxylic acids are organic acids with the general formula R-COOH.

Carboxylic acid molecules are polar, and, like alcohol molecules, can form hydrogen bonds with each other and with other kinds of molecules.

Aliphatic carboxylic acids

The aliphatic monocarboxylic acids show the same solubility behaviour as the alcohols: the first four in the series (see table below) are miscible with water, the five-carbon acid is partly soluble, and the higher acids are virtually insoluble in water. Because of the wide range of uses, the differing circumstances of isolation and, frequently, the complexity of structures. Many organic acids are described by a variety of names. Unsaturated carboxylic acids also behave like alkenes and alkynes, i.e. they show polymerization. Dicarboxylic acids are all solids.

Saturated as well as unsaturated aliphatic monocarboxylic acids are used in a variety of applications. Many are employed in the production of synthetic fibre materials, resins, plastic and dyestuffs. A number of the acids are important chemical intermediates or solvents and are used in cosmetics or food applications.

Formic acid is used as a reducing agent for wool, dyeing and decalcifying, tanning, depilation and treatment of hides, latex coagulation, regeneration of old rubber, electroplating, animal food additive, food preservatives and flavour adjunct, brewing antiseptic, and as a glue in aircraft manufacture.

Acetic acid is used in synthetic fibre production, cellulose acetate, acetate rayon, plastics, printing, food preserving, pharmaceuticals, and photography.

Industrial use of unsaturated monocarboxylic acids is mainly for polymeric materials, as chemical preservatives and as soap and food constituents.

Oxalic acid (a dicarboxylic acid) is used for textile finishing, stripping, cleaning, calico printing, dyeing, paint, varnish, rust removal, equipment cleaning, wood cleaning, dye manufacturing, paper, ceramics, photography, and rubber industries.

Industrial uses of unsaturated polycarboxylic acids are in resin manufacture, edible preservatives, and mordants in dyeing. Several members of the group occur as normal constituents of human metabolism.

Aromatic carboxylic acids

Including the nitro- and halogen derivatives, the aromatic carboxylic group is one of the largest groups of industrial chemicals. However, the nitro- and halogen derivatives, and the aromatic esters will be dealt with elsewhere. Compounds are used for the synthesis of dyes, elastomers, medicine, pesticides and plastics.

Local effects

Aliphatic carboxylic acids

Exposure to short-chain carboxylic acids causes irritation of the eyes, skin and mucous membranes. The degree of irritation is largely influenced by the strength of the acid, its water solubility and its ability to penetrate the skin. Formic, acetic, oxalic, maleic, and malonic acid are irritants also in aqueous solution and may cause effects on the eyes, skin and mucous membranes.

Fumaric acid is a mild irritant on skin and membranes.

Acrylic, crotonic and methacrylic acids may possess some sensitization potential (see patch test).

See document on occupationally caused allergic contact dermatoses.

Aromatic carboxylic acids

α -naphthoic and β -naphthoic acids are moderate irritants to the skin; benzoic acid and p-tert-butylbenzoic acid are mild irritants to the skin.

Guide values:

- aliphatic saturated monocarboxylic acids: 25 mg/m³ for inhalation as formic acid,
- aliphatic saturated polycarboxylic acids: 1 mg/m³ for inhalation as oxalic acid.

See document on occupationally caused allergic contact dermatoses.

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

Table

Some common carboxylic acids and their synonyms

Common name	Synonym	Systematic name	Formula
Formic	Formylic Hydrogen carboxylic	Methanoic	HCOOH
Acetic	Ethylic Methanecarboxylic	Ethanoic	CH ₃ COOH
Propionic	Methylacetic Ethanecarboxylic	Propanoic	CH ₃ CH ₂ COOH
Butyric	Ethylacetic 1-Propanecarboxylic	Butanoic	CH ₃ (CH ₂) ₂ COOH
Oxalic	Ethanedionic	Ethanedioic	HOOC-COOH
Malonic	Carboxyacetic Dicarboxymethane	Propanedioic	HOOCCH ₂ -COOH
Acrylic	Acroleic Vinylformic	2-Propenoic	CH ₂ CH-COOH
Crotonic	3-Methylacrylic	(<i>trans</i>)-2-Butenoic	CH ₃ (CH) ₂ -COOH
Methacrylic	2-Methylene-propionic	2-Methyl-2-propionic	CH ₂ C(CH ₃)-COOH
Maleic	<i>cis</i> -1,2-Ethylene- dicarboxylic	(<i>cis</i>)-2-Butenedioic	HOOC-(CH ₂) ₂ -COOH
Fumaric	<i>trans</i> -1,2-Ethylene- dicarboxylic	(<i>trans</i>)-2-Butenedioic	HOOC-(CH ₂) ₂ -COOH
α -Naphthoic	α -Naphthalene- carboxylic	1-Naphthoic	1-C ₁₂ H ₁₁ -COOH
β -Naphthoic	p-Naphthalene- carboxylic	2-Naphthoic	2-C ₁₂ H ₁₁ -COOH
Benzoic P- <i>tert</i> -benzoic	Benzenecarboxylic	Benzoic 2- <i>tert</i> -Butylbenzoic	C ₆ H ₅ -COOH p-(CH ₃) ₃ C-COOH

Arsenic hydride (arsine)

Definition of causal agent

Arsine is a colourless gas which is heavier than air. It is formed when hydrogen comes into contact with trivalent arsenic.

Main occupational uses and sources of exposure:

Arsenic hydride is used in microelectronics, for example, or formed when nascent hydrogen comes into contact with arsenic impurities in metallurgy, (processing of arsenical minerals, preparation and use of metallic arsenides).

Toxic acute systemic effects

Haemolytic syndrome

Headaches, asthenia, dizziness,
gastro-intestinal disorders,
cardiovascular symptoms,
jaundice, acute renal failure.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of acute exposure to arsine;
- and, if available:
 - biological monitoring
 - workplace air monitoring.

Minimum duration of exposure: A few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 48 hours.

Coal-miners' pneumoconiosis

Definition of causal agent

Coal-miners' silicosis consists of chronic bilateral interstitial pulmonary fibrosis following the inhalation and incorporation of dust mixtures with a particle size $< 5 \mu\text{m}$ having a relatively small quartz content (including cristobalite and tridymite).

Synonyms: miners' silicosis, anthracosilicosis, coal-workers' pneumoconiosis.

Diagnostic criteria

- Chest X-ray: multiple, predominantly peripheral shadows in the apex and mid-zones of the lungs; these small rounded shadows are hazy and not clearly defined, with perinodular translucence. They increase in size during the course of the disease and can fuse with neighbouring nodules to form larger shadows (ILO classification: small opacities p, q, r; larger opacities A, B, C).
- Symptoms: in mild cases no symptoms initially. Later, coughing, shortness of breath, partially black pigmented sputum.
- Clinical signs: in mild cases no signs initially. Later, abnormal respiratory sounds upon auscultation; in advanced cases, dyspnoea, hypoxemia, signs of right heart failure.
- Lung function: initially restrictive ventilation disorders, frequently obstructive ventilation syndrome and increased residual volume, diffusion disorders, exertion-related reduction in oxygen absorption and in oxygen partial pressure.
- Complications: chronic non-specific respiratory syndrome, pulmonary emphysema, cor pulmonale, silicotuberculosis, very occasionally Caplan's syndrome.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions showing evidence of repeated/prolonged working underground with hard coal and rock,
- and, if available:
 - workplace air monitoring:
guide value:
4 mg/m³ of quartz-containing respirable dust.

Minimum duration of exposure: Five years, depending on intensity of exposure.

Maximum latent period: None.

Chronic toxic encephalopathy (CTE) caused by organic solvents

Definition

Chronic toxic encephalopathy caused by solvents is characterized by a global mental impairment including changes in:

- (i) cognitive functions, memory and concentration,
- (ii) personality,
- (iii) motivation, vigilance and energy.

The clinical picture may be described as a psycho-organic syndrome or a mild degree of dementia, i.e. a clinical syndrome of premature ageing of higher cortical functions.

Main occupational sources of exposure

In the classification of Raleigh four groups are defined according to the severity of symptoms, type 1 being the least severe. In this document, a description is given of the diagnostic criteria of the pathological entity which corresponding to the Raleigh groups Type 2A and 2B. Some cases of Type 3 may be included, but these are few.

Chronic toxic encephalopathy caused by organic solvents was often observed during the 1970s and 1980s in Scandinavia. A considerable number of house painters were diagnosed after an exposure period of 10 years or more. The ambient air concentration of solvents was high and working hours were often long during a period of construction (the building boom of the 1950s and 1960s).

Diagnostic criteria

Signs and symptoms: the history must disclose significant subjective complaints concerning several of the following functional areas:

impairment of memory, concentration (decreased concentration, distractability) and other intellectual activities, decreased initiative (lack of initiative, apathy), loss of leisure-time interests, decreased energy level, increased sleep demands (abnormal fatigue), changes in mood (depressive mood), increased nervousness, emotional lability and irritability.

It is usually found that the gravity of symptoms are slightly improved after cessation of exposure.

Neuropsychological tests performance: the neuropsychological test battery should include:

tests of verbal and visual memory, concentration, speed, visual analysis and construction, and abstraction ability, known to be sensitive to the effects of diffuse cerebral hemisphere dysfunction. Furthermore, the test battery should include tests that reflect primary intellectual ability: it should be evaluated from performance in these tests together with anamnestic information on education and other information on previous intellectual level of functioning.

Intellectual impairment may be assumed if the performance in the sensitive tests is generally lower than the lower 5% distribution level of performance for a normal population of similar age and primary intellectual ability.

Neurological examination: usually normal. Mild signs of dyscoordination and polyneuropathy may be present. Cerebral atrophy and EEG changes may or may not be present.

Differential diagnosis: other causes of encephalopathy should be excluded by means of history (development of symptoms, alcohol anamnesis, cerebral concussions, other exogenous factors), a general physical and neurological examination.

A diagnosis should be established as a result of an investigation by a neurologist and a clinical psychologist.

Exposure criteria

Minimum intensity of exposure:

- anamnesis of significant exposure to organic solvents,
- notice should be taken of skin absorption and of the fact that exposures may often be to mixtures of solvents,
- and if available:
 - biological monitoring
 - workplace air monitoring.

Present information suggests that levels of exposure substantially above those given below, taking place over a period of 10 years, are required to induce chronic toxic encephalopathy. These concentrations refer to an eight-hour working day:

toluene:	375 mg/m ³ (100 ppm)
xylene:	435 mg/m ³ (100 ppm)
styrene:	210 mg/m ³ (50 ppm)
pentane:	1 500 mg/m ³ (500 ppm)
white spirit:	600 mg/m ³ (100 ppm)
1,1,2,trichloroethane:	45 mg/m ³ (10 ppm).

This list is non-exhaustive and other solvents may need to be considered.

Minimum duration of exposure: 10 years; this could be less in case of exposure to particularly high concentrations.

Maximum latent period before onset of the disease: Initial symptoms of mental impairment should be present within one year after cessation of exposure.

Induction period: Does not apply.

Naphthol and its chlorinated derivatives

Definition of causal agent

Naphthols are alpha and beta isomers of hydroxynaphthalene. They take the form of white volatile crystals which give off a vapour with a faint 'mothball' odour.

Naphthols are extracted from coal tar or are prepared from naphthalene. They are widely used in the manufacture of dyes, rubber accelerators and perfumes, and in the pharmaceuticals industry.

Local toxic effects

Irritant effects

Naphthol irritates the skin, eyes and respiratory tract. In some cases dermatitis is accompanied by persistent hyperpigmentation.

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

Nickel carbonyl

Definition of causal agent

Nickel carbonyl, Ni (CO)₄ is a volatile liquid, easily decomposing into nickel and CO.

Main occupational uses and sources of exposure:

Intermediate product of nickel refining.

Toxic effects

Acute inhalation

First phase: immediate

Non-specific gastro-intestinal and neurological symptoms: nausea, vomiting, headache, dizziness, vertigo, profound weakness, etc.

Second phase: delayed

Insidious, signs and symptoms are delayed (12 to 36 hours), cough, hyperpnoea, cyanosis, tachycardia, chemical pneumonitis, acute pulmonary oedema, risk of respiratory failure, circulatory collapse, cerebral oedema resulting in death in five to 15 days. Possibility of the development of chronic respiratory insufficiency (sequelae).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of intense exposure to nickel carbonyl;
- and if available:
 - biological monitoring: nickel in urine (qualitative);
 - workplace air monitoring.

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 48 hours.

Skin diseases and skin cancers caused by soot, tar, bitumen, pitch, anthracene or compounds thereof, mineral and other oils, crude paraffin, carbazole or compounds thereof, by-products of the distillation of coal

Definition of causal agents

The incidence of skin cancer is increasing in the general population. This is probably due to increased exposure to the sun. Nevertheless, squamous cell carcinoma is also causally related to occupational exposure to fossil fuel derivatives containing polynuclear aromatics. In practical terms, workers are rarely exposed to only a single group of such compounds and virtually never to a single polynuclear aromatic compound. Thus the epidemiological evidence for a human carcinogenic effect varies from firm (soot, tar, pitch, mineral oils), through probable (bitumen and bitumen-derived products), to inadequate for the purpose of evaluation (anthracene and carbazole). However, both anthracene and carbazole are major components of the total amount of polynuclear aromatic compounds in the environment, with human exposure occurring primarily through smoking tobacco and inhaling polluted air. Paraffins are aliphatic hydrocarbons, and one of the main components of crude oil.

Toxic effects

Local effects

Irritant effects

Some of these substances can cause irritation of the skin.

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

Allergic contact dermatitis

Some of these substances (anthracene, phenanthrene, carbazole) can cause allergic contact dermatitis.

See document on occupationally caused allergic dermatoses.

Acne

Indistinguishable clinically from the acne of teenage years. The lesions affect the exposed areas or where the oils can saturate clothing; generally the dorsal surfaces of the hands, extensor surfaces of the arms and the anterior surfaces of the thighs.

The condition is not as persistent as chloracne and cyst formation is not a feature.

Occupational exposure to oils can aggravate idiopathic acne or cause comedones, follicular plugging and even folliculitis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of acute or repeated/prolonged exposure of skin to cutting oils,

Minimum duration of exposure: A few weeks to a few months depending on the intensity of exposure.

Maximum latent period: Six months.

Cancer

Generally chronic dermatitis, acne, keratosis, papillomata precede malignancy with ulceration, local spread and, eventually, distant metastases.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of the working conditions showing evidence of repeated/prolonged exposure to the abovementioned substances.

Minimum duration of exposure: Six months.

Minimum free interval: Usually 20 years, but five years in some of the cases described (workers exposed to tar and sunshine).

Attention is drawn to the multicausality of this pathology.

See document on occupationally caused cancers.

Occupationally caused cancers

Definition of the causal agent

Cancer is one of the most serious outcomes of workplace exposure. There are a number of well-recognized occupational carcinogens and an even longer list where the agent or individual process is suspected of causing malignant disease in working populations. Substances which meet the requirements to be classified according to the criteria in Annex VI of Council Directive 67/548/EEC as carcinogenic, may be identified by the two risk phrases on the container as follows: R 45 can cause cancer, R 49 may cause cancer by inhalation. However, as this list can never be exhaustive, other chemicals may be considered to be carcinogenic if they satisfy the criteria in section (V) below. Some physical and biological agents as well as some production processes may cause cancer.

The criteria for identifying the occupational nature of an individual case of cancer are often more difficult to define than for many non-malignant occupational diseases because:

- (i) the cancer is often caused by non-occupational factors such as lifestyle, diet or genetic predisposition;
- (ii) the occupational cancer has no specific histopathological features to distinguish it from non-occupational cancer;
- (iii) there may be interaction between occupational and non-occupational factors — such as cigarette smoking and asbestos exposure — in the pathogenesis of lung cancer;
- (iv) it is often difficult to determine whether an occupational factor initiates and/or promotes cancer;
- (v) Epidemiological studies carry the greatest weight in identifying a carcinogenic agent. Other evidence may be taken into account namely:
 - (a) evidence of animal carcinogenicity in one (or preferably more than one) species,
 - (b) evidence of laboratory tests showing mutagenicity,
 - (c) chemical similarity to a known carcinogen,
 - (d) reports of series of patients — case reports as a basis for further investigation.

None the less, some general exposure criteria can be formulated for individuals known to have a relevant malignant disease which are as follows:

Minimum intensity of exposure: Occupational exposure to a R45 agent or other relevant agent/process assessed by:

- the anamnesis and a study of the working conditions showing evidence of significant prolonged exposure to the agent or process. However, such evidence may be difficult to acquire; thus the advice of specialists with knowledge of these working conditions is often necessary;
- and possibly, if available, evidence of known absorption of that agent.

Minimum duration of exposure: Usually knowledged to be from five to 20 years depending on the type of cancer, the agent and the level of exposure.

Minimum induction period: From 10 to 40 years depending on the type of cancer, the agent and the level of exposure.

Silicosis

Definition

Silicosis is bilateral pulmonary fibrosis caused by inhalation and deposition of dust containing silicon dioxide (SiO_2) in crystalline forms (quartz, cristobalite and tridymite).

Main occupational uses and sources of exposure:

Underground workings; foundries; porcelain factories; repair and demolition of blast furnaces; glassmaking; sand crushing; sand blasting; sandstone milling; manufacture of abrasive powders; carborundum manufacture; quartz, sandstone, silex and slate quarries.

Manifestations

1. Chronic silicosis

Simple silicosis

Complicated silicosis (progressive massive fibrosis — PMF)

Diagnostic criteria:

Chest X-ray: in simple silicosis, multiple and discreet rounded opacities and reticular patterns usually seen in the upper lung fields. With advancing disease the size and numbers of the opacities increase and may coalesce to conglomerate masses: this is progressive massive fibrosis.

Symptoms: in simple silicosis, few or no symptoms. A dry cough, sputum production and symptoms of pulmonary insufficiency develop with advancing disease.

Clinical signs: initially, in simple silicosis, few or no signs. In advanced stages, signs of obstructive lung disease or fibrosis may develop, in some cases leading to right cardiac insufficiency.

Lung function: initially, in simple silicosis, little or no change in lung function. In advanced stages, restrictive and/or obstructive impairment may develop.

Complications: risk of tuberculosis is increased. A positive rheumatoid factor, with or without rheumatoid arthritis, may predispose to increasing silicotic fibrosis and development of Caplan's nodules. Chronic bronchitis.

Recognition criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions showing evidence of significant exposure to silicon dioxide are normally sufficient, provided chest X-rays show evidence of typical silicosis;

— and, if available:

- workplace air monitoring:

guide values:

> 0.05 mg/m^3 (respirable dusts) if duration of exposure is less than 20 years

> 0.10 mg/m^3 (respirable dusts) if duration of exposure is less than 10 years.

Minimum duration of exposure: Five years

Maximum latent period: A maximum period cannot be fixed, the symptoms being a function of the cumulative dose.

2. Accelerated silicosis

Diagnostic criteria: Simple nodular silicosis which rapidly develops into progressive massive fibrosis with restrictive lung function impairment and reduced gas transfer. Chest X-ray may show fine nodular or nodulo-reticular opacities.

Recognition criteria:

Minimum duration of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions showing evidence of exposure to moderate to high concentrations of free silica in dust;
- and, if available:
 - workplace air monitoring:
guide values:
> 40% free silica in respirable dusts.

Minimum duration of exposure: Two years.

Maximum latent period: Two years.

3. Acute silicosis (alveolar silico-proteinosis)

Diagnostic criteria: Rapidly developing dyspnea, coughing, asthenia, weight loss and progressive respiratory insufficiency. Chest X-ray shows an alveolar filling pattern. Lung function tests show restrictive impairment with reduced gas transfer.

Recognition criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions showing evidence of exposure to high concentrations of free silica in dust;
- and, if available:
 - workplace air monitoring:
guide values:
> 80% free silica in respirable dusts.

Minimum duration of exposure: Six months.

Maximum latent period: One year.

Asbestos

Definition of causal agent

Asbestos is a fibrous silicate which exists in various forms:

Serpentines: chrysotile;

Amphiboles: crocidolite, amosite, actinolite, tremolite, anthophyllite.

These different fibres are all capable of causing the diseases mentioned below, although their biological reactivity is different.

Main occupational uses and sources of exposure:

Extraction and handling of asbestos-bearing rock; carding, spinning and weaving the fibres; manufacture of asbestos cement; lagging for boilers; the construction industry; manufacture and maintenance of vehicle brakes.

Adverse effects

Asbestos warts

Pronounced thickening and hyperkeratosis on the dorsal and palmar surfaces of the hands and the forearms caused by minute asbestos fibres penetrating the skin. A cure can be effected by removing the fibres.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis, evidence of which is provided by the subcutaneous presence of asbestos fibres. (A single contact is enough for fibres to penetrate the skin.)

Asbestosis

Bilateral, interstitial, diffuse pulmonary fibrosis.

Diagnostic criteria:

The following symptoms and signs give strong evidence of the presence of asbestosis and indicate its severity:

- (i) symptoms and signs: breathlessness; persistent bilateral, late inspiratory basal crepitations; clubbing;
- (ii) chest X-ray: diffuse interstitial fibrosis mainly in the lower lung fields;
- (iii) lung function tests: restrictive syndrome with reduction in diffusion capacity.

These signs do not necessarily appear simultaneously and the order in which the abnormalities occur may differ from one subject to another.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to asbestos,

-
- the presence of asbestos bodies or fibres (in sputum or fluid from broncho-alveolar lavage) does not prove the existence of an asbestos-related disease but, in cases of doubt, is confirmation of exposure to asbestos,
 - and, the measurement of asbestos in the air at the place of work showing:
 - evidence of occupational exposure exceeding 1 fibre per cm³ for asbestos fibres other than crocidolite and 0.5 fibres per cm³ for crocidolite.

Minimum duration of exposure: Five years.

Maximum latent period: Not applicable.

Benign pleural pathology

(a) Pleural plaques

Hyaline parietal pleural plaques

Bilateral, localized thickening (fibrosis) of the pleura, often partially calcified.

Their presence does not imply the existence of asbestosis. Often they are only an objective sign of earlier inhalation of asbestos.

Visceral pleural plaques.

These can lead to a reduction in lung function.

(b) Asbestos pleurisy

Diffuse exudative pleural reaction, with or without fibrosis, asymptomatic or associated with symptoms. Tends to be chronic.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to asbestos,
- the presence of asbestos bodies or fibres (in sputum or fluid from broncho-alveolar lavage) does not prove the existence of an asbestos-related disease but, in case of doubt, is confirmation of exposure to asbestos.

Minimum duration of exposure: Usually a few years, but in some cases can be very short (six months).

Maximum latent period: Not applicable.

Minimum induction period: Usually more than 10 years.

Malignant pathology

(a) Diffuse malignant mesothelioma

Primary malignant tumour of the pleura

Primary malignant tumour of the peritonium

(b) Primary bronchial cancer

Asbestos causes bronchogenic carcinoma. In the presence of tobacco smoking, the risk is increased.

Exposure criteria:

Minimum intensity of exposure: Mesothelioma: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of definite exposure to asbestos.

This exposure may be confirmed by the presence of asbestos bodies or fibres in sputum, fluid from broncho-alveolar lavage or lung biopsy. The presence of asbestos bodies or fibres does not prove the existence of an asbestos-related disease but, in case of doubt, is confirmation of exposure to asbestos.

Bronchial cancer: Given the many causes of bronchial cancer (smoking being the most frequent cause), in order to determine whether each individual case can be recognized as an occupational disease, it must be examined in depth on the basis of strictly defined scientific criteria taking into account other possible causes.

This evaluation takes into account:

- the presence of other asbestos-related medical manifestations (pleural plaques, asbestosis, etc.)
- the presence of asbestos bodies or fibres in sputum, fluid from the broncho-alveolar lavage or lung biopsy. These manifestations, as well as the presence of asbestos bodies or fibres, do not prove the existence of an asbestos-related disease but, in case of doubt, is a confirmation of exposure to asbestos.

Minimum duration of exposure: Usually a few years.

Minimum induction period:

mesothelioma: usually more than 25 years,

bronchial cancer: usually more than 15 years.

See document on occupationally caused cancers.

Pneumoconiosis caused by silicates

Definition of causal agent

Silicates include a variety of substances such as orthosilicic acid salts and their condensation products, as contained in various mixtures of substances, such as talc (steatite, soap-stone), mica (muscovite, phlogopite), kaolin (kaolinite), diatomaceous earth, nepheline, sillimanite, pyrophyllite or asbestos-containing dusts, cement dusts. Eronite and zeolites are silicates which can cause pneumoconiosis, but are not usually encountered in an occupational setting.

Main occupational uses and sources of exposure:

Extraction, drilling, grinding, polishing, crushing of materials containing silicates.

Toxic effects

Talcosis

Pneumoconiosis caused by silicates consists of bilateral interstitial pulmonary fibrosis. However, pulmonary disease resulting from exposure to pure talc is rare. Talc contaminated with silica or asbestos may induce respiratory disease related to these contaminants. (see documents on silicosis and asbestos).

Long-term exposure to (asbestos-free) cement dust rarely causes benign pneumoconiosis and chronic bronchial diseases.

Diagnostic criteria:

- Chest X-ray: striated cordlike opacity in both mid-zones and lower areas, as well as pleural plaques; as the disease progresses, fairly large shadow formation in the mid-zones; in quartz/asbestos contamination, also nodules and interstitial and pleural changes.
- Symptoms: in mild cases, no symptoms initially. Shortness of breath, cough and sputum later.
- Clinical signs: in mild cases no symptoms initially, but later presence of crepitations upon auscultation. In advanced cases, dyspnea, hypoxemia, signs of right heart failure.
- Lung function: initially, restrictive ventilation disorders; later, obstructive syndrome and raising of the residual volume, diffusion disorders exertion-related reduction in oxygen absorption and oxygen partial pressure.
- Complications: chronic non-specific respiratory disease, pulmonary emphysema, cor pulmonale syndrome and, in the case of asbestos contamination, bronchial carcinoma and mesothelioma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and analysis of the working conditions showing evidence of prolonged/repeated exposure to talc during extraction and in industrial and, to a lesser extent, in cosmetic and pharmaceutical use,

— and, if available:

- workplace air monitoring:

guide values:

atmospheric concentration $> 2 \text{ mg/m}^3$ (inhalable dust) in asbestos fibre-free talc,
asbestos contaminated talc: see documents on asbestosis.

Minimum duration of exposure: Two years for pure talc.

Maximum latent period: None.

Inhalation of dusts and fibres from cotton, flax, hemp, jute and sisal

Definition of causal agent

Respirable fraction of dust from cotton (bracts, leaves, stems), flax (stems), hemp, jute and sisal.

Other plants may be responsible for triggering a byssinosis-like syndrome.

Main occupational uses and sources of exposure:

Work exposing workers to the inhalation of dusts and vegetable textile fibres: e.g. beating, carding, drawing, combing, spinning, winding and twisting.

Toxic effects

1. Local effect

Irritant effects

These vegetable dusts cause irritation to the mucous membranes.
See document on occupationally caused irritation of the skin and mucous membranes.

2. Systemic effects

Acute effects

These set in during the first day of exposure after an induction period of several hours. The effects include shivering, tightness of the chest, dyspnoea, fever and malaise. The symptoms disappear after one or two days. If re-exposure occurs after a period of no exposure, they reappear. There are few objective signs: rhonchi may be present on auscultation. Reduced pulmonary function occurs in the acute stage. There are no specific spirometric, radiological or serological signs.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of exposure to these vegetable dusts,
- and, if available:
 - workplace air monitoring:
 - guide value:
 - atmospheric concentration above 0.2 mg/m³ (total dusts).

Minimum duration of exposure: Several hours. Five hours exposure to a dust level of 0.2 mg/m³.

Maximum latent period: 48 hours.

Chronic effects

Chronic lung effect

Obstructive airway disease with late onset of moderate to severe dyspnoea, tightness of the chest, gradually increasing during the working week and over a period of years. Shivering and malaise, as described under acute effects, gradually decreases as the years pass.

Objective signs: reduction of the Forced expiratory volume in 1 second (FEV₁).

Severe cases display a decrease in Forced Vital Capacity (FCV).

There are few radiological signs.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to these vegetable dusts,
- and, if available:
 - workplace air monitoring:
guide values:
atmospheric concentration above 1.5 mg/m³ (total dusts),
symptoms may occur at lower dust concentrations if actual exposure has occurred for more than 20 years,
- Byssinosis: may be complicated by chronic bronchitis and emphysema. Other factors such as smoking should be taken into account.

Minimum duration of exposure: 10 years exposure to a dust level of 1.5 mg/m³.

Maximum latent period: Five years.

Graphite dust (natural and artificial)

Definition of causal agent

Graphite was earlier produced from natural mines and usually consisted of crystalline carbon and crystalline silicon. The crystalline silicon content was between 3.6 and 11%. Today, graphite is synthesized from carbon molecules only.

Main occupational uses and sources of exposure:

Graphite is used mainly in foundries and in the manufacture of lubricants, electrodes, refractory materials and car components.

Occupational exposure can occur during the production of graphite articles, ore extraction or the production of artificial graphite from coal or mineral oil.

Adverse effects

Pneumoconiosis

Chronic exposure to graphite causes progressive disabling pneumoconiosis. It is possible that this pneumoconiosis is caused only by natural graphite, although the involvement of artificial graphite in this disease cannot definitely be ruled out.

The disease continues to develop even after the worker has been removed from the source of exposure.

Diagnostic criteria:

- X-ray examination: pneumoconiosis pattern;
- biopsy (not mandatory): pigmentation, focal emphysema, fibrosis;
- sputum test: blackish colour, presence of graphite particles.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of exposure to graphite dust,
 - workplace air monitoring;
- guide values: atmospheric concentrations well above 10 mg/m³ for artificial graphite, 2.5 mg/m³ for the respirable fraction of natural graphite.

Minimum duration of exposure: Five years.

Maximum latent period: Five years.

Inhalation of barium dust

Definition of causal agent

Barium is a silvery white metal.

Insoluble compounds: only the toxicity of barium sulphate will be examined

Soluble compounds: mainly barium hydroxide $\text{Ba}(\text{OH})_2$, barium nitrate $\text{Ba}(\text{NO}_3)_2$ and barium chloride BaCl_2

Main occupational uses and sources of exposure:

Barium sulphate is used in the manufacture of radio-opaque materials and as a basis for the production of white pigments. Exposure can occur during extraction of the ore and during the subsequent phases of its industrial processing.

Soluble compounds: these are used in the manufacture of glass, vulcanization of synthetic rubber, pesticides, pigment production, in the foodstuffs industry and in the production of electronic components.

Toxic effects of insoluble compounds

Benign pneumoconiosis

Asymptomatic non-fibrosing pneumoconiosis, called baritosis, diagnosed through a chest X-ray revealing evidence of widespread, sometimes confluent radio-opaque nodules. Progressive reversibility of the radiological picture once exposure has been terminated.

No alteration of lung function.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of repeated or prolonged exposure to insoluble barium dust (particularly during extraction);
- and if available;
 - workplace air monitoring:
 - e.g. atmospheric concentration $> 10 \text{ mg/m}^3$
 - in the event of contamination by crystalline silica, the concentrations producing effects would be much lower (see document on silicosis).

Minimum duration of exposure: Five years.

Maximum latent period: Five years.

Toxic effects of soluble compounds

Irritant effects

The soluble compounds of barium cause irritation to the skin and mucous membranes.

Guide value:

atmospheric concentration well above 0.5 mg/m³.

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

Dusts of hard metals

Definition of causal agent

Hard metals are those used to make articles of hardness just less than that of diamond: e.g. sintered carbides of tungsten, titanium, tantalum, niobium, molybdenum, vanadium and metallic cobalt.

Main occupational uses and sources of exposure:

Occupational exposure may occur during production of metal-ceramic articles, tungsten carbide tools, diamond-edged cutting tools, grinding of metal tools, as well as working with cobalt steel, diamond polishing or decoration of ceramics.

Toxic effects

Asthma

Sometimes, the disease caused by hard metals may begin with asthma attacks. If exposure continues, a slow progressive pattern of obstructive airways disease develops.

See document on occupationally caused asthma.

Interstitial lung disease (hard metal disease)

Exposure to dusts of hard metals may give rise to non-specific pathology of the upper respiratory tract and interstitial fibrosis. Mixed obstructive and restrictive features characterized by asthma and interstitial lung disease are possible. Cobalt exposure may induce hypersensitivity pneumonitis.

Criteria of diagnosis:

- Chest X-ray: initially the pattern reticular; while more advanced cases show a diffuse micronodular pattern.
- Lung function tests: restrictive or mixed pattern, reduction of gas transfer factor obtained.
In some cases, additional evidence may be obtained from bronchoalveolar lavage or lung biopsy.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed and, if possible assessed, by:

- anamnesis and study of the working conditions showing evidence of repeated or prolonged exposure to high levels of hard metals dusts, particularly in excess of current permitted levels, e.g. cobalt dust and fumes ($> 0.05 \text{ mg/m}^3$).

Minimum duration of exposure: A few months.

Maximum latent period: None.

Organic compounds of tin

Definition of causal agent

Tin is a relatively light and very malleable white metal. The most toxic organic compounds are the trialkyltins, followed by the dialkyltins and monoalkyltins; the tetraalkyltins are metabolized to their trialkyltin homologues.

Main occupational uses and sources of exposure:

Organotin compounds are used in various branches of industry. Disubstituted and, to a certain extent, monosubstituted compounds are used in the plastics industry, trisubstituted compounds are mainly used as biocides, whereas the tetrasubstituted compounds serve as intermediates in the chemical industry.

Toxic effects

Irritant effect

The organic derivatives of tin cause irritation to the skin and mucous membranes.

They can cause erythema of the face.

Sub-acute exposure can result in erythematous dermatitis with pruritus and pustular eruption on the scalp.

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

Acute toxic encephalopathy

The symptoms are: headaches, dizziness, photophobia, weakness and flaccid paralysis of the limbs depending on the level of exposure.

Exposure criteria:

Maximum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of intense exposure to the organotin derivatives (take account of the possibility of cutaneous absorption);

— and, if available:

- biological monitoring: urinary excretion of inorganic tin (4 to 5 days after exposure) (qualitative)
- workplace air monitoring:

guide value:

exposure to an atmospheric organic tin concentration well above 0.2 mg/m³.

Minimum duration of exposure: From a few minutes to a few days depending on intensity of exposure.

Maximum latent period: One week.

Inorganic tin dusts and fumes

Definition of causal agent

Tin is a relatively light and very malleable white metal.

Main occupational uses and sources of exposure:

Occupational exposure to tin dust can occur in the mineral extracting industry as well as in the various phases of processing the metal. Exposure to tin fumes can also occur during fusion operations.

2. Adverse effects

Irritant effects

The fumes and dusts of inorganic tin can cause irritation to the eyes and upper respiratory tract. See document Occupationally caused irritation of the skin and mucous membranes.

Stannosis

Chronic exposure to the dusts and fumes of tin oxide can lead to benign pneumoconiosis, called 'stannosis'.

Diagnostic criteria:

- chest X-ray: diffuse nodular opacities with a mean diameter around three mm
- stability of X-ray picture after exposure has been interrupted
- no alterations of lung function

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of prolonged/repeated exposure to tin oxide dusts or fumes;
- and, if available:
 - workplace air monitoring.
Guide values: Atmospheric concentration > 2 µg/m³ inorganic tin

Minimum duration of exposure: Five years.

Maximum latent period: Five years.

Wood dust

Definition of causal agent

Dust from untreated or treated wood. In the case of allergies, certain species of wood. For diseases of the lower respiratory tract, respirable fraction only (aerodynamic diameter of 5 µm or less).

Main occupational uses and sources of exposure:

Handling, treatment and working of wood (sawing, milling, planing, sanding). Cabinet-making, joinery and workshops for production of wooden flooring material.

Toxic effects

Allergic contact dermatitis, contact urticaria

See document on occupationally caused allergic contact dermatoses.

Irritant contact dermatitis

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

Allergic rhinitis

See document on rhinitis and allergic conjunctivitis.

Asthma

See document on occupationally caused asthma.

Extrinsic allergic alveolitis

See document on occupationally caused hypersensitivity pneumonitis (extrinsic allergic alveolitis).

Nasal and sinonasal cancer

Exposure criteria:

Minimum intensity of exposure: Occupational exposure (hardwoods such as oak and beech and softwood e.g. pine) confirmed, if possible assessed, by:

— anamnesis and study of exposure conditions;

— and, if available:

- workplace air monitoring

guide value:

atmospheric concentration: > 1 mg/m³.

Minimum duration of exposure: 10 years.

Minimum induction period: 20 years.

Iron dust

Definition of causal agent

Iron dust or iron oxide fumes are usually found in conjunction with mining, steelmaking, iron or steel rolling, metal polishing, welding with bare electrodes on uncoated steel, and ochre pigment.

In the extractive industries, airborne dust is often contaminated with other chemical agents such as crystalline silica, carbon. Iron ores include haematite (Fe_2O_3), magnetite (Fe_3O_4), limonite ($\text{Fe}_2\text{O}_3 \cdot \text{H}_2\text{O}$) and siderite (FeCO_3).

Toxic effects

1. Local effects

Irritant effects

Exposure to large quantities of iron dust can cause irritation of the mucous membranes. See document on occupationally caused irritation of the skin and mucous membranes.

2. Systemic effects

Siderosis

Long-term exposure to iron dust may lead to a benign (overload) pneumoconiosis: siderosis.

Since there is absence of clinical symptoms and lung function impairment, siderosis is generally identifiable only through chest X-ray examination.

In case of co-exposure to crystalline silica, combined pneumoconiosis can occur; in which case the clinical picture mainly evolves into chronic bronchitis. Compared to pure silicosis, symptomatic sidero-silicosis is more likely to progress into cor pulmonale (in 10 to 15% of cases). In some cases, the pathological changes can attributed to iron dust alone as it is possible to find pulmonary fibrosis without the typical fibrohyaline silicotic nodule.

An association with tuberculosis has also been described.

Diagnostic criteria:

- anamnesis revealing exposure to iron dust;
- chest X-ray: diffuse reticular pattern and, in more severe cases, micronodulation due to the radio-opacity of iron: in this case, differentiation with respect to silicosis is necessary. Generally, siderosis is diagnosed in asymptomatic subjects by chance, through X-ray patterns. These patterns are sometimes reversible;
- presence of siderocytes in the sputum.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of the working conditions showing evidence of prolonged or repeated exposure to iron dust;

— and, if available:

- biological monitoring:
presence of siderocytes in the sputum,
- workplace air monitoring:
significant concentrations of iron dust.

Minimum duration of exposure: 10 years.

Maximum latent period: None.

Comments:

- Exposure to mixtures of iron dust, crystalline silica and carbon causes combined pneumoconiosis: sidero-silicosis, anthraco-sidero-silicosis (see document on silicosis)
- Several epidemiologic surveys have reported a high incidence of pulmonary neoplasms in iron-mining workers exposed to haematite.
However, the occurrence of these tumours is likely due to simultaneous exposure to other risk factors such as radon.

Infectious and parasitic diseases of occupational origin

General consideration

This document is not an exhaustive list of all the infectious and parasitic diseases that can be of occupational origin.

Almost any infection could occur as a result of occupational exposure but certain occupations carry a higher risk than others. These include agricultural workers (especially in subtropical climates where there is often a higher incidence of infections than elsewhere), health-care workers and laboratory personnel, workers involved with animals and animal products such as veterinarians, abattoir workers, meat and fish handlers, and outdoor workers in general where there may be exposure to excreta of infected animals, such as construction workers, sewage workers and those employed in or on water.

The table summarizes the most important occupations associated with infectious diseases. Five main diseases are described - viral hepatitis, brucellosis, tetanus, leptospirosis and tuberculosis.

For other pathologies, one should refer to specialized textbooks. See also, document on infectious diseases transmitted by animals.

Table:

A summary of the main occupations associated with communicable diseases

Occupation	Disease
Farming and animal husbandry, forestry, hunting, construction work, sewer work, mining, veterinary service	Anthrax Anthropod-borne disease, e.g. encephalitis Brucellosis Coccidioidomycosis Histoplasmosis Hookworm Leptospirosis Malaria Q Fever Rabies Rickettsial diseases Schistosomiasis Tetanus Trypanosomiasis Tuberculosis Tularaemia
Meat and fish handling	Bovine tuberculosis Brucellosis Erysipeloid Fungal infections (various) Q Fever Tularaemia

Occupation	Disease
Poultry and bird handling	Chlamydiosis Fungal infections (various) Newcastle virus disease
Work with wood, hair and hides	Anthrax Q Fever
Health-care workers, laboratory personnel	Tuberculosis Viral hepatitis Most communicable diseases

Viral hepatitis

1. Definition and causal agent

Viral hepatitis refers to infections of the liver caused by a number of viruses including hepatitis A, hepatitis B, non-A, non-B, hepatitis C, hepatitis D (the delta agent, a defective virus) and epidemic non-A hepatitis. Infections with other viruses such as Epstein-Barr and cytomegalovirus may also present with hepatic illness. Although all these agents could cause occupationally related infection, by far the most important world-wide is hepatitis B virus (serum hepatitis).

2. Transmission of infection

2.1. Exposure

In general, infection with hepatitis B virus (HBV) occurs with the injection of infected human blood or plasma fractions. Other known or suspected routes of infection include tattooing, sexual contact and possibly non-parenteral routes involving mucosal exposure to body fluids. Vertical transmission from mother to child is an important non-occupational mode of transmission for hepatitis B. Airborne spread is not considered a risk. Food is a major source of infection for hepatitis A.

2.2. Occupational groups at risk

For hepatitis B infection, at risk are primarily those individuals whose occupation brings them into contact with infected blood or blood products or the body fluids of infected patients. The main risk group is, therefore, health-care workers, including laboratory personnel. Others include prison and mental-institution staff, police and ambulance personnel who may come into contact with the blood or body fluids of infected persons in their care.

3. Clinical disease (HBV)

3.1. Presenting features

After an incubation period of between 60 and 180 days, anorexia, nausea and vomiting are followed a few days later by jaundice and the passage of dark urine and pale stools. Diarrhoea, skin rashes and a low-grade fever can occur in a minority of cases. Clinical examination of the jaundiced patient usually reveals a smooth, tender, enlarged liver.

3.2. Laboratory diagnosis

Confirmed by the presence of high serum aminotransferases and the presence of serum antigen markers such as HBsAg.

3.3. Prognosis

It is a self-limiting illness in up to 90% of patients. Fulminant (and frequently fatal) hepatitis occurs in less than 1% of patients, but some who recover from jaundice can develop either a carrier stage (5 to 10%), repeated attacks of jaundice or chronic active hepatitis, which can lead to liver failure. Persistent hepatitis B infection can lead to hepatocellular carcinoma in up to 30% of affected patients.

4. Definition of general criteria for recognizing viral hepatitis

4.1. Determination of causal agent

Only the hepatitis B, non-A, non-B, hepatitis D and epidemic non-A hepatitis viruses are covered here. The predominant virus is hepatitis B.

4.2. Disease caused

Clinical criteria: Acute hepatitis
Persistent hepatitis
Chronic active hepatitis
Post-hepatitic cirrhosis
Post-cirrhotic liver cancer

4.3. Definition of specific criteria for identifying the infectious disease from the type of exposure

Type of occupation

Any occupation involving or likely to involve exposure to blood, blood derivatives, body fluids and biological samples.

Definition of exposure criteria

for acute infection:

- minimum induction period: 60 days
- maximum latent period before symptoms appear: 180 days

for chronic infection:

maximum latent period is difficult to determine. The diagnosis of chronic infection requires specialist advice.

Brucellosis

1. Definition and causal agent

Brucellosis is a zoonosis usually caused, in descending order of virulence, by the coccobacilli *Brucella melitensis*, *Brucella suis* or *Brucella abortus*. The organism grows slowly and is resistant to drying but sensitive to acid and heating. Infection may be acute, subacute, chronic or clinically unapparent. Infective animals may or may not show signs of the disease.

2. Transmission of infection

2.1. Exposure

Infection is most common in males aged 10 to 40 years. The natural reservoirs for the organism are goats, sheep, camels (*B. melitensis*), pigs (*B. suis*) and cattle (*B. abortus*). Dogs, horses and rabbits can also become infected. Infection occurs in humans due to drinking infected milk, tending infected animals or handling infected carcasses, where the organism may enter the body through cuts and abrasions.

2.2. Occupational groups at risk

This is a disease mainly of farmers, slaughtermen, butchers, meat packers, agricultural engineers and laboratory technicians. For veterinary surgeons, accidental inoculation or conjunctival contamination with brucella vaccine is an added risk.

3. Clinical disease

3.1. Presenting features

The incubation period varies from several days to several months. The early symptoms of clinical disease are non-specific: fevers (sometimes episodic), chills, night sweats, aches and pain, anorexia and lethargy. Hepatosplenomegaly and lymphadenopathy occur in a minority of cases.

3.2. Laboratory diagnosis

- (i) Isolation of the organism is difficult.
- (ii) Serological tests to find specific antibodies.

3.3. Prognosis

- (i) A self-limiting disease in 90% of cases.
- (ii) Serious or prolonged effects on the joints, heart or nervous system can occur in 10% of cases.

4. Definition of general criteria for recognizing brucellosis

4.1. Determination of causal agent

See section 1. Definition and causal agent.

4.2. Disease caused

Clinical criteria: Acute brucellosis
Subacute brucellosis
Chronic brucellosis
Articular, cardiac and neurological complications

There is no clinical symptom specific to brucellosis.

Para-clinical criteria: isolation of the organism or serology.

4.3. Definition of specific criteria for identifying the infectious disease from the type of exposure

Type of occupation

Any occupation involving or likely to involve exposure to the following animals or products thereof:

- (i) goats (*B. melitensis*)
- (ii) pigs (*B. susis*)
- (iii) cattle (*B. abortus*)

Definition of exposure criteria

for acute infection:

time interval: a few days (incubation)

maximum latent period before symptoms appear: up to six days.

for chronic infection:

maximum latent period before symptoms appear is difficult to determine and requires specialist medical advice.

Tetanus

1. Definition and causal agent

Tetanus is caused by *Clostridium tetani*, which is an anaerobic, gram-positive, spore-forming bacillus. The resistance of the spores to drying and heating has ensured its widespread distribution in soil and animal faeces. Its anaerobic characteristics and the toxin produced within the bacterium during its early stages of

growth have meant that it remains a particularly serious sequela of penetrating wounds, particularly where ignorance, poverty and poorly developed health services prevail.

2. Transmission of infection

2.1. Exposure

A world-wide hazard. Soil and faeces are the main source of exposure, with infection occurring through deep and uncleaned wounds.

2.2. Occupational groups at risk

Military forces and agricultural workers are probably at greatest risk due to their increased chances of acquiring penetrating wounds contaminated with soil.

3. Clinical disease

3.1. Presenting features

The period from injury to onset of symptoms varies from one day to several months, though this incubation period rarely exceeds two weeks. The severity of symptoms is related to the initial tissue damage and its contamination, whilst the shorter the incubation period, the more serious the resulting disease. Muscle rigidity precedes muscle spasms and in most cases starts with stiffness of the facial muscles. Involvement of the pharynx or respiratory muscles causes respiratory deficiency. Later the limbs may be involved and full-blown generalized spasms will then follow. Full recovery in survivors takes 4 to 6 weeks.

3.2. Laboratory diagnosis

This is less important than the severe and life-threatening clinical picture, which usually provides the diagnosis.

3.3. Prognosis

The complications of the disease play a dominant role in tetanus. Respiratory paralysis or pneumonia are the most common and most dangerous, though autonomic nervous system damage can cause cardiovascular problems, whilst fractures of the spine can result from the muscular spasms. In untreated cases, mortality can be as high as 70%, depending on age, severity of the disease and availability of intensive care facilities.

4. Definition of general criteria for recognizing tetanus

4.1. Determination of causal agent

See definition and causal agent.

4.2. Disease caused

Clinical criteria: tetanus.

Para-clinical criteria: nil.

4.3. Definition of specific criteria for identifying the infectious disease from the type of exposure

Type of occupation

Any occupation involving the risk of inoculation with the micro-organism or its spores.

Definition of exposure criteria

time interval: several hours

maximum latent period before symptoms appear: four weeks.

Leptospirosis

1. Definition and causal agent

Leptospirosis is caused by the *Leptospira interrogans* complex. Leptospira are thin, highly motile spirochaetes with hooked ends. The organisms are microscopically demonstrable by dark-field illumination and silver staining. There are 19 serological groups.

2. Transmission of infection

2.1. Exposure

Rodents, especially rats, are the most important reservoir. *Rattus norvegicus* and *Mus musculus* carry a broad spectrum of serotypes, though other animals, including cattle, pigs, goats, dogs, foxes and voles, can be infected. The organism may exist in the animal host without causing pathological change. Exposure to urine of these animals is the commonest type of human risk.

2.2. Occupational groups at risk

People working in a rat-infested environment or where there is infected material or water are at greatest risk. These include agricultural workers (especially those working in rice or sugar-cane fields), sewer workers, miners, veterinarians, abattoir workers, fish handlers and military personnel.

3. Clinical disease

3.1. Presenting features

The length of the incubation period of 2 to 20 days depends on the host response and the quantity of micro-organisms. In the mild form there may only be a low-grade fever, but the severe form associated with *L.icterohaemorrhagica* (Weils disease) presents with jaundice, renal failure and haemorrhages. Cardiovascular collapse may occur. Approximately 80 to 90% of cases have no jaundice.

The disease has two phases: a septicaemic phase, which lasts 4 to 7 days with fevers, headaches, myalgia and conjunctival infection, whilst renal failure and jaundice are uncommon but serious features. A second immune phase lasts four to 30 days. The immune phase coincides with the disappearance of the spirochaete from most tissues. Uveitis, rashes, meningitis, encephalitis and myelitis may occur. Liver and kidney abnormalities continue from the first phase.

3.2. Laboratory diagnosis

A history of exposure to rat-infested environments is very helpful in differentiating leptospirosis from other pyrexial illnesses. Leucocytosis with neutrophilia (and in 40% of cases a thrombocytopaenia) plus increased plasma fibrinogen levels is supplemented by abnormal urinalysis and the demonstration of leptospira spp. in the urine. Liver function tests may be abnormal. After the second week of the disease, isolation of the organism becomes less likely but serology is then important. Macroscopic slide agglutination is a good screening test supplemented by microscope-type specific agglutination tests, where titres of 1:100 are sufficient to indicate a previous infection.

3.3. Prognosis

Recovery is normally the rule but older patients and those with severe renal, haematological and hepatic change may succumb. Renal dialysis has greatly reduced previous mortality figures and the long-term follow-up of dialysed patients indicates a good recovery of renal functions.

4. Definition of general criteria for recognizing leptospirosis

4.1. Determination of causal agent

See section 1. Definition and causal agent.

4.2. Diseases caused

Clinical criteria:

acute form: ictero-haemorrhagic leptospirosis
neurological complications

Para-clinical criteria:

Isolation of the organism or antigenic reaction

4.3. Definition of specific criteria for identifying the infectious disease from the type of exposure

Type of occupation

Any occupation involving or likely to involve exposure to secretions and excretions of rodents.

Definition of exposure criteria

for the acute disease and its complications:

time interval: three days,

maximum latent period before symptoms appear: three weeks.

Tuberculosis

1. Definition and causal agent

Human tuberculosis is largely confined to infection with *Mycobacterium tuberculosis*.

2. Transmission of infection

2.1. Exposure

Animal to human spread is unusual except for *M. bovis* in heavily contaminated milk. *M. tuberculosis* spreads from humans through contact with pulmonary secretions or sputum of infected persons. The airborne route is the predominant mode of spread.

2.2. Occupational groups at risk

Those at risk are, in the main, health-care workers and laboratory personnel, although farmers and veterinarians may be exposed to *M. bovis*.

3. Clinical diagnosis

3.1. Presenting features

The disease is slow to present — the primary lesion is a tubercle. Such a primary infection may become inactive and is usually symptomless.

Tuberculosis sensitivity appears within a few weeks. Pulmonary tuberculosis as a symptomatic disease affects perhaps only 5 to 15% of infected persons and is thus usually due to a reactivation of a latent tubercle focus. It has a chronic variable course ranging from asymptomatic to widespread dissemination within the lungs and a spread to other organs including the brain and bones. Cough, fatigue, fever, weight loss, chest pain and haemoptysis, with or without multiple organ involvement, heralds a serious and potential life-threatening infectious disease.

3.2. Laboratory diagnosis

The culture of *M. tuberculosis* from pathological specimens is necessary to confirm the diagnosis. Chest radiographs will show shadowing and/or cavitation in severe cases.

3.3. Prognosis

Recovery is good if tuberculosis is diagnosed early, as treatment with effective drugs is available.

4. Definition of criteria for recognizing tuberculosis

4.1. Determination of causal agent:

See section 1. Definition and causal agent.

4.2. Disease caused

Clinical criteria:

Acute, sub-acute or chronic tuberculosis anywhere in the body but usually in the lungs.

Para-clinical criteria:

Possibly isolation of the organism on culture.

4.3. Definition of specific criteria for identifying the infectious disease from the type of exposure

Type of occupation

Any occupation involving or likely to involve exposure to infected patients (*M. tuberculosis*) or animals (*M. bovis*)

Definition of exposure criteria:

acute form:

M. bovis infection: incubation period

acute: at least four weeks

(usually presenting as enlarged cervical lymph nodes)

chronic: several years — a wide variety of organ involvement.

Cutaneous forms of M. tuberculosis infection

Erythema nodosum — allergic manifestation which occurs within a few weeks of primary infection and resolves within a further three weeks.

Cervical lymphadenitis

Mainly *M. bovis*, occasionally *M. tuberculosis*. May be chronic and resistant to treatment.

Chronic tuberculosis

Mainly a pulmonary involvement.

INFECTIOUS DISEASES TRANSMITTED BY ANIMALS

There are many infectious diseases which can be transmitted by animals or their excreta. The main diseases have already been examined separately (brucellosis, leptospirosis, tuberculosis, tetanus, see document on infectious and parasitic diseases of occupational origin). Others are covered in this chapter. However, some human diseases which are undoubtedly transmitted by infected animals are too rare to be examined here and will be recognized as occupational illnesses only by individual assessment in each case or as a complication of an occupational accident, particularly following bites or stings (rabies, pasteurellosis, malaria, etc.).

TULARAEMIA

1. Definition and aetiological agent

Tularaemia is an anthroponosis caused by *Franciscella tularensis*. A number of animals are infected by this gram-negative bacillus and humans can easily be contaminated, most often through direct contact. The disease is usually characterized by skin lesions with regional ganglion hypertrophy.

2. Transmission of infection

Exposure

Many animals are natural carriers of *F. tularensis*, particularly hares, rabbits, squirrels, marmots, musk rats, foxes, mice, rats, quails, pheasant, etc.

Humans are very sensitive to tularaemia; the bacteria most often enter directly through the skin, even where there is no existing skin lesion, and only rarely through insect vectors (ticks). The bacillus can also penetrate the body through the mucous membranes, the digestive tract or the respiratory tract.

Occupational groups exposed

Gamekeepers, foresters; those involved in animal rearing and slaughtering; transport; handling rabbits, hares and other small furry animals; preparation of animal skins; laboratory work involving contact with rabbits and small rodents.

3. Clinical picture

The incubation period is usually three to five days. The clinical forms depend mainly on the path of infection, but all involve fever, asthenia, joint and muscle pain and headache.

The most common clinical form combines ulceration at the point of infection with regional adenopathy.

The eyes, lungs and digestive tract may be affected, depending on the path of infection.

Biological diagnosis

Isolate bacteria from lesions.

Serological tests to identify antibodies.

4. General recognition criteria

Disease caused

Clinical criteria: ulcero-glandular form,
 oculo-glandular form,
 primitive pulmonary form,
 digestive form.

Paraclinical criteria: any additional examination which can establish that *F. tularensis* has entered the body.

Criteria for linking the infectious disease with the type of exposure

Type of occupation: any occupation likely to involve contact with hares, rabbits or small rodents.
Exposure criteria: minimum induction period: a few hours
maximum latent period: 15 days.

LYME ARTHRITIS

1. *Definition and aetiological agent*

Lyme arthritis is caused by the spirochaete *Borellia burgdorferi* and is transmitted to humans through tick bites. It is characterized by chronic migratory erythema sometimes accompanied by joint or neurological disorders.

2. *Transmission of infection*

Exposure

Dogs and a number of wild species may carry the bacteria. Some species of tick are responsible for transmitting the disease to humans.

Occupational groups exposed

All forestry work in areas where the disease is endemic.

3. *Clinical picture*

Symptoms

Chronic migratory erythema appears 3 to 20 days following the tick bite. Skin lesions may be accompanied by general signs, arthralgia and myalgia.

Sequelae (encephalitis, myocarditis and arthritis) may also appear.

Biological diagnosis

Isolation of bacteria (difficult).

Serological tests for specific antibodies.

4. *General recognition criteria*

Disease caused

Clinical criteria: chronic migratory erythema,
sequelae: encephalitis, myocarditis, arthritis.

Paraclinical criteria: clinical signs must be confirmed by any additional examination which can establish that the bacteria have entered the human body.

Criteria linking the infectious disease with the type of exposure

Type of occupation: any work with a risk of tick bite in an area where the disease is endemic.
Exposure criteria: minimum induction period: two days;
maximum latency period: one month for chronic migratory erythema,
six months for late-appearing symptoms.

ORNITHOSIS

1. Definition and aetiological agent

Ornithosis is an anthroozoonosis caused by *Chlamydia psittaci*. Infection is most often characterized by acute pneumopathy.

2. Transmission of infection

Exposure

C. psittaci is carried by domestic and wild birds. For humans, the infection is airborne from a bird-contaminated environment.

Occupational groups exposed

Work involving contact with birds, poultry or their excreta.

3. Clinical picture

Symptoms

Following an incubation period of usually one to two weeks, infection may be characterized by acute febrile pneumopathy. Asymptomatic forms may also be observed.

Biological diagnosis

Intracellular isolation of the bacteria is difficult.

A number of serological tests can be carried out to identify antibodies. However, cross reactions may be observed between *C. psittaci*, *C. trachomatis* and *C. pneumoniae*. In addition, early treatment with tetracyclines can reduce antibodies.

4. General recognition criteria

Disease caused

Clinical criteria: acute pneumopathy.

Paraclinical criteria: any further examination which can establish that *C. psittaci* has entered the human body.

Criteria for linking the infectious disease with the type of exposure

Type of occupation: any occupation likely to involve exposure to domestic or wild birds or their excreta.

Exposure criteria: minimum induction period: 48 hours;
maximum latent period: 21 days.

Q FEVER

1. Definition and aetiological agent

Q fever is caused by the rickettsia *Coxiella burnetii*. In humans, infection is often benign and unnoticeable, but it can cause intermittent fever and in some cases endocarditis and hepatitis.

2. *Transmission of infection*

Carriers and contamination method

There are two human contamination methods depending on the carrier:

- (i) domestic animals, particularly cattle and sheep, may be infected. Humans can be infected from contaminated placentas, aborted matter, secretions, viscera, etc.;
- (ii) humans can be infected from wild animals through tick bites. This contamination method appears to be much rarer.

Occupational groups exposed

The disease mainly affects sheep and cattle farmers, abattoir workers, veterinary surgeons and laboratory staff working with the bacteria.

3. *Clinical picture*

Symptoms

In humans, the disease is most often benign and unnoticeable. It may be characterized by the sudden onset of intermittent fever accompanied by general signs. In the acute phase, acute febrile pneumopathy and gastro-intestinal disorders may be observed. The main chronic symptoms are endocardial disorders and hepatic complications.

Biological diagnosis

Isolating the bacteria is difficult.

Diagnosis is mainly based on serological tests.

4. *General recognition criteria*

Disease caused

Clinical criteria: Q fever with or without pneumopathy and digestive disorders;
chronic symptoms: endocarditis, hepatitis.

Paraclinical criteria: any additional examination which can establish that *C. burnetii* has entered the human body.

Criteria linking the infectious disease with the type of exposure

Type of occupation: any occupation involving or likely to involve exposure to cattle and sheep and their excreta.

Exposure criteria: minimum induction period: one week;
maximum latent period: three weeks.

ERYSIPELOID

1. Definition and aetiological agent

Erysipeloid is an anthroponosis caused by *Erysipelothrix rhusiopathiae*. The bacteria are found in a number of species of domestic and wild animals, particularly mammals, birds, aquatic animals, etc. Humans can be infected through direct contact. Infection is characterized by skin lesions, generally benign.

2. *Transmission of infection*

Exposure

A number of species of mammals and birds carry *E. rhusiopathiae*. Pigs are the worst affected (swine erysipelas).

Humans contract the disease through contact with carriers or sick animals, when handling products of animal origin or objects contaminated by the animals. The path of infection is often through wounds or skin abrasions.

Occupational groups exposed

Gamekeepers, foresters; farmers, veterinary surgeons, abattoir, tripe and meat-processing workers; pig, cattle, poultry, game farmers, etc.; fishermen and fish-market workers; processing and conserving of food products of animal origin, etc.

3. *Clinical picture*

Symptoms

Most often erythematous and oedematous skin lesions form on the hands and fingers, following a wound. They may be accompanied by problems in the joints.

The development of the disease is usually benign. In exceptional cases, cardiac disorders and septicaemia have been observed.

Diagnosis

Diagnosis is basically clinical. It may be confirmed by isolating and identifying bacteria from the lesion.

4. *General recognition criteria*

Disease caused

Clinical criteria: cutaneous form: erysipeloid maculopapule;
cutaneous form with arthritis;
endocardiac septicaemia.

Criteria linking the infectious disease with the type of exposure

Type of occupation: any occupation likely to involve exposure to animals or animal products (pork, poultry, game, fish, etc.).

Exposure criteria: minimum induction period: A few hours;
maximum latent period: Seven days.

Noise

Definition of causal agent

Sound or noise is an undulatory phenomenon by means of which mechanical vibration energy is propagated through an elastic medium, generally air, giving rise to auditory perception.

Depending on the type of work carried out and the resulting noise limits, noise can have effects on organs other than those of the auditory system. This document only covers the effects on the auditory apparatus. In working environments, depending on the variations in the noise level, noise can be stable, fluctuating, variable or impulsive and, depending on duration, either continuous or intermittent.

Adverse effects

1. Acute effects

Neurosensory effects:

Dizziness, tinnitus, hypoacusis which can lead to total deafness.

The auditory deficit is neurosensory or mixed (both conductive and neurological), generally monolateral and partly reversible, depending on the energy of the sound wave and the duration of exposure.

Physical damage:

Laceration of the tympanic membrane, with bleeding.

The site of the lesion is in the tympanic membrane, middle ear and cochlea.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of sudden exposure to a very loud noise. Importance of the notion of suddenness of the causal phenomenon (bang, explosion, etc.).

Minimum duration of exposure: Brief.

Maximum latent period: The symptoms should appear immediately after exposure to the noise.

2. Chronic effects

Occupational deafness:

The disease develops slowly and insidiously. It is possible to distinguish various phases which characterize how serious the condition has become. Tinnitus can be heard in each phase. Hypoacusis is characterized by a quantitative reduction in auditory sensitivity, by a loss of the ability to discriminate between sounds and by a qualitative deterioration in the recruitment of the acoustic signal.

The site of the lesion is the cochlea; hypoacusis is of the neurosensory type, more pronounced on the frequencies 3 to 6 KHz. It is bilateral and generally symmetrical, irreversible but usually not progressive once exposure to noise ceased.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to noise of over 85 dB. It is possible, however, that exposure to noise levels of over 75dB are already a source of occupational deafness.

Minimum duration of exposure: Six months taking into account variable individual susceptibility.

Maximum latent period: Does not apply.

Pressure exceeding atmospheric pressure (measured at sea level)

Definition of causal agent

Certain disorders are associated with spending time in a compressed atmosphere and are directly due to pressure itself or to inhalation of compressed gas mixtures.

Other disorders occur during or after decompression.

These disorders affect professional divers and those working with compressed air.

Acute effects

Acute diseases caused by the mechanical effects of pressure

- *Barotrauma of the middle ear*
Haemorrhagic exudate or burst eardrum accompanied by otalgia, otorrhagia, tinnitus aurium or hypoacusis.
- *Barotrauma of the inner ear*
Sometimes dissociated cochleovestibular disorder.
- *Barotrauma of the sinuses*
- *Excess pressure on the lungs*
Breathlessness, haemoptysis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of work being carried out in conditions where the pressure exceeds atmospheric pressure.

Minimum duration of exposure: Brief.

Minimum latent period: 36 hours.

Conditions caused by the toxic effects of inhaled gases

- *Nitrogen narcosis ('rapture of the deep')*

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of diving work to depths in excess of 50 metres.

Minimum duration of exposure: Brief.

Maximum latent period: A few minutes.

- *Hypo-oxaemic attack*
Convulsions preceded by cramp, dizziness and nausea.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of work involving diving to depths in excess of 100 metres, with inhalation of compressed air.

Minimum duration of exposure: Brief.

Maximum latent period: A few minutes.

- *High-pressure neurological syndrome*
Tremors, muscle contractions, dizziness and nausea.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of work involving diving under helium to depths in excess of 50 metres.

Minimum duration of exposure: Brief.

Maximum latent period: A few minutes.

Decompression diseases

— *Bends*

Osteoarticular pain

— *Subcutaneous formication*

— *Neurological disturbances*

Paraplegia, etc.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of diving work involving rapid resurfacing.

Minimum duration of exposure: Brief.

Maximum latent period: A few hours.

Chronic effects

Diseases caused by pressure

Hypoacusis

Caused by irreversible cochlear damage with or without labyrinthic syndrome.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis.

Minimum duration of exposure: Three months.

Maximum latent period: One month.

Decompression diseases

Dysbaric osteonecrosis

Affecting the shoulder, hip or knee with a characteristic skeletal X-ray picture.

Minimum intensity of exposure:

Occupational exposure confirmed by the anamnesis.

Minimum duration of exposure: Three months.

Maximum latent period: 20 years.

Pressure below that of ground level atmospheric pressure

Definition of causal agent

In order to permit passengers of modern aircraft to breathe without using masks the cabins of both pilot and passenger sections are pressurised. However, the pressure level produced is not that of ground level atmospheric pressure but only that equivalent to 2000 m above sea level (moderate low pressure).

Manufacturing or maintenance companies often modify, adapt or repair the equipment of the aircraft during flight without passengers. Similar activity takes place during the testing of new aircraft.

Combat planes usually operate at high altitudes and crew members are protected by masks supplying pure oxygen at a pressure close to ground level atmospheric pressure.

In flight, during repair, changes, and in unplanned incidents, pressure may become considerably lower than that of ground level atmospheric pressure.

Physiologic effects may occur both when low pressure is established and when atmospheric pressure corresponding to ground level is reestablished. Organs most susceptible are the middle ear and sinuses.

Acute effects

Barotrauma of the middle ear

Symptoms and signs: Sudden pain, hearing loss, bleeding from the ear. Burst eardrum (confirmed by inspection).

Exposure criteria:

Minimum intensity of exposure: Occupational change of external pressure, confirmed by anamnesis and measurement outprints, if possible.

Minimum duration of exposure: Brief.

Maximum latent period: A few minutes.

Chronic sub-acute effects

Barotrauma of the middle ear

Symptoms and signs: Increasing pain, hearing loss, inflammation and bleeding from the ear.

Exposure criteria:

Minimum intensity of exposure: Occupational change of external pressure, confirmed by anamnesis and measurement outprints, if possible.

Minimum duration of exposure: Six months.

Maximum latent period: One month.

Mechanical vibration affecting the hands and arms

Definition of causal agent

Vibration transmitted to the hands and arms by machines or through objects held against a vibrating surface, at frequencies ranging from 25 to 250 Hz.

Adverse effects

1. 'Hand-arm vibration syndrome'

Vascular disorders

Raynaud's phenomenon: episodes of white digits, with numbness of one or several digits, exacerbated by cold.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by anamnesis showing evidence of work involving exposure to vibration.

Minimum duration of exposure: Six months. Inversely proportional to intensity of exposure.

Maximum latent period: Two years.

Neurological disorders

Neuropathy with tingling and numbness of the digits, loss of sensory discrimination.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by anamnesis showing evidence of work involving exposure to vibration.

Minimum duration of exposure: Six months. Inversely proportional to intensity of exposure.

Maximum latent period: Two years.

Osteoarticular disorders

Osteoarticular diseases confirmed by radiography:

- carpal bone disorders;
 - necrosis of the semilunate bone (Kienböck's disease);
 - osteonecrosis of the scaphoid bone (Köhler's disease);
- hyperostotic arthrosis of the elbow.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by anamnesis showing evidence of work involving considerable exposure to vibrations transmitted by percussion tools.

Minimum duration of exposure: Five years.

Maximum latent period: Two years.

Diseases of the periarticular bursae caused by mechanical pressure

Definition of causal agent

Prolonged pressure on a periarticular bursa.

Adverse effects

Acute hygroma

Acute hygroma of the synovial periarticular bursae in the pressure zone of the elbow or knee.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by anamnesis providing evidence of work involving pressure being placed on the elbow or knee.

Minimum duration of exposure: Eight hours.

Maximum latent period: Three days.

Chronic hygroma

Chronic hygroma of the elbow or knee.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by anamnesis providing evidence of work involving pressure being placed on the elbow or knee.

Minimum duration of exposure: One month.

Maximum latent period: One month.

Non-ionizing radiation

Definition of causal agent

The non-ionizing radiations which can cause typical disorders in man are those with wavelengths between 100 nm and 1m, i.e.

- ultraviolet radiation (uv) (100 to 400 nm)
- visible light (400 to 760 nm)
- infrared radiation (ir) (760 nm to 3 μ m)
- microwaves (1 μ m to 1 m)

Laser radiation within these wavelengths is also included under this heading.

Non-ionizing radiations with wavelengths > 1 m have no proven effect on health.

Main occupational uses and sources of exposure

- UV: bacteriocidal lamps, plasma arc and xenon welding, sun's rays especially at high altitudes, industrial lasers;
- IR: Sun's rays, sources of radiant heat, industrial lasers.

Adverse effects

1. Pathological effects of ultraviolet radiation

The extent to which UV radiation penetrates the body, and its biological effects, vary according to the wavelength:

- UV(C) is absorbed through the skin, conjunctiva and cornea, but does not penetrate any further,
- UV(B) penetrates as far as the lens,
- UV(A) may reach the retina.

Acute effects

Keratoconjunctivitis

Painful disorder affecting both eyes, with conjunctival hyperaemia and photophobia. If the cause is a UV laser, the cornea may be severely affected with subsequent opacification.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- anamnesis and study of working conditions providing evidence of intense exposure (intensity greater than the limit values) to UV(C) or UV(B) or UV lasers.

Minimum duration of exposure: About one second.

Maximum latent period: 48 hours.

Photoretinitis

Phototrauma of the retina.

Relatively painless disorder of the retina, with transient blindness, persistence of visual image and scotoma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of intense exposure to UV(A), particularly industrial lasers (A).

Minimum duration of exposure: Fraction of a second.

Maximum latent period: Immediate blindness.

Cutaneous effects

Erythema, skin burns.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of intense exposure to UV(C);

— and if the data is available:

Guide value: exposure of the uncovered parts to UV(C) with intensity of the dose received on skin > 0.03 J/cm².

Minimum duration of exposure: One hour.

Maximum latent period: 24 hours.

Chronic effects

Actinic cataract

This is usually a disorder of the anterior capsule of the lens, extending to the sub-capsular epithelium.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to UV(B) and UV(A).

Minimum duration of exposure: One year.

Maximum latent period: 15 years.

Skin cancers

These appear on uncovered parts of the body (head, neck, hands and forearms) and are mainly associated with outdoor occupations exposed to solar radiation. They include basal cells and spinocellular epitheliomas and malignant melanomas.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to solar radiation.

Minimum duration of exposure: 20 years.

Minimum induction period: Epitheliomas: 20 years; Melanomas: five years.

See document on occupationally caused cancers.

2. Pathological effects of visible light

Acute effects

Photoretinitis

Photochemical damage may be caused by blue light emitted at 400 to 550 nm or broad spectrum light emitted at high power (xenon projectors, arc lamps, flashguns). Documented pathological effects are those caused by class III and IV lasers used in visible light, which can cause acute lesions, ocular pain, transient blindness and persistence of visual image, chromatic deficiency.

Photoretinitis can also develop asymptotically during exposure to continuous-wave lasers; a thorough examination may discover the presence of a scotoma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of intense exposure to the abovementioned forms of radiation.

Minimum duration of exposure: A few seconds.

Maximum latent period: One year.

Chronic effects

Miners' nystagmus

This is an occupational disease associated with poor lighting, which involves problems in focusing. Pendular or rotating nystagmus may be accompanied by dizziness and headaches.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of exposure to lighting intensity below the standards prescribed for comfort (in underground work).

Minimum duration of exposure: Five years.

Maximum latent period: One year.

3. Pathological effects of infrared radiation

Acute effects

Thermal effects on the anterior part of the eye and surrounding areas

Burning sensation on the skin around the eyes, blepharitis and keratitis.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of intense exposure to broad-spectrum IR(B) and IR(C) emitters (sun, incandescent light sources, special lamps) or to industrial lasers.

Minimum duration of exposure: A few minutes.

Maximum latent period: 24 hours.

Heat-related retinal disorders

Sight disorders with scotoma, immediate oedematous lesions, with pigmentary lesions to the fundus of the eye appearing later, anomalies in the retina identified by retinal angiography.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

- anamnesis and examination of working conditions providing evidence of intense exposure to industrial lasers.

Minimum duration of exposure: About one second.

Maximum latent period: 24 hours.

Chronic effects

Glass workers' cataract (Heat-induced cataract)

This starts in the posterior cortex of the lens and forms a web, leading to irregularly shaped discoid posterior opacification.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to IR radiation emitted by incandescent glass or metal (over 1 500 °C).

Minimum duration of exposure: One year.

Maximum latent period: 15 years.

4. *Pathological effects of microwaves*

Heat cataract

Cloudy opacities on the posterior cortex of the lens. Spot opacities spread over the lens cortex.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of exposure to microwaves (wavelength of the order of decimetre, centimetre)

Minimum duration of exposure: Depends on intensity of the radiation. High-energy radiation (several hundred mW/cm²) can rapidly damage the lens.

Maximum latent period: 15 years.

Nerve paralysis due to pressure

Definition of causal agent

Prolonged pressure on anatomical grooves causing nerve injuries as a result of compression.

Adverse effects

Carpal tunnel syndrome

Compression of the median nerve in the wrist.

Tarsal tunnel syndrome

Guyon's cavity syndrome

Compression of the ulnar nerve in the wrist.

Ulnar nerve groove syndrome

Compression of the ulnar nerve in the elbow.

Compression of the external popliteal nerve

Compression of the nerve at the neck of the fibula.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by anamnesis providing evidence of prolonged and repeated direct or indirect pressure on the part of the body concerned. Extreme movements of hyperflexion and hypertension; condition worsened by vibrations (carpal tunnel syndrome).

Minimum duration of exposure: From a few hours (external popliteal nerve) to several months (carpal tunnel).

Maximum latent period: A few months.

Diseases caused by overstraining muscles and tendons

Definition of causal agent

Vigorous and repetitive movements of the upper limb joints, causing iterative microtrauma and wear-and-tear phenomena.

Effects

- Epicondylitis**
- Radial styloiditis**
- Tendinitis of the extensors and flexors**

In the wrists and fingers.

- Tenosynovitis**
- Trigger finger**

Modular tenosynovitis.

- Painful shoulder**

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of work involving repetitive movements with imposed output rate and vigorous occupational movement (expert's report case-by-case so as to exclude any non-occupational origin of the disorder).

Minimum duration of exposure: Six months.

Maximum latent period: One month.

- Low back pain**

Data available are not sufficient to decide on the occupational origin.

AGENTS RESPONSIBLE FOR OCCUPATIONALLY CAUSED ASTHMA
(Open, non-exhaustive list)

There are a large number of substances identified as causing occupational asthma. The categories of agents with some common examples are:

Macromolecules:

- (1) Substances of animal origin e.g. urine proteins from rats and mice (exposure of laboratory workers).
- (2) Substances of vegetable origin e.g. grain dust (as in bakers' and millers' asthma e.g. wood dusts, colophony).

Low molecular mass substances:

- e.g. diisocyanates (used in painting of vehicles).
e.g. persulphates (used by hairdressers).

Occupationally caused asthma

Definition

Occupationally caused asthma refers to reversible bronchial obstruction caused by agents present in the working environment.

Main occupational sources of exposure:

Either macromolecules (usually glycoproteins) of animal or vegetable origin or chemical substances of low molecular mass. In a few cases irritant substances may severely aggravate pre-existing asthma: their role in occupational asthma should be assessed on an individual basis.

The main causal agents are listed in the annex. The list is an open one.

Diagnostic criteria

Clinical certification of asthma must be confirmed by an examination of respiratory function showing either:

- bronchial obstruction reversible by bronchodilators; or
- bronchial obstruction triggered by non-specific bronchoconstrictors (metacholine test) when basic functional tests are normal;
- anamnesis: occupational exposure to a substance known to trigger occupational asthma; the sequence of the attacks in direct relation to the work schedule. Attacks may begin several hours following exposure;
- recurrence of disorders following re-exposure to the same agent;
- a positive provocation test cannot be demanded as a criterion for recognition, due to the danger involved;
- optional supportive evidence may be provided for certain allergens by:
 - (i) serial peak flow rater;
 - (ii) rhinomanometric study with nasal provocation tests;
 - (iii) IgE-dependent immediate immune reactions:
 - skin (prick tests);
 - raised levels of serum IgE specific to the occupational allergen;
 - histamine release;
 - basophil degranulation tests.

Exposure criteria

Minimum intensity of exposure: Cannot be specified, as there is no direct dose-effect relationship in the occurrence of occupationally caused asthma.

Minimum duration of exposure: Occupationally caused asthma generally requires a sensitization period ranging from a few weeks to several months. The minimum duration of exposure is one month, but will be shorter in the case of earlier sensitization (asthma could occur during the exposure period).

Maximum latent period: Three days.

AGENTS RESPONSIBLE FOR OCCUPATIONALLY CAUSED ASTHMA
(Open, non-exhaustive list)

There are a large number of substances identified as causing occupational asthma. The categories of agents with some common examples are:

Macromolecules:

- (1) Substances of animal origin e.g. urine proteins from rats and mice (exposure of laboratory workers).
- (2) Substances of vegetable origin e.g. grain dust (as in bakers' and millers' asthma e.g. wood dusts, colophony).

Low molecular mass substances:

- e.g. diisocyanates (used in painting of vehicles).
e.g. persulphates (used by hairdressers).

Occupationally caused allergic rhinitis and conjunctivitis

Definition

Occupationally caused allergic rhinitis is defined as a reversible nasal obstruction triggered by sensitizing agents present in the working environment. It often precedes occupationally caused asthma. Occupational conjunctivitis can be associated with occupationally caused allergic rhinitis which has the same pathophysiology.

Main occupational sources of exposure:

Either macromolecules (usually animal or vegetable glycoproteins) or chemical substances of low molecular mass acting as haptens.

The causative agents for occupationally caused rhinitis and conjunctivitis are similar to those for occupationally caused asthma. (see Annex 1)

Diagnostic criteria

- Rhinitis, which is initially allergic, may be followed by superinfections. Conjunctivitis is usually bilateral.
- Anamnesis: occupational exposure to an allergen. The sequence of the signs of conjunctivitis and rhinitis is directly related to the schedule of work: nasal discharge starts between a few minutes and a few hours after beginning work. Nasal obstruction is usually observed on waking in the morning. Rhinitis and conjunctivitis improve during the weekend and the holidays and recur when work begins again.
- The rhinomanometric test with nasal provocation is sometimes used to support a diagnosis of occupational allergic rhinitis.
- Further support may be obtained by IgE-mediated immune reactions:
 - skin (prick tests);
 - rise in serum IgE specific to the occupational allergen;
 - histamine release;
 - basophil degranulation tests.

Exposure criteria (see document on occupationally caused asthma)

Occupationally caused allergic contact dermatoses

Definition

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

Main occupational sources of exposure:

The causal agents are complex molecules, usually proteins, which are complete antigens, or molecules with a molecular mass of less than 2 000 to 3 000 Daltons, which haptens or incomplete antigens. Haptens are the most common cause of allergic contact dermatitis.

The main agents are listed in the annex. The list is open-ended.

Diagnostic criteria

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

Anamnesis: 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 a recurrence of the disease on re-exposure to the same agent.

Immunological criteria: patch tests should be carried out for all the suspected substances present at the workplace (including their basic components and the elements of protective equipment and detergents). They should be carried out by a competent person. In cases of photo-sensitivity and urticaria, special tests should be carried out (e.g. photo patch tests, prick test).

If positive, these tests 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

An allergic skin disease may be dependent on:

- personal factors: genetic factors or cutaneous and extracutaneous factors, such as race, sex, age, type and thickness of the epidermis, etc.,
- 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).

Minimum intensity of exposure: There is no dose/effect relationship in the onset of allergic contact dermatitis.

Minimum duration of exposure: In exceptional cases, a single contact is sufficient to cause sensitization (with dinitrochlorobenzene, dinitrofluorobenzene and phthalic anhydride). 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. 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.

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

- I Macromolecules
Substances of animal or plant origin e.g. woods.
- II Low molecular mass substances
metallic salts (e.g. nickel salts, chromates)
Resins, hardener (e.g. epoxy-resins)
Dyes and dye intermediates (e.g. paraphenylene-diamine)
- III Photo-allergents
Ultra-violet cured inks containing acrylates.

Occupationally caused irritation of the skin and mucous membranes

Definition of causal agents

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 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:

EEC: 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 thickening of the skin.

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,
- 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.

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.

The possibility of wear-and-tear dermatosis (e.g. from repeated cleaning work) can cause increased susceptibility on subsequent contact with an irritant.

Some workers suffering from allergic contact dermatitis or other skin diseases may show increased sensitivity to the action of the irritants.

Account should be taken of the possibility of splashes, and of immersion where occlusion increases the irritation (for instance: under rubber 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: Acute irritation dermatitis: A few minutes to a few hours depending on the intensity of exposure.

Chronic irritant dermatitis: Seven days.

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.

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

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 hyperactivity 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:

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 preceded by upper respiratory tract symptoms, e.g. ozone, phosgene, nitrogen oxides.

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.

Exposure criteria:

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

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.

Maximum latent period: The onset of symptoms should occur during exposure or within 48 hours at the latest. Delayed symptoms are possible with slightly soluble substances.

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

Reproductive risks from occupational exposures

The effects of physical, biological and chemical agents on human reproduction and the risks from exposure are difficult to assess because of the complexity of the reproductive process and the long span of years required for reproductive maturation.

The developmental defects seen may not be adequate indices of the effects of occupational exposure. In humans it is estimated that over one third of early embryos die and about 9% of recognized pregnancies abort spontaneously. Approximately 3% of newborn infants have defects at birth and with increasing age, more defects may become detectable.

Adverse effects on reproduction may occur in the preconceptional stage in men and in women, and in the postconceptional stages affecting the embryo or foetus. These stages may be affected by occupational as well as non-occupational exposures. The resulting effects include premature delivery and low birth weight.

Preconceptional stage

By its interaction with a gamete, a hazardous agent may either impair fertilization or cause such severe alterations in the resulting zygote that an early, unrecognized abortion occurs. Paternal or maternal exposure to hazardous agents at this stage may result in the inhibition of fertilization, impaired placental implantation, spontaneous abortion or abnormalities of the embryo.

Postconceptional stage

This may be divided into different phases of development:

1. *Implantation*

Defective implantation and spontaneous abortion may occur, usually within the first weeks of pregnancy.

2. *Organ differentiation*

During the active organ differentiation phase, between the third to eighth week, the central nervous system, heart, gut and musculo-skeletal system begin to develop, although at different rates. At this stage, teratogenic changes in the embryo can be induced by chemical, physical or biological agents, these teratogenic agents may affect any of the organ systems. It may even induce death of the embryo, or retardation and/or functional defects which are recognized after birth.

3. *Maturation*

This covers the period from the end of organ differentiation to the perinatal period and infancy. Physical growth, structural and physiologic maturation of central nervous system and the development of some of the endocrine glands, is not completed until some months after birth.

At present, exposure criteria for suspected aetiological agents applicable to individuals are difficult to establish. What is available is limited to lists of such agents — the exposure to which should be avoided or minimized. The agents include ionizing radiation, hormonal preparations such as oestrogenic compounds, and some pesticides e.g. DDT, all of which may affect both the male and female reproductive system. Kepone and dibromo-chloro-propane (DBCP) affects the male reproductive system, methyl mercury affects primarily the female reproductive system, and lead (Pb) and viruses such as rubella affects the foetus.

Chemical substances which meet the requirements to be classified according to the criteria in Annex VI of Council Directive 67/548/94 as toxic to human reproduction may be identified by a risk phrase on the container as follows:

- R 60: May impair fertility
- R 61: May cause harm to the unborn child
- R 62: Possible risk of impaired fertility
- R 63: Possible risk of harm to the unborn child

Leucoderma (vitiligo)

Occupationally caused leucoderma (vitiligo, achromia) refers to depigmentation of the skin caused by occupational exposure to chemicals.

Definition of causal agent

The agents involved mainly belong to the phenols and catechols group. Most are used as antioxidants in the chemical and photographic industries, or in cosmetics and pharmaceuticals. They are also used in adhesives and disinfectants.

The main causal agents are listed below.

Diagnostic criteria

- Clinical: hypopigmented and depigmented patches appear at the site of skin contact. These are usually on the exposed areas of the hands and forearms, although covered areas may be affected in some cases.
Neither facial leucoderma nor depigmentation due to steroids, hydroxyquinoline sulphate or butyl hydroxyanisole are normally associated with occupational exposure. The depigmentations may be mottled and patchy or confluent and symmetrical. There may be some inflammation.
There is a tendency for spontaneous but slow repigmentation after discontinuation of exposure.
- Anamnesis: occupational exposure to a substance known for its depigmenting properties.

Exposure criteria:

Intensity of exposure: Assessed via anamnesis.

Minimum duration of exposure: From a few days to several months. Leucoderma normally appears after direct and repeated skin contact, although similar effects have been reported following inhalation.

Maximum latent period: Two years.

Agents responsible for occupationally caused leucoderma (open, non-exhaustive list)

Phenols: p-tert-butyl phenol
 p-tert-amyl phenol
 o-phenyl phenol
 chloro-2 amino-4 phenol

Catechols: catechol (pyrocatechol)
 methyl catechol (o-hydroxyanisole)
 4-isopropyl catechol
 4-tert-butyl catechol

Hydroquinone, monobenzone

Hypersensitivity pneumonitis (extrinsic allergic alveolitis)

Definition

Hypersensitivity pneumonitis or extrinsic allergic alveolitis involve granulomatous inflammation which alters gas exchange.

Main occupational sources of exposure:

Hypersensitivity pneumonitis or extrinsic allergic alveolitis result from an immunological response specific to the inhalation of organic dusts. These may be spores or mycelia of mould fungi, animal proteins, etc. In exceptional cases, the disease may be caused by chemical substances.

Diagnostic criteria

- The symptoms depend on the nature of the disease, various forms of which are possible.
 - Acute: recurrent febrile episodes with dyspnea developing four to six hours after exposure.
 - Subacute: less intense and develops continuously in parallel with continued exposure.
 - Chronic: pulmonary fibrosis with chronic respiratory insufficiency affecting gas transfer factor (alveolar-capillary carbon monoxide diffusion), with possible complication in the form of right ventricular insufficiency.
- Radiological pulmonary anomalies: bilateral nodular, micronodular or more or less reticulo-nodular opacities.
- Anamnesis: occupational exposure to a substance known to cause hypersensitivity pneumonitis. Symptoms are directly related to the working timetable.
 - Immunological criteria: presence of antibodies in the form of serum precipitins. Increased percentage of T8 lymphocytes in the broncholar alveolar lavage fluid is a further indication, but this test should not be mandatory as a recognition criterion.
 - A respiratory challenge test should not be mandatory as a recognition criterion.

Exposure criteria:

Minimum intensity of exposure: Assessed by anamnesis. Although the symptoms usually appear with high concentrations of the allergen in the working environment, there is no good relationship between dose and effect.

Minimum duration of exposure: From a few minutes to a few months depending on the form.

Maximum latent period:

Acute form: eight hours;
 Subacute form: eight days;
 Chronic form: one year.

Meniscal diseases resulting from working over a prolonged period in a kneeling or crouching position

Definition of causal agent

Maintaining a working posture involving hyperflexion of the knee often in a crouching or kneeling position (in mines, in public works and building sites, electricians, tilers, etc.).

Effects

Meniscal lesions, confirmed by additional examinations, which may lead to complications (fissuring or rupture of the meniscus)

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed by the anamnesis providing evidence of work carried out over a prolonged period.

Minimum duration of exposure: Three months.

Maximum latent period: Six months.

Toxic polyneuropathy

Polyneuropathy of the mixed sensory/motor type, predominantly affecting the lower limbs.

Cardiovascular effects

An increase in the incidence of the cardiovascular diseases in people exposed to CS₂.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of exposure conditions providing evidence of prolonged or repeated exposure to CS₂;

— and, if available:

- biological monitoring of CS₂ in the blood, metabolites in the urine (2-thiothiazolidine-4-carboxylic acid (TTCA)), CS₂ in the exhaled air

- workplace air monitoring:

guide value: atmospheric concentration > (31 mg/m³) 10 ppm.

Minimum duration of exposure: One year.

Chronic encephalopathy: 10 years.

Maximum latent period: Parkinsonism syndrome and effects on the peripheral nervous system:

five years after the end of exposure. Other effects on the central nervous and cardiovascular systems: these assessments require an expert's report on a case-by-case basis.

Ionizing radiation

Definition of causal agent

Charged corpuscular radiation (alpha and beta particles) is the cause of internal irradiation (e.g. inhalation of radon). Neutral corpuscular radiation (neutrons) or electromagnetic radiation (X- or gamma-rays) is dangerous in terms of external irradiation.

Sources of exposure and main occupational uses:

X-ray machines, particle accelerators, gamma radiography sources, cobalt bombs, nuclear reactors, laboratory equipment, work involving isotopes.

Adverse effects

1. Non-random (non-stochastic) effects

(a) Acute effects

These are early effects which depend on the dose and the dose rate.

I. Whole-body irradiation

Medullary aplasia

With initial lymphopenia and chromosomal aberrations.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of external whole-body irradiation in excess of 1 Gray for X-ray or gamma-ray irradiation and 0.3 Gray for neutrons.

Minimum duration of exposure: A few minutes.

Maximum latent period: Two months.

II. Partial-body irradiation

Acute radioepidermatitis

Exudative lesions developing approximately three weeks after transient erythema, with necrosis as a possible complication.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of external X-ray or gamma-ray irradiation in excess of 10 Gray.

Minimum duration of exposure: A few minutes.

Maximum latent period: Two months.

Alopecia

Temporary hair loss after localized irradiation of the scalp.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of external X-ray or gamma-ray irradiation in excess of 3 Gray.

Minimum duration of exposure: A few minutes.

Maximum latent period: Two months.

Minimum induction period: 15 days.

Oligospermia and azospermia

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of external X-ray or gamma-ray irradiation in excess of 0.3 Gray.

Minimum duration of exposure: A few minutes.

Maximum latent period: Two months.

(b) Delayed effects

These appear some time after irradiation, whether this has been brief or prolonged.

Cataract

Crystalline opacities in the lens.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of external irradiation involving cumulative doses to the eye exceeding 10 Gray for X-rays and 8 Sv for neutrons (0.8 Gy).

Minimum duration of exposure: Can be brief.

Maximum latent period: Five years.

Minimum induction period: One year.

Chronic radiodermatitis

Atrophy, hyperkeratosis or telangiectasia, possibly complicated by radionecrosis.

Exposure criteria:

Minimum intensity and duration of exposure: Occupational exposure assessed by:

— anamnesis and study of working conditions providing evidence of repeated external X-ray irradiation in excess of 5 mGy/day. Total skin dose > 10 Gy.

Maximum latent period: Five years.

(c) Effects on the foetus

In certain accidental circumstances, exposure of a pregnant woman to radiation can cause foetal deformities depending on the dose received by the foetus and the age of the foetus at the time of irradiation.

Cerebral deformities (e.g. microcephalus) and skeletal deformities

Exposure criteria:

Minimum intensity and duration of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of brief X-ray irradiation of the foetus in excess of 0.3 Gy during the period of organogenesis.

Mental retardation

Exposure criteria:

Minimum intensity and duration of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of brief X-ray irradiation of the foetus in excess of 0.5 Gy beyond the eighth week of intra-uterine life.

2. Random (stochastic) effects

These are delayed effects arising after brief or prolonged irradiation.

Cutaneous spinocellular epithelioma

Following radioepidermatitis lesions.

Exposure criteria:

Minimum duration and intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of external irradiation involving a cumulative X-ray dose to the skin in excess of 15 Gy.

Minimum induction period: 10 years.

Leukaemia

Exposure criteria:

Minimum duration and intensity of exposure: Occupational exposure assessed by:

- anamnesis (taking account of the dose received, the subject's age, and the incidence of leukaemia among the general public) and study of working conditions providing evidence of external or internal irradiation involving a cumulative dose in excess of 1 Sv.

Minimum induction period: Three years.

Primary cancer of the lung

Exposure criteria:

Minimum duration and intensity of exposure: Occupational exposure assessed by:

- anamnesis (taking account of smoking habits) and study of working conditions providing evidence of internal irradiation by alpha emitters.

Minimum induction period: Five years.

Osteosarcoma

Exposure criteria:

Minimum duration and intensity of exposure: Occupational exposure assessed by:

- anamnesis and study of working conditions providing evidence of external or internal irradiation through incorporation of radionuclides normally absorbed in bone (radium 226, plutonium 239, etc.) involving a cumulative dose to the skeleton in excess of 8 Gy.

Minimum induction period: Five years.

See document on occupationally caused cancers.

NB: Some isotopes present a particular affinity for specific organs (for example: iodine for the thyroid gland)

Alphabetical key-word index

Key-word	Diagnosis No	Page No
ABS	0046	84
accumulator plants	0018	41
acetic acid	0059	106
acetylcholinesterase, inhibition of	0039	73
acro-osteolysis	0031	62
acrylonitrile monomer	0001	13
actinic cataract	0085	156
acute radioepidermatitis	0096	175
acute bronchopneumonia	0009	27
aliphatic amines, halogenated derivates of	0052	95
aliphatic amines	0052	95
alkylaryloxides, halogenated derivates of	0049	91
alkylarylsulphonates, halogenated derivates of	0049	91
allergic alveolitis	0094	173
allergic rhinitis	0089	165
allergic conjunctivitis	0089	165
allergic contact dermatoses	0090	166
alloys	0021	47
alopecia	0096	175
alveolitis	0094	173
amalgam	0011	31
ammonia	0015	37
angiosarcoma	0031	62
animal proteins	0094	173
animals, infectious diseases	0079	143
anthracene	0065	114
anthracene or compounds thereof	0065	114
anthrax	0078	135
arthropod-borne disease, e.g. encephalitis	0078	135
anti-explosive constituent	0023	49

Key-word	Diagnosis No	Page No
antimony	0055	102
aplastic anaemia	0053	97
aromatic hydrocarbons, halogenated	0047	86
aromatic nitrocompounds	0053	97
aromatic amines	0051	93
arsenic compounds	0002	14
arsenic inorganic compounds	0002	14
arsenic hydride	0060	108
asbestos	0068	119
asbestos warts	0068	119
asbestosis	0068	119
asthma, bakers and millers	0088	163
asthma	0088	163
azospermia	0096	175
barium	0072	127
Benzene derivates, halogenated	0047	86
benzene	0043	79
benzoic	0059	106
benzoquinone	0050	92
beryllium	0003	16
biocides	0074	130
biphenyls and polyphenyls, halogenated	0047	86
bird	0078	135
bitumen	0065	114
bovine tuberculosis	0078	135
bromine	0023	49
bronchial cancer	0010	29
bronchial cancer	0003	16
bronchopneumopathy, chronic obstructive	0010	29
brucellosis	0078	135
1,4-butanediol	0034	66

Key-word	Diagnosis No	Page No
butanol	0033	65
butyric acid	0059	106
cadmium	0009	27
cancer of the bladder	0051	93
cancers	0066	116
carbamates	0040	75
carbazole	0065	114
carbides, sintered	0073	129
carbon monoxide	0004	18
carbon disulphide	0020	45
carboxylic acid	0059	106
carpal tunnel syndrome	0086	160
cataract	0085	156
cataract	0096	175
catechols	0093	172
ceramics	0003	16
cerebellar syndrome	0011	31
cerebral deformities (e.g. microcephalus)	0096	175
chlamydiosis	0078	135
chloracne	0048	89
chloracne	0047	86
chlorine	0022	48
chromium	0010	29
chronic encephalopathy	0062	110
chronic lead nephropathy	0018	41
chronic radiodermatitis	0096	175
chrysotile	0068	119
classification of Raleigh	0062	110
coal-miners	0061	109
coccidioidomycosis	0078	135
cochlea	0080	148

Key-word	Diagnosis No	Page No
colophony	0088	163
communicable diseases, most	0078	135
complicated silicosis	0067	117
cotton	0070	124
crocidolite	0068	119
crotonic acid	0059	106
cutaneous spinocellular epithelioma	0096	175
cyanides	0007	23
deafness	0080	148
decompression diseases	0087	161
dental enamel	0019	43
dermatoses	0090	166
dichloroisopropyl ether	0036	69
dichloromethane	0028	56
diethylene glycol	0034	66
diisocyanates	0088	163
dinitrobenzene	0053	97
dinitrotoluene	0053	97
dinoseb	0054	101
distillation of coal	0065	114
dithiocarbamates	0056	103
divinylbenzene	0046	84
DNT	0053	97
dysbaric osteonecrosis	0087	161
electroplating	0009	27
encephalopathy	0062	110
encephalopathy	0011	31
epicondylitis	0087	161
erysipeloid	0078	135
erysipeloid	0079	143
2-ethoxyethanol	0037	70

Key-word	Diagnosis No	Page No
ethyl ether	0036	69
ethylene glycol	0037	70
ethylene glycol	0034	66
explosives	0035	67
explosives	0017	39
extrapyramidal syndrome	0012	33
extrinsic allergic alveolitis	0094	173
eye, anterior part of	0085	156
farming	0078	135
fertilizers	0017	39
fibrosis	0071	126
fish	0078	135
flax	0070	124
fluoride compounds, inorganic	0025	51
fluorine compounds	0025	51
fluorosis, skeletal	0025	51
forestry	0078	135
formaldehyde	0042	78
formalin	0042	78
formic acid	0059	106
fumaric acid	0059	106
fumigation	0032	64
fungal infections (various)	0078	135
fungicides	0050	92
fungicides	0056	103
glomerular damage	0011	31
glomerulonephritis	0011	31
glycol ethers	0037	70
glycols	0034	66
grain dust	0088	163
granulomatous fibrosis	0003	16
graphite dust	0071	126

Key-word	Diagnosis No	Page No
guaiacol	0036	69
Guyon's cavity syndrome	0086	160
haemolytic anaemia	0051	93
haemolytic anaemia	0053	97
hair	0078	135
hairdressers	0088	163
haptens	0089	165
hard metals	0073	129
health-care workers	0078	135
haemolytic syndrome	0058	105
hemp	0070	124
hepatitis, toxic	0047	86
hepatitis, toxic	0051	93
herbicides	0056	103
herbicides	0054	101
hides	0078	135
histoplasmosis	0078	135
hookworm	0078	135
hydrocyanic acid	0006	21
hydrogen cyanide	0006	21
hydrogen antimonide	0058	105
hydroquinone	0093	172
hygroma	0084	155
hypersensitivity pneumonitis	0094	173
hypoacusis	0080	148
infectious diseases, transmitted by animals	0079	143
infectious diseases	0078	135
inorganic tin	0075	131
insecticides	0056	103
iodine	0024	50
ionizing radiation	0096	175
iron dust	0077	133

Key-word	Diagnosis No	Page No
irritation of the skin	0091	168
ischaemic heart disease	0028	56
ischaemic heart disease	0004	18
isocyanates	0008	25
isopropanol	0033	65
isopropyl ether	0036	69
jute	0070	124
keratoconjunctivitis	0085	156
ketones	0038	71
lead, inorganic compounds	0018	41
leptospirosis	0078	135
leucoderma	0093	172
leucoderma	0050	92
leukaemia	0043	79
leukaemia	0096	175
liver fibrosis	0031	62
lung cancer	0009	27
lyme arthritis	0079	143
malaria	0078	135
maleic acid	0059	106
malonic acid	0059	106
manganese	0012	33
MBK	0038	71
meat	0078	135
mechanical vibration	0080	148
mechanical pressure	0084	155
medullary aplasia	00096	175
meniscal diseases	0095	174
mental retardation	0096	175
mercury compounds	0011	31
'metal fume fever'	0009	27

Key-word	Diagnosis No	Page No
metallic cobalt	0073	129
methacrylic acid	0059	106
methaemoglobinaemia	0035	67
methaemoglobinaemia	0051	93
methaemoglobinaemia	0053	97
methanol	0033	65
2-methoxyethanol	0037	70
methyl n-butyl ketone	0038	71
methyl bromide	0032	64
methyl ether	0036	69
methyl acrylate	0041	77
methylene chloride	0028	56
methylmethacrylate	0057	104
middle ear	0080	148
mineral and other oils	0065	114
miner's nystagmus	0085	156
MMA	0057	104
MMT	0012	33
molybdenum	0073	129
monobenzene	0093	172
monoethyl ether	0037	70
monoethyl ether	0037	70
mould fungi	0094	173
mucous membranes	0091	168
muscles and tendons, overstraining	0087	161
n-heptane	0027	55
n-hexane	0026	53
naphthalene and its derivatives	0045	82
a-naphthoic acid	0059	106
narcotic syndrome	0036	69
nasal cancer	0042	78

Key-word	Diagnosis No	Page No
nasal cancer	0076	132
naphthol and its chlorinated derivatives	0063	112
nephropathy	0009	27
nephtropathy	0011	31
nephrotic syndrome	0011	31
nerve	0086	160
Newcastle virus disease	0078	135
nickel	0016	38
nickel carbonyl	0064	113
nitric acid	0013	35
nitro derivatives of phenols	0054	101
nitro derivatives of glycerol	0035	67
nitro derivatives of glycols	0035	67
nitro derivatives of hydroxybenzotrile	0054	101
nitrobenzene	0053	97
4-nitro diphenal	0053	97
4-nitrodipmenyl	0053	97
nitrogen oxides	0014	36
noise	0080	148
non-ionizing radiation	0085	156
ocular detriment	0050	92
oil industry	0015	37
oligospermia	0096	175
oral cavity disorders	0011	31
organic dusts	0094	173
organic solvents	0062	110
organic acids	0059	106
oragnophosphorous esters	0039	73
ornithosis	0079	143
osteoarticular disorders	0083	154
osteosarcoma	0096	175
oxalic acid	0059	106

Key-word	Diagnosis No	Page No
PAH	0065	114
painful shoulder	0087	161
paint	0028	56
papulovesicular lesions	0003	16
paraffin	0065	114
parasitic diseases	0078	135
Parkinsonism	0020	45
PBB	0047	86
PCB	0047	86
PCP	0048	89
pentachlorophenol	0048	89
pantane	0062	110
perchlorethylene	0030	60
periarticular bursae	0084	155
peripheral neuropathy	0039	73
persulphates	0088	163
pesticides	0056	103
petrol	0043	79
phenols	0093	172
phosgene	0005	20
phosphine gas	0017	39
phosphoric acid	0017	39
phosphorus	0017	39
photographic films	0024	50
photoretinitis	0085	156
pigments	0009	27
pigments	0051	93
pitch	0065	114
plastic materials	0018	41
plastics	0074	130
PMMA	0057	104
pneumoconiosis	0069	122

Key-word	Diagnosis No	Page No
pneumoconiosis	0071	126
politeal nerve, the external	0086	160
polynuclear aromatic compounds	0065	114
polynuclear compounds, halogenated	0047	86
polyurethane	0008	25
portal hypertension	0031	62
poultry	0078	135
primary cancer of the lung	0096	175
progressive massive fibrosis — PMF	0067	117
propionic acid	0059	106
Q fever	0079	143
Q fever	0078	135
rabies	0078	135
radial styloiditis	0087	161
Raynaud's phenomenon	0031	62
Raynaud's phenomenon	0035	67
Raynaud's phenomenon	0083	154
rayon	0020	45
refrigeration	0015	37
renal tubular impairment	0011	31
reproductive risks	0092	171
retinal disorders	0085	156
retrolobular optical neuritis	0020	45
rickettsial diseases	0078	135
rodenticides	0017	39
rubber industry	0020	45
b-naphtonic acid	0059	106
schistosomiasis	0078	135
sensorimotor polyneurophaty	0026	53
sewer work	0078	135
siderosis	0077	133
silicates	0069	122

Key-word	Diagnosis No	Page No
silicosis	0067	117
sinonasal cancer	0076	132
sisal	0070	124
skeletal deformities	0096	175
skin irritation of	0091	168
skin cancers	0085	156
smoking tobacco	0065	114
soot	0065	114
stannosis	0075	131
steel, special	0016	38
stibine	0058	105
stibiosis	0055	102
styrene	0062	110
styrene	0046	84
sulphur oxides	0019	43
sulphur acid	0019	43
surfactants	0041	77
talcosis	0069	122
tantalum	0073	129
tar	0065	114
tarsal tunnel syndrome	0086	160
tendinitis of the extensors and flexors	0087	161
tenosynovitis	0087	161
tetanus	0078	135
tetrachlor ethylene	0030	60
tin, organic compounds of	0074	130
tinnitus	0080	148
titanium	0073	129
toluene	0044	81
toluene	0062	110
toxic nephropathy	0011	31

Key-word	Diagnosis No	Page No
toxic encephalopathy	0018, 0062	41, 110
toxic polyneuropathy	0011	31
1,1,2, trichloroethane	0062	110
trichloroethylene	0029	58
trigger finger	0087	161
trypanosomiasis	0078	135
TTCA	0020	45
tuberculosis	0078	135
tularaemia	0078	135
tularaemia	0079	143
tungsten	0073	129
tympanic membrane	0080	148
ulnar nerve groove syndrome	0086	160
urine proteins	0088	163
vanadium	0021	47
vanadium	0073	129
varnish remover	0028	56
veterinary	0078	135
vibration	0083	154
vinyl chloride monomer	0031	62
vinyl ether	0036	69
vinylbenzene	0046	84
viral hepatitis	0078	135
viscose	0020	45
vitiligo	0093	172
wood	0078	135
wood dust	0076	132
xylene	0062	110

Cross-reference index

Diagnosis No	European Schedule No	Cross-reference diagnosis No
0001	100	0066, 0090, 0091
0002	101	0091
0003	102	0066, 0090, 0091
0004	103.01	
0005	103.02	0091
0006	104.01	0091
0007	104.02	0091
0008	104.03	0089, 0090, 0091, 0094
0009	105	0066
0010	106	0066, 0088, 0090, 0091
0011	107	0090, 0091
0012	108	
0013	109.01	0091
0014	109.02	0091
0015	109.03	0091
0016	110	0066, 0088, 0090
0017	111	0091
0018	112	
0019	113.01, 113.02	
0020	113.03	0091
0021	114	0091
0022	115.01	0088, 0090, 0091
0023	115.02	0091
0024	115.04	0091
0025	115.05	0091
0026	116	0062, 0091
0027	116	0091
0028	116	0091
0029		0062, 0091
0030		0062, 0091

Diagnosis No	European Schedule No	Cross-reference diagnosis No
0031	117	0066, 0091
0032	117	0091
0033	118	0091
0034	119	0091
0035		
0036	120	0062, 0091
0037		0091
0038	121	0026, 0062, 0091
0039	122	
0040		
0041		0090, 0091
0042	124	0066, 0088, 0090, 0091
0043	126.01	0062, 0091
0044		0062, 0091
0045	126.02	
0046	126.03	0062, 0091
0047	127, 128.02	0091
0048		0091
0049	128.03, 128.04	0091
0050	128.05	0091, 0093
0051	129.01	0066, 0088, 0090, 0091
0052	129.02	0089, 0090
0053	130.01	0090, 0091
0054	130.04	0091
0055	131	0091
0056		066, 0090, 0091
0057		0088, 0089, 0090, 0091
0058		
0059	123	0090
0060		
0061		

Diagnosis No	European Schedule No	Cross-reference diagnosis No
0062	116, 125, 128.01	
0063		0091
0064		
0065	201.01, 201.02, 201.03, 201.04, 201.05, 201.06, 201.07, 201.08, 201.09	0066, 0090, 0091
0066	301	
0067	301.11, 301.12	
0068	301.21, 301.22, 302	0066
0069	301.31	0067, 0068
0070	304.02	
0071	304.04	
0072	304.04	0091
0073	304.04	0088
0074		0091
0075	304.04	0091
0076	305.01	0088, 0089, 0090, 0091, 0094
0077	304.05	0067, 0091
0078	401, 402, 403, 404, 405, 406	0079
0079		0078
0080	503	
0081	504	
0082	504	
0083	505.01, 505.02	
0084	506.10	
0085	502.01, 502.02	0066
0086	506.40	
0087	506.21, 506.22, 506.23	
0088	304.03	
0089	304.03	0088
0090	202	
0091		

Diagnosis No	European Schedule No	Cross-reference diagnosis No
0092		
0093		
0094	304.01, 304.03	
0095	506.30	
0096	508	0066

Annex

II

(Acts whose publication is not obligatory)

COMMISSION

COMMISSION RECOMMENDATION

of 22 May 1990

to the Member States concerning the adoption of a European schedule of occupational diseases

(90/326/EEC)

The Commission, under the terms of the Treaty establishing the European Economic Community and in particular Article 155 thereof, and without prejudice to more favourable national laws or regulations, recommends that the Member States :

1. introduce as soon as possible into their national laws, regulations or administrative provisions concerning scientifically recognized occupational diseases liable for compensation and subject to preventive measures, the European schedule in Annex I ;
2. take steps to introduce into their national laws, regulations or administrative provisions the right of a worker to compensation in respect of occupational diseases if the worker is suffering from an ailment which is not listed in Annex I but which can be proved to be occupational in origin and nature, particularly if the ailment is listed in Annex II ;
3. ensure as far as possible that all cases of occupational disease are reported and progressively make their statistics on occupational diseases compatible with the schedule in Annex I ;
4. — develop and improve the various preventive measures for the diseases mentioned in the European schedule, turning, if necessary, to the Commission for information on the experience acquired by Member States,
— use for this purpose the European schedule as a reference document on the prevention of occupational diseases and certain work accidents ;
5. — circulate notices on the occupational diseases in their national list, taking special account of the medical information notices on occupational diseases in the European schedule, drawn up by the Commission,
— supply in particular all relevant information on diseases or agents recognized in their national legislation when requested to do so by another Member State through the Commission, and supply the Commission with statistical and epidemiological information on the incidence of occupational diseases ;
6. Provide the personnel responsible for implementing the national provisions resulting from this recommendation with adequate training ;
7. — introduce a system for the collection of information on data concerning the epidemiology of the diseases listed in Annex II and any other disease of an occupational nature,
— promote research in the field of ailments linked to an occupational activity, in particular the ailments listed in Annex II.

This recommendation shall not apply to diseases which are not recognized as being occupational in origin.

The Member States shall themselves determine the criteria for recognizing each occupational disease in accordance with their current national laws or practices.

The Commission requests the Member States to inform it, at the end of a three-year period, of the measures taken or envisaged in response to this recommendation. The Commission will then examine the extent to which this recommendation has been implemented in the Member States, in order to determine whether there is a need for binding legislation.

Done at Brussels, 22 May 1990.

For the Commission
Vasso PAPANDEOU
Member of the Commission

ANNEX I

EUROPEAN SCHEDULE OF OCCUPATIONAL DISEASES

The diseases mentioned in this schedule must be linked directly to the occupation. The Commission will determine the criteria for recognizing each of the occupational diseases listed hereunder :

1.	Diseases caused by the following chemical agents :	<i>EEC No</i>
100	Acrylonitrile	608 003 004
101	Arsenic or compounds thereof	033 002 005
102	Beryllium (glucinium) or compounds thereof	—
103.01	Carbon monoxide	006 001 002
103.02	Carbon oxychloride	—
104.01	Hydrocyanic acid	—
104.02	Cyanides and compounds thereof	006 007 005
104.03	Isocyanates	—
105	Cadmium or compounds thereof	048 001 005
106	Chromium or compounds thereof	—
107	Mercury or compounds thereof	080 001 000
108	Manganese or compounds thereof	—
109.01	Nitric acid	007 004 001
109.02	Oxides of nitrogen	007 002 000
109.03	Ammonia	007 001 005
110	Nickel or compounds thereof	—
111	Phosphorus or compounds thereof	015 001 001
112	Lead or compounds thereof	082 001 006
113.01	Oxides of sulphur	—
113.02	Sulphuric acid	016 020 008
113.03	Carbon disulphide	006 003 003
114	Vanadium or compounds thereof	—
115.01	Chlorine	017 001 007
115.02	Bromine	—
115.04	Iodine	602 005 003
115.05	Fluorine or compounds thereof	009 001 000
116	Aliphatic or alicyclic hydrocarbons derived from petroleum spirit or petrol	—
117	Halogenated derivatives of the aliphatic or alicyclic hydrocarbons	—
118	Butyl, methyl and isopropyl alcohol	—
119	Ethylene glycol, diethylene glycol, 1,4-butanediol and the nitrated derivatives of the glycols and of glycerol	—
120	Methyl ether, ethyl ether, isopropyl ether, vinyl ether, dichloroisopropyl ether, guaiacol, methyl ether and ethyl of ethylene glycol	—
121	Acetone, chloroacetone, bromoacetone, hexafluoroacetone, methyl ethyl ketone, methyl n-butyl ketone, methyl isobutyl ketone, diacetone alcohol, mesityl oxide, 2-methylcyclohexanone	—
122	Organophosphorus esters	—
123	Organic acids	—
124	Formaldehyde	—
125	Aliphatic nitrated derivatives	—
126.01	Benzene or counterparts thereof (the counterparts of benzene are defined by the formula : C_nH_{2n-6})	601 020 008
126.02	Naphthalene or naphthalene counterparts (the counterpart of naphthalene is defined by the formula : C_nH_{2n-12})	—
126.03	Vinylbenzene and divinylbenzene	—
127	Halogenated derivatives of the aromatic hydrocarbons	—

		<i>EEC No</i>
128.01	Phenols or counterparts or halogenated derivatives thereof	—
128.02	Naphthols or counterparts or halogenated derivatives thereof	—
128.03	Halogenated derivatives of the alkylaryl oxides	—
128.04	Halogenated derivatives of the alkylaryl sulfonates	—
128.05	Benzoquinones	—
129.01	Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof	—
129.02	Aliphatic amines and halogenated derivatives thereof	—
130.01	Nitrated derivatives of aromatic hydrocarbons	—
130.02	Nitrated derivatives of phenols or their counterparts	—
131	Antimony and derivatives thereof	051 003 009
2.	Skin diseases caused by substances and agents not included under other headings	
201	<i>Skin diseases and skin cancers caused by:</i>	
201.01	Soot	
201.02	Tar	
201.03	Bitumen	
201.04	Pitch	
201.05	Anthracene or compounds thereof	—
201.06	Mineral and other oils	
201.07	Crude paraffin	
201.08	Carbazole or compounds thereof	—
201.09	By-products of the distillation of coal	
202	Occupational skin ailments caused by scientifically recognized allergy provoking or irritative substances not included under other headings	
3.	Diseases caused by the inhalation of substances and agents not included under other headings	
301	<i>Diseases of the respiratory system and cancers:</i>	
301.11	Silicosis	
301.12	Silicosis combined with pulmonary tuberculosis	
301.21	Asbestosis	
301.22	Mesothelioma following the inhalation of asbestos dust	
301.31	Pneumoconioses caused by dusts of silicates	
302	Complication of asbestos in the form of bronchial cancer	
303	Broncho-pulmonary ailments caused by dusts from sintered metals	
304.01	Extrinsic allergic alveolites	
304.02	Lung diseases caused by the inhalation of dusts and fibres from cotton, flax, hemp, jute, sisal and bagasse	
304.03	Respiratory ailments of an allergic nature caused by the inhalation of substances consistently recognized as causing allergies and inherent to the type of work	
304.04	Respiratory ailments caused by the inhalation of dust from cobalt, tin, barium and graphite	
304.05	Siderosis	
305.01	Cancerous diseases of the upper respiratory tract caused by dust from wood	
4.	Infectious and parasitic diseases:	
401	Infectious or parasitic diseases transmitted to man by animals or remains of animals	
402	Tetanus	
403	Brucellosis	
404	Viral hepatitis	
405	Tuberculosis	
406	Amoebiasis	
5.	Diseases caused by the following physical agents:	
502.01	Cataracts caused by heat radiation	
502.02	Conjunctival ailments following exposure to ultraviolet radiation	
503	Hypoacusis or deafness caused by noise	
504	Diseases caused by atmospheric compression or decompression	

505.01	Osteoarticular diseases of the hands and wrists caused by mechanical vibration
505.02	Angioneurotic diseases caused by mechanical vibration
506.10	Diseases of the periarticular sacs due to pressure
506.21	Diseases due to overstraining of the tendon sheaths
506.22	Diseases due to overstraining of the peritendineum
506.23	Diseases due to overstraining of the muscular and tendonous insertions
506.30	Meniscus lesions following extended periods of work in a kneeling or squatting position
506.40	Paralysis of the nerves due to pressure
507	Miner's nystagmus
508	Diseases caused by ionizing radiation

ANNEX II

ADDITIONAL LIST OF DISEASES SUSPECTED OF BEING OCCUPATIONAL IN ORIGIN WHICH SHOULD BE SUBJECT TO NOTIFICATION AND WHICH MAY BE CONSIDERED AT A LATER STAGE FOR INCLUSION IN ANNEX I TO THE EUROPEAN SCHEDULE

2.1.	Diseases caused by the following chemical agents :	<i>EEC No</i>
2.101	Ozone	—
2.102	Aliphatic hydrocarbons other than those referred to under heading 1.116 of Annex I	—
2.103	Diphenyl	—
2.104	Decalin	—
2.105	Aromatic acids — aromatic anhydrides	—
2.106	Diphenyl oxide	—
2.107	Tetrahydrophurane	603 025 000
2.108	Thiopene	—
2.109	Methacrylonitrile	608 001 003
	Acetonitrile	—
2.110	Hydrogen sulphide	016 001 004
2.111	Thioalcohols	—
2.112	Mercaptans and thioethers	—
2.113	Thallium or compounds thereof	081 002 009
2.114	Alcohols or their halogenated derivatives not referred to under heading 1.118 of Annex I	—
2.115	Glycols or their halogenated derivatives not referred to under heading 1.119 of Annex I	—
2.116	Ethers or their halogenated derivatives not referred to under heading 1.120 of Annex I	—
2.117	Ketones or their halogenated derivatives not referred to under heading 1.121 of Annex I	—
2.118	Esters or their halogenated derivatives not referred to under heading 1.122 of Annex I	—
2.119	Furfural	605 010 004
2.120	Thiophenols or counterparts or halogenated derivatives thereof	—
2.121	Silver	—
2.122	Selenium	034 002 008
2.123	Copper	—
2.124	Zinc	—
2.125	Magnesium	—
2.126	Platinum	—
2.127	Tantalum	—
2.128	Titanium	—
2.129	Terpenes	—
2.130	Boranes	—
2.140	Diseases caused by inhaling nacre dust	
2.141	Diseases caused by hormonal substances	
2.150	Dental caries associated with work in the chocolate, sugar and flour industries	
2.2.	Skin diseases caused by substances and agents not included under other headings :	
2.201	Allergic and orthoallergic skin ailments not recognized in Annex I	
2.3.	Diseases caused by inhaling substances not included under other headings :	
2.301	Pulmonary fibroses due to metals not included in the European schedule	
2.302	Broncho-pulmonary ailments caused by dusts or fumes from aluminium or compounds thereof	

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- 2.303 Broncho-pulmonary ailments and cancers associated with exposure to the following :
— soot,
— tar,
— bitumen,
— pitch,
— anthracene or compounds thereof,
— mineral and other oils
- 2.304 Broncho-pulmonary ailments caused by man-made mineral fibres
- 2.305 Broncho-pulmonary ailments caused by synthetic fibres
- 2.306 Broncho-pulmonary ailments caused by dusts from basic slags
- 2.4. **Infectious and parasitic diseases not described in Annex I :**
- 2.401 Parasitic diseases
- 2.402 Tropical diseases
- 2.403 Infectious diseases, not included in Annex I, of workers engaged in disease prevention, health care, domiciliary assistance or laboratory work and other activities where a risk of infection exists
- 2.5. **Avulsion due to overstraining of the spinous processes**
-

ANNEX III

THE SITUATION IN THE MEMBER STATES

This Annex was adopted in 1989 and is for guidance only, as the situation is in constant development. It will be updated when the Commission presents its report on the impact of the present recommendation in accordance with Item 4 of the explanatory memorandum.

I. Belgium

Belgium has a list of occupational diseases carrying entitlement to compensation.

The occupational diseases are broken down into the following categories :

1. caused by chemical agents ;
2. caused by physical agents ;
3. caused by biological agents ;
4. of the skin due to various causes ;
5. of the respiratory tract due to various causes.

Furthermore, Belgium has lists of 'occupational' diseases not carrying entitlement to compensation, but which are now being studied with a view to possible inclusion in the list of occupational diseases carrying entitlement to compensation.

The mixed system of compensation is not used in Belgium.

2. Denmark

The list of occupational diseases contains seven categories :

1. occupational diseases caused by chemical agents (Category A);
2. occupational diseases of the skin caused by substances or agents which do not come under other headings (Category B);
3. occupational diseases caused by the inhalation of substances or agents which do not come under other headings (Category C);
4. infectious or parasitic occupational diseases (Category D);
5. occupational diseases caused by physical agents (Category E);
6. initial stages of malignant ailments caused by organic compounds (Category F);
7. dental or periodontal diseases (Category G).

The mixed system of compensation is used.

3. Federal Republic of Germany

The list of occupational diseases carrying entitlement to compensation contains six categories :

1. diseases caused by chemical agents ;
2. diseases caused by physical agents ;
3. diseases caused by biological agents ;
4. respiratory tract and lung diseases ;
5. skin diseases ;
6. diseases not covered in the above.

Total : 59 occupational diseases carrying entitlement to compensation.

A mixed system is used on the basis of specific conditions governing compensation.

4. Greece

The list of occupational diseases carrying entitlement to compensation contains five categories :

1. (a) poisoning and allergies caused by 13 listed chemical substances ;
(b) skin diseases caused by chromium and cement ;
2. parasitic and contagious diseases ;
3. (a) diseases caused by physical agents ;
(b) miners' diseases ;
4. skin diseases ;
5. lung diseases.

Total : 52 occupational diseases carrying entitlement to compensation.

The mixed system of compensation is not used.

5. Spain

The list of occupational diseases carrying entitlement to compensation contains six categories :

- diseases caused by chemical agents,
- diseases of the skin caused by agents which do not come under other headings :
 - skin cancers,
 - other skin diseases of occupational origin,
- pneumoconioses,
- infectious and parasitic diseases,
- diseases caused by physical agents,
- diseases not classifiable under other headings.

Total : 71 occupational diseases carrying entitlement to compensation.

The mixed system is not used.

6. France

For the general scheme for employees, there are 91 occupational disease tables, which are not broken down by the agents responsible but by disease families and the products or agents responsible. Compensation for occupational diseases is on a flat-rate basis, but employees are given the benefit of the assumption that their disease is attributable to work if it meets the conditions set out in each table (symptoms of the disease, products or agents, period required for recognition, work involving exposure, and occasionally duration of exposure).

There is a mixed system for recognition and compensation in the case of pneumoconioses, with the procedure involving an approved doctor or a board of three specialists.

A claim for compensation (not limited to a flat-rate) can be made in respect of any disease not covered by the tables by invoking the liability of the employer.

There is also a schedule for occupational diseases containing 47 tables for farmers and farm employees. It effectively corresponds largely to the first schedule, but with special features owing to the particular nature of the risks covered.

A total of 300 symptoms or groups of symptoms carry entitlement to compensation under the general scheme for employees and nearly the same number is covered by the farm scheme. New tables are established or the existing ones are revised when it is found, as a result of epidemiological study, that a new type of disease is, almost certainly, occupationally induced. Furthermore, consideration is being given to the extension of the mixed system.

7. Ireland

The classification of occupational diseases is divided into four categories (A, B, C and D) :

- A : diseases caused by physical agents (14 diseases),
- B : diseases caused by biological agents (10 diseases),
- C : diseases caused by chemical agents (29 diseases),
- D : diseases with various causes other than those above (three diseases).

Total : 56 occupational diseases carrying entitlement to compensation ; seven further occupational diseases have carried entitlement to compensation since 1985.

A mixed system of compensation exists only for certain respiratory diseases, including certain pneumoconioses, respiratory and skin diseases.

8. Italy

There are two lists of occupational diseases :

- one list covering occupational diseases in industry,
- one list covering occupational diseases in agriculture.

The first list contains 49 headings carrying entitlement to compensation not classified by agents responsible.

The second list contains 21 occupational diseases in agriculture carrying entitlement to compensation not classified by agents responsible.

Total : 70 occupational diseases carrying entitlement to compensation.

The system of compensation is currently being amended.

9. Luxembourg

The list of occupational diseases carrying entitlement to compensation contains six categories :

1. diseases caused by chemical agents ;
2. diseases caused by physical agents ;
3. diseases caused by biological agents ;
4. respiratory tract and lung diseases (including pneumoconioses) ;
5. skin diseases ;
6. diseases covered in the above.

Total : 55 occupational diseases carrying entitlement to compensation.

The mixed system is used on the basis of specific conditions governing compensation.

10. Netherlands

In the Netherlands the European Schedule of Occupational Diseases is used as a basic reference document for the diagnosis, reporting and registration of occupational diseases, provided, however, that there is a cause-and-effect link between the disease and the occupational activity. Under the Dutch social security system all cases of disease or incapacity for work give rise to compensation, regardless of the cause.

The form this compensation takes does not depend on whether the disease is occupational in origin or not.

11. Portugal

There are two groups of occupational diseases :

(a) The diseases contained in a list published by the relevant Ministry, which is based on the French list and contains 89 tables of diseases giving the causal agent, the type of disease caused, the recognition period and a list of the main activities responsible. These occupational diseases are divided into seven categories :

1. poisoning ;
2. lung ailments ;
3. dermatoses ;
4. diseases caused by physical agents ;
5. diseases caused by biological agents ;
6. tumours ;
7. mucous membrane allergies.

(b) Injuries, functional disorders or diseases not included in the above list for which no compensation will be obtained unless a link is established between the activity carried out by the worker and the ailment caused (mixed system).

12. United Kingdom

The list of occupational diseases contains four categories (A, B, C and D) :

A : diseases caused by physical agents (11 diseases) ;

B : diseases caused by biological agents (nine diseases) ;

C : diseases caused by chemical agents (29 diseases) ;

D : diseases with various causes which do not come under the above categories (10 diseases).

Total : 59 occupational diseases carrying entitlement to compensation.

There is no mixed system of compensation, except in the case of industrial accidents and certain specific diseases.

**Items of Annex I list of the Commission recommendation
with cross-references to DIAG numbers**

Name	Number	Diagnosis	Page No
acrylonitrile	100	0001	13
arsenic or compounds thereof	101	0002	14
beryllium (glucinium) or compounds thereof	102	0003	16
carbon monoxide	103.01	0004	18
carbon oxychloride	103.02	0005	20
hydrocyanic acid	104.01	0006	21
cyanides and compounds thereof	104.02	0007	23
isocyanates	104.03	0008	25
cadmium or compounds thereof	105	0009	27
chromium or compounds thereof	106	0010	29
mercury or compounds thereof	107	0011	31
manganese or compounds thereof	108	0012	33
nitric acid	109.01	0013	35
oxides of nitrogen	109.02	0014	36
ammonia	109.03	0015	37
nickel or compounds thereof	110	0016	38
phosphorus or compounds thereof	111	0017	39
lead or compounds thereof	112	0018	41
oxides of sulphur	113.01	0019	43
sulphuric acid	113.02	0019	43
carbon disulphide	113.03	0020	45
vanadium or compounds thereof	114	0021	47
chlorine	115.01	0022	48
bromine	115.02	0023	49
iodine	115.04	0024	50
fluorine or compounds thereof	115.05	0025	51
aliphatic or alicyclic hydrocarbons derived from petroleum spirit or petrol	116	0028 0027 0062	56 55 110
halogenated derivatives of the aliphatic or alicyclic hydrocarbons	117	0031 0032	62 64

Name	Number	Diagnosis	Page No
butyl, methyl and isopropyl alcohol	118	0033	65
ethylene glycol, diethylene glycol, 1,4-butanediol and the nitrated derivatives of the glycols and of glycerol	119	0034	66
methyl ether, ethyl ether, isopropyl ether, vinyl ether, dichloroisopropyl ether, guaiacol, methyl ether and ethyl of ethylene glycol	120	0036	69
acetone, chloroacetone, bromoacetone, hexafluoroacetone, methyl ethyl ketone, methyl n-butyl ketone, methyl isobutyl ketone, diacetone alcohol, mesityl oxide, 2-methylcyclohexanone	121	0038	71
organophosphorus esters	122	0039	73
organic acids	123	0059	106
formaldehyde	124	0042	78
aliphatic nitrated derivatives	125	0062	110
benzene or counterparts thereof (the counterparts of benzene are defined by the formula: C_nH_{2n-6})	126.01	0043	79
naphthalene or naphthalene counterparts (the counterpart of naphthalene is defined by the formula: C_nH_{2n-12})	126.02	0045	82
vinylbenzene and divinylbenzene	126.03	0046	84
halogenated derivatives of the aromatic hydrocarbons	127	0047	86
phenols or counterparts or halogenated derivatives thereof	128.01	0062	110
naphthols or counterparts or halogenated derivatives thereof	128.02	0047	86
halogenated derivatives of the alkylaryl oxides	128.03	0049	91
halogenated derivatives of the alkylaryl sulphonates	128.04	0049	91
benzoquinones	128.05	0050	92
aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulphonated derivatives thereof	129.01	0051	93
aliphatic amines and halogenated derivatives thereof	129.02	0052	95
nitrated derivatives of aromatic hydrocarbons	130.01	0053	97
nitrated derivatives of phenols or their counterparts	130.02	0054	101
antimony and derivatives thereof	131	0055	102
Skin diseases and skin cancers caused by:	201	—	
soot	201.01	0065	114

Name	Number	Diagnosis	Page No
tar	201.02	0065	114
bitumen	201.03	0065	114
pitch	201.04	0065	114
anthracene or compounds thereof	201.05	0065	114
mineral and other oils	201.06	0065	114
crude paraffin	201.07	0065	114
carbazole or compounds thereof	201.08	0065	114
by-products of the distillation of coal	201.09	0065	114
occupational skin ailments caused by scientifically recognized allergy provoking or irritative substances not included under other headings	202	0090	166
diseases of the respiratory system and cancers	301	0066	116
silicosis	301.11	0067	117
silicosis combined with pulmonary tuberculosis	301.12	0067	117
asbestosis	301.21	0068	119
mesothelioma following the inhalation of asbestos dust	301.22	0068	119
pneumoconioses caused by dusts of silicates	301.31	0069	122
complication of asbestos in the form of bronchial cancer	302	0068	119
broncho-pulmonary ailments caused by dusts from sintered metals	303	0073	129
extrinsic allergic alveolitis	304.01	0094	173
lung diseases caused by the inhalation of dusts and fibres from cotton, flax, hemp, jute, sisal and bagasse	304.02	0070	124
respiratory ailments of an allergic nature caused by the inhalation of substances consistently recognized as causing allergies and inherent to the type of work	304.03	0088 0089 0094	163 165 173
respiratory ailments caused by the inhalation of dust from cobalt, tin, barium and graphite	304.04	0071, 0075 0072, 0075	124, 131 127, 129
siderosis	304.05	0077	133
cancerous diseases of the upper respiratory tract caused by dust from wood	305.01	0076	132
infectious or parasitic diseases transmitted to man by animals or remains of animals	401	0078	135
tetanus	402	0078	135

Name	Number	Diagnosis	Page No
brucellosis	403	0078	135
viral hepatitis	404	0078	135
tuberculosis	405	0078	135
amoebiasis	406	0078	135
cataracts caused by heat radiation	502.01	0085	156
conjunctival ailments following exposure to ultraviolet radiation	502.02	0085	156
hypercousis or deafness caused by noise	503	0080	148
diseases caused by atmospheric compression or decompression	504	0081 0082	150 152
osteoarticular diseases of the hands and wrists caused by mechanical vibration	505.01	0083	154
angioneurotic diseases caused by mechanical vibration	505.02	0083	154
diseases of the periarticular sacs due to pressure	506.10	0084	155
diseases due to overstraining of the tendon sheaths	506.21	0087	161
diseases due to overstraining of the peritendineum	506.22	0087	161
diseases due to overstraining of the muscular and tendonous insertions	506.23	0087	161
meniscus lesions following extended periods of work in a kneeling or squatting position	506.30	0095	174
paralysis of the nerves due to pressure	506.40	0086	160
miner's nystagmus	507	—	
diseases caused by ionizing radiation	508	0096	175

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