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COMMISSION OF THE EUROPEAN COMMUNITIES

M E D I C A L P A R T I C U L A R S

ON THE DISEASES RECORDED IN THE

APPENDIX II

of the Recommendation by the Commission to Member States

concerning the adoption of a

EUROPEAN SCHEDULE OF INDUSTRIAL DISEASES

(Recommendation of 23rd July 1962 - J.O. of 31/8/1962 No.80)

Working Paper

LIST OF EXPERTS

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P R E F A C E

The E.E.C. Recommendation of 23rd July 1962 to member states concerning industrial diseases was accompanied by two appended schedules :

- the European schedule of industrial diseases (APPENDIX I)
- the schedule of diseases possibly to be entered in the European schedule (APPENDIX II).

This Recommendation foresaw that Medical Particulars should be drawn up for these diseases. The Particulars relating to APPENDIX I were drawn up by a Group of independent medical experts and the collection was published in 1972.

The diseases included in APPENDIX II have been dealt with in a similar manner and the work is presented here.

For these diseases a certain number of studies and publications were in general already available. However, a deepening of this knowledge was necessary. Three courses of action were advocated : the exchange of information between member states, the compulsory notification of the diseases included in this indicative list and the drawing up of Medical Particulars similar in their presentation and spirit to those prepared for the diseases of APPENDIX I.

The diseases included in APPENDIX II do not possess the same obvious character either in their symptomatology or in their relation to the occupation as the diseases mentioned in APPENDIX I.

The diseases concerned here are in fact relatively less frequent or less well-known or else they may be caused by agents which are encountered not very often or only fairly recently in the industrial environment. Furthermore, certain diseases which do not appear in the schedule of APPENDIX II also justify inclusion.

The study of these diseases often rests upon a small number of observations. It seemed useful therefore to mention in several of these new Particulars (and contrary to those of APPENDIX I) some information acquired in animal experiments when these revealed disorders which suggested that a danger to humans in the industrial environment might be feared. It may be appropriate, however, to recall here the caution with which such attempts of extrapolation from animal to human organism have to be treated.

These Medical Particulars, like the Particulars of APPENDIX I, are intended for general information. In addition, though, they also serve to draw attention to hazards, little known as yet, of the industrial environment. Some brief ideas regarding medical prevention have been suggested but they must not be regarded as an adequately developed chapter on "Prevention".

The schedule of diseases which forms the subject of the present work should not be considered as an exhaustive complement of the schedule of APPENDIX I. Diseases which are not included in either of the two appendices are known in industrial environments and others will yet be discovered. However, this collection represents the bulk of industrial diseases. Special attention was given to the preparation of notes on the pathology which may be occasioned by techniques or products newly introduced in industrial environments, and on subjects which seemed to be dealt with inadequately elsewhere. In view of both, new medical acquisitions and technical developments, these Particulars should be periodically reconsidered.

It is important to bear in mind the interest represented by the collection and the study of information on concrete cases of infrequently occurring, new or as yet little known diseases encountered in any of the countries of the Community.

The rapid development of knowledge has already given rise in the countries of the Community to the registration of certain of these diseases in their national schedule of industrial diseases liable to compensation.

This new knowledge will also make necessary the study of a revision of the European schedule of industrial diseases.

Certain of the diseases considered in these Particulars of APPENDIX II have well defined clinical, biological or radiological characteristics, clear correlations with working conditions and an already significant frequency. There are many others, however, which do not possess such clear association with work - statistical facts which seem indispensable in order to consider them systematically as industrial diseases automatically liable to compensation under this heading. Furthermore, occupational factors may have an influence on the development of chronic diseases of any other origin; these interactions have not yet been sufficiently investigated.

Yet it is necessary that individual cases where a connection between occupational cause at harmful effect has been established should be entitled to compensation of the same order as the other health hazards (accidents or diseases) of occupational origin. Adequate regulations are indispensable in order to avoid :

- that each country should have to widen indefinitely the schedule of industrial diseases automatically entitling to compensation, thus progressively taking all value from this conception, or
- that cases of true industrial disease should unjustly remain without effective compensation.

The mixed system, advocated by the Commission in their recommendations, meets this necessity.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A1
OZONE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY OZONE

Ozone (O_3) is an allotropic variety of oxygen in the form of triatomic molecules. Its odour is perceptible in air in very low concentrations.

Ozone is present in air in very small quantities. It is formed by the dissociation of oxygen molecules O_2 and reassemblage to O_3 by means of ionization phenomena under the action of high-voltage electric discharges, which may be natural (storms) or artificial of various kinds (arc welding, glow discharges), X-radiation or UV-radiation.

It is stable at normal temperature but at high temperature the O_3 molecule dissociates into a free oxygen atom and a normal oxygen molecule O_2. This is an active oxidant.

For industrial applications it is supplied either in solution in chlorofluorinated derivatives of methane or of ethane or in the form of compressed gas in cylinders (do not grease screw-threads).

I. SOURCES OF DANGER

The main industrial sources of danger reside either in the utilization of the gas as :

- bleaching agent for paper pulp, textiles, flour, starch, sugar and waxes;
- sterilizing agent for air and water;
- oxidant;
- catalyst;

- agent intervening in the preparation of vanillin, of camphor, certain perfumes, etc...;
- preserving agent in refrigeration chambers;
- purifying agent for mineral oils and their derivatives (former usage);

or in the formation of ozone during arc welding and by electric equipment producing ultraviolet radiations or ionizing radiations; in such cases frequently simultaneous formation of nitrogen oxides and of hydrogen oxide occurs, the synergic action of which intervenes in the pathological phenomena.

Ozone has also been recommended :

- as a bactericide in industrial, medical, private localities (it seems, however, that this bactericidal action is very slight if not zero in doses that are not harmful to man);
- as a deodorizer in the same type of localities (such deodorizing action however appears more likely to be the consequence of a diminution of the olfactory sense through the action of ozone on the nasal mucosae than the consequence of a chemical action);
- as an oxidant for carbon monoxide which would thus be converted to carbon dioxide in garages (such an oxidation of carbon monoxide by ozone will be practically zero however at ordinary temperature and with the concentrations used).

Finally, ozone constitutes one of the harmful elements of the atmospheric pollution of towns, especially owing to its oxidizing effect.

II. PHYSIOPATHOLOGY

Ozone is above all a strong irritant of the mucosae. Its inhalation seems to bring about also a certain degree of depression of the central nervous system.

Its action becomes manifest especially upon the respiratory mucosae where it causes irritation phenomena which may give rise to acute pulmonary oedema. This direct action favours moreover phenomena of superimposed respiratory infection.

Tests in humans have demonstrated :

at 0,5 ppm : phenomena of respiratory irritation;
at 1 ppm for a short time : to the phenomena of respiratory irritation are added tachycardia, more or less pronounced prostration and abdominal pains.

Bearing in mind the observations made, it appears that with concentrations of 5 ppm there is already a danger of the occurrence of acute pulmonary oedema in man and that prolonged exposures to not immediately harmful concentrations appear to favour the appearance of pulmonary emphysema and of chronic bronchitis.

The action on the ocular mucosae brings about a conjunctivitis in man. However, an experimental exposure of 6 hours daily during one year to such concentrations, which are slightly above urban concentrations, did not produce disorders that could be detected in a thorough ophthalmological examination.

III. CLINICAL SYNDROME AND DIAGNOSIS

Slight intoxications manifest themselves by signs of irritation of eye, nose and throat, with coughing, watering of the eyes, vertigo, increasing tiredness. These phenomena disappear fairly rapidly when exposure stops, but are more lasting after regular extended exposure.

In more serious cases, when exposure has been substantial, respiration is more difficult and cases of acute pulmonary oedema have been reported. In other cases, in addition to phenomena of marked pulmonary irritation (dyspnoea, cough) palpitations, a lowering of blood pressure and a rapidly growing asthenia with loss of conscience occur. Rapid medical attention will, however, ensure complete and rapid recovery.

Repeated exposure to slight doses for several hours per week may be the cause of respiratory (dyspnoea, cough) and nervous (cephalalgia, vertigo, somnolence) disorders.

The tests of respiratory function are sometimes abnormal but these variable disturbances have no definite general character and are not specific.

Finally, the projection of liquid ozone may cause cutaneous or ocular lesions like burns.

IV. COMPLEMENTARY RECOMMENDATIONS

Ozone can be detected and measured in air by ultraviolet equipment or by a potassium iodide process. Other gases which are frequently associated may be separated by preliminary bubbling through solutions of chromic acid and potassium permanganate.

It is detected on an average by the sense of smell in concentrations from 0.01 ppm, but exposure quickly brings about a diminution of the olfactive sensitiveness.

Beside technical measures of prevention (among which is the perfect isolation of electrical equipment) it is medically recommended not to expose persons with pulmonary or cardiac lesions or heavy smokers to a risk of an inhalation of substantial concentrations of ozone.

It should be noted that ozone produces a more rapid ageing of rubber and hence a risk of more rapid formation of cracks in the same when used in respiratory protection apparatuses.

Recomm. 1962 - Ind. diseases
APPENDIX II-PARTICULAR NO. A2
ESTERS OF SULPHURIC AND SULPHUROUS ACIDS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE ESTERS OF SULPHURIC AND SULPHUROUS ACIDS.

Of all the esters of sulphur acids only those of sulphuric acid are of real importance on an industrial level. The esterification of sulphuric acid permits the production of monosubstituted or disubstituted compounds of the types : $R-O-SO_2-OH$ or $(R-O)_2-SO_2$. The derivatives liable to produce health hazards in industrial environment are the derivatives wherein the radicals R are alkyl groups.

The main representative of these derivatives is dimethyl sulphate which will be described as a typical example; the corresponding diethyl compounds are used less frequently; they would have a similarly aggressive effect; the same is true of the esters of other sulphur acids, for example, those of sulphonic acids which are used above all in laboratories.

DIMETHYL SULPHATE (1)

Dimethyl sulphate, also known as methyl sulphate, $(CH_3)_2-SO_4$ is the dimethyl ester of sulphuric acid; at ordinary temperature it is an oily, colourless and almost odourless liquid. Its boiling point is 188°C, but it emits vapours which are heavier than air already at ordinary temperature. It is only slightly soluble in water but dissolves readily in most organic solvents.

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(1) some indications were already included in Particular A18 e (page 132) of Appendix I.

I. SOURCES OF DANGER

Dimethyl sulphate is a methylation agent for amino compounds used in the synthesis of organic chemical products, notably of esters, of phenol derivatives (methylaminophenol),etc...

The main sources of danger exist in the perfume and dyestuff industries and in the preparation of vanillin, caffeine, codeine and antipyrine.

The hazards are particularly increased by working at high temperatures and under pressure.

II. PHYSIOPATHOLOGY

Various theories have been put forward to explain the action of dimethyl sulphate : some suggest that it acts directly through its alkylating properties; others believe that its action is a result of its decomposition on contact with the mucosae hydrolizing into sulphuric acid and methyl alcohol or again into formaldehyde and formic acid in situ or in the organism. The acid so liberated produces after a latent period more or less serious burns of the mucosae. Analogous phenomena are possible on the skin but to a much smaller degree.

On contact of the liquid with the skin a certain percutaneous absorption is possible. Corrosive phenomena on the mucosae and on the skin predominate. An effect on the central nervous system, on the kidneys, on the liver and on the heart has also been reported.

III. CLINICAL SYNDROME AND DIAGNOSIS

In industrial environment acute poisoning is caused by the inhalation of vapours or of mists of dimethyl sulphate. The first sign of such poisoning is an anaesthesia of the ocular mucosae followed by an irritation of the same which may sometimes be delayed by a few hours. These disorders can

be serious and veritable burns of the cornea may occur in addition to the conjunctivitis. The pulmonary effects manifest themselves after a latent period of four to eight hours by signs of broncheo-alveolar irritation and even by an acute pulmonary oedema which can sometimes be fatal.

Contact of liquids or concentrated vapours with the skin causes phlyctenae which after healing leave zones of hypoaesthesia which may persist for several months. Contact of liquid with the ocular mucosae also produces serious burns.

After the acute phenomena brought about by the inhalation of vapours or by an extensive cutaneous contact, cases of haemolysis, icterus, renal disorders and various neurological disorders (somnolence, cramps, disturbances of coordination, of attention and of will and even delirium and coma) have been reported.

In favourable cases recovery is slow; the development of respiratory manifestations may be intersected by infectious broncho-pulmonary complications. Prolonged aesthenia follows.

IV. FIRST AID MEASURES

Any person who has been exposed to dimethyl sulphate should immediately be taken into the fresh air and kept resting after immediate removal of clothing contaminated by liquid or even by vapours, and after immediate abundant and prolonged washing, possibly completed by washing with a slightly alkaline solution.

The occurrence of ocular trouble (watering of the eyes) suggests the possibility of a delayed starting of respiratory disorders and justifies keeping the patient under medical supervision for 48 hours.

Even in the absence of direct ocular affection, it is recommended to carry out an immediate washing of the eyes with water or with slightly alkaline solutions.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 3a
MERCAPTANS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY MERCAPTANS

The mercaptans or thiols are mono-alkylated derivatives of hydrogen sulphide; their general formula is R-SH.

The following two groups of mercaptans are distinguished :

a) the aliphatic mercaptans :

- methyl mercaptan or methane thiol : CH_3-SH
- ethyl mercaptan or ethane thiol : C_2H_5-SH
- propyl mercaptan or propane thiol : C_3H_7-SH
- butyl mercaptan or butane thiol : C_4H_9-SH
- hexyl mercaptan or hexane thiol : C_6H_{13}
- methylheptyl mercaptan or methylheptane thiol : C_8H_{17}-SH

b) the aromatic mercaptans :

- phenyl mercaptan or benzene thiol : C_6H_5-SH
- benzyl mercaptan or phenylmethane thiol or thiobenzyl alcohol or toluene thiol : C_6H_5-CH_2-SH.

The boiling point of methyl mercaptan is 6°C. Its vapours are much heavier than air, and it is most frequently encountered in the gaseous state. With that exception, the mercaptans are colourless or straw-coloured liquids, of a nauseous smell at ordinary temperature which is perceptible in very small concentrations. They are weakly acid, soluble in alcohol and acetone, slightly soluble in vegetable oils and almost insoluble in water. This solubility varies according to the particular mercaptan considered.

I. SOURCES OF DANGER

The mercaptans are frequently formed spontaneously in the decomposition of organic sulphur compounds. They are liberated in the cracking of petroleum and are produced by the treatment of certain natural gases. They are also by-products of a number of synthetic processes in the chemical and pharmaceutical industry.

Methyl mercaptan is used as a starting material for the manufacture of artificial cattle feedstuffs. The mercaptans with longer chains are used as antioxidants in the rubber industry and as resin stabilizers.

Other sources of danger exist in lead foundries and in the treatment of zinc, nickel and copper. Traces of mercaptan are sometimes added to illuminating gas to indicate possible leakages (smell).

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

According to their toxicity, the mercaptans can be divided into two groups :

1) Methyl and ethyl mercaptan,

2) Long-chain mercaptans and aromatic mercaptans.

1) Methyl mercaptan and ethyl mercaptan have physiopathological effects which are fairly analogous to those of hydrogen sulphide; however, the toxicity of hydrogen sulphide is more pronounced than that of these two mercaptans.

The inhalation of small quantities may cause nausea, vomiting, vertigo and headache.

The inhalation of considerable quantities of methyl mercaptan vapours causes sudden loss of consciousness followed by a coma which is accompanied by cyanosis of the face and tachycardia.

An acute pulmonary oedema is often associated. Provided there is immediate and appropriate treatment, the victims regain conscience but at this stage generally extreme agitation followed by a prolonged state of confusion are observed.

Convalescence is often lengthy with prolonged bronchitis and deficiency in general condition. Cases of acute methaemoglobinemias and haemolytic anaemias have also been reported in respect of the origin of which the role of a deficit of gluco-6-phosphate-dehydrogenase has been discussed.

2) The toxicity of aliphatic long-chain mercaptans and of aromatic mercaptans is fairly feeble with the exception of that of methylheptyl mercaptan, phenyl mercaptan, benzyl mercaptan and xylyl mercaptan.

The acute poisoning following the inhalation of the vapours of the latter products is characterized by an asthenia with muscular weakness, headache, vertigo, nausea, somnolence, conscience disorders and mydriasis; to these are added in serious cases cyanosis, tachycardia, hypersudation and a chilling of the extremities.

Death may supervene through coma, collapse or acute pulmonary oedema.

In principle the mercaptans are depressants of the central nervous system and induce somnolence with the exception, however, of methylheptyl mercaptan which produces poisoning of the central nervous system with clonic and tonic manifestations.

Direct contact, especially with the liquid causes a more or less pronounced irritation of the skin and of the ocular mucosae. In more severe cases the lesions of the latter may leave some corneal sequelae.

III. COMPLEMENTARY RECOMMENDATIONS

The measurement of the mercaptan content in the atmosphere may be effected by spectrophotometry; the method does not allow differentiation of the various compounds of this group.

IV. FIRST AID MEASURES

The first aid measures are in principle identical with those indicated in cases of hydrogen sulphide poisoning (see Particular No. A12 c of Appendix I).

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 3b
THIOETHERS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THIOETHERS

The thioethers, also called alkyl sulphides, may be regarded as dialkylated derivatives of hydrogen sulphide.

Their general formula is as follows :

a) symmetrical thioethers : R-S-R

b) asymmetrical thioethers : R-S-R'

They are colourless liquids of nauseous smell, generally insoluble in water but readily soluble in ether or in alcohol.

By heating or by contact with acids the thioethers are decomposed with liberation of sulphur oxides. Toxic and inflammable vapours may also develop on contact with water, water vapour and oxidants.

The most widely used compounds are dimethyl sulphide and diethyl sulphide.

I. SOURCES OF DANGER

Alkyl sulphides with a low number of carbon atoms are found in the "black liquors" of the cellulose industry.

Methyl sulphide is used above all for the synthesis of methionine, of dimethyl sulphoxide and of surface-active products.

II. PHYSIOPATHOLOGY

No observations have been traced of cases of thioether poisoning in man. The notions of their toxicity rest above all upon animal experiments according to which the thioethers appear to be the cause of haemolytic anaemia.

The possibility of dermatoses of an allergic nature has also been mentioned.

The decomposition of thioethers with liberation of sulphur oxydes (SO_2, SO_3) may be at the root of phenomena involving the irritation of ocular and respiratory mucous membranes (see Particular No. A 12 of Appendix I).

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 4
ZINC OXIDE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ZINC OXIDE

Zinc oxide (ZnO), commonly called zinc white, is obtained in pure condition in the form of colourless hexagonal crystals. It emits vapours from 1300°C and sublimates at approx. 1800°C. The commercial product is a very white, light powder which is practically insoluble in water; it may contain impurities, in particular lead, but also cadmium, antimony and arsenic.

I. SOURCES OF DANGER

The main occupational hazards of exposure are :

- the extraction of zinc by roasting and by calcination of its ores;
- the melting of zinc alloys and notably of brass;
- the welding and oxygen-cutting of galvanized metal objects;
- the metallization by projection with the spraying gun of zinc molten in the electric arc;
- the preparation and utilization of paints, lacquers and varnishes containing zinc white;
- the pharmaceutics and cosmetics industries;
- the utilization as charge in the preparation of siccatives, cements, glues and powders, in the rubber industry, in the fabrication of certain types of glass, enamels and ceramic products and of rayon;
- the chemical industry for the neutralization of diazonium and naphthol solutions;
- in the dyeing industry as a protective paste ("reserve") for aniline black and for aniline black mordants.

II. PHYSIOPATHOLOGY

In industrial environment exposure substantially leads to the inhalation of zinc oxide dusts and fumes and to a lesser extent to penetration via the digestive tract and contact with the skin. There is early excretion of zinc, mainly through the digestive tract and subsidiarily in the urine and perspiration. The question of its accumulation remains controversial.

III. CLINICAL SYNDROME AND DIAGNOSIS

By inhalation (Metal fume fever)

The inhalation of zinc oxide produces a delayed acute febrile reaction, similar to an attack of malaria or a spell of influenza, known under the name of "brass founder's ague"; the pathogenesis of this febrile attack has not yet been fully clarified. After a few hours of exposure, the disturbances usually appear at the end of the working day or in the night that follows; the first signs are a sweetish taste in the mouth, an irritation in the throat with coughing, tiredness and general stiffness, headache and arthralgia, followed by shivers, nausea and vomiting. These disorders are generally accompanied by a sudden attack of fever which may sometimes reach 40°C. After a few hours profuse perspiration marks the end of the attack and the patient falls asleep; generally, the disorders have totally disappeared the following morning; a general lassitude may persist for some time with stiffness and sometimes arthralgia.

The attacks may repeat themselves on the next day and on the following days if exposure is repeated; the symptoms may then intensify and be accompanied by more pronounced pulmonary and bronchial signs, sometimes even mental confusion and convulsions. Sanguineous anomalies (leukocytosis which may attain 12 000 to 16 000 white corpuscles/mm^3 and persist more than twelve hours after the febrile attack) sometimes a glycosuria and an albuminuria may be observed.

The majority of workers develop a certain resistance to these attacks but this is lost quickly after a few days of rest. It has been observed that the attacks often occur on Mondays or after resumption of work after a break.

By ingestion

Absorption by mouth produces non-specific, mainly digestive, disorders which result from the formation of zinc chloride under the effect of the gastric juices.

Repeated absorption of small doses brings loss of appetite and constipation. With stronger doses nausea or even vomiting occurs, accompanied by loss of weight and anaemia with most frequently hypochromia.

The presence of impurities such as hydrogen sulphide, antimony, arsenic, etc..., has been suggested as at least an aggravating factor in the toxic action of zinc oxide itself.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 5
BORANES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY BORANES

The boranes, or boron hydrides or hydrogen borides, are hydrogenated boron compounds. They may be classified into two groups :

a) the boranes proper of formula : B_nH_{n+4}

b) the dihydroboranes of formula : B_nH_{n+6}

They exist at ordinary temperature in various physical states, the simple ones in the form of gases, the heavier ones as liquid or solids.

They hydrolyze more or less rapidly in contact with water to produce hydrogen and boric acid. This reaction is exothermic.

Among the more important boranes the following may be quoted :

- Diborane : B_2H_6 (boiling point 92.5°C), gas of nauseous smell, hydrolizes instantly on contact with moisture;
- Pentaborane : B_5H_9 (boiling point 58°C), volatile liquid of penetrating smell which hydrolyzes within a few hours; certain forms of pentaboranes are pyrophoric;
- Decaborane : $B_{10}H_{14}$ crystalline solid, sublimates easily with very pronounced nauseous smell.

They can give organic derivatives (such as dimethyl borane) and metal or alkali boron hydrides (boronates).

I. SOURCES OF DANGER

In addition to their use as rocket fuels, the borons are employed as :

- reducing agents in the pharmaceutical industry and perfumery;
- metal protective agents;
- constituents of rubber vulcanization and plastic polymerization agents.

II. PHYSIOPATHOLOGY

The effects are relatively different according to the various boranes.

Diborane is absorbed by the respiratory tract. The rapidity of its hydrolysis probably explains its main action of irritation of the broncho-pulmonary mucosae. Considerable or prolonged exposures also stimulate the central nervous system and also produce hepatic and renal disorders.

Pentaborane is absorbed mainly by inhalation of its vapours and to a lesser extent by penetration through healthy skin.

Decaborane is absorbed by percutaneous penetration and by inhalation of its vapours.

The action of pentaborane and decaborane is exerted mainly on the central nervous system. To this come occasionally transitory functional disorders of the liver and of the kidneys.

The repetition of exposure accentuates the effect on the nervous system through an accumulation of the toxic effects.

III. CLINICAL SYNDROME

The clinical syndrome differs according to the various boranes.

Diborane

In acute poisoning the broncho-pulmonary irritation effects predominate : rapid setting in of dyspnoea, a sensation of thoracic constriction and burning accompanied by a cough frequently with expectoration. Radiography sometimes shows some

transitory diffuse opacities.

Associated with this are often shivers and fever and a syndrome similar to "brass founder's ague" with headache and vertigo. In severe cases diplopia and difficulties of accommodation have been reported.

The evolution is generally short; the disorders disappear within two or three days. When there has been greater exposure the respiratory manifestations may be more severe and broncho-pneumonia may supervene through added infection.

Prolonged exposure to relatively low concentrations gives rise to neurological phenomena : headache, vertigo, myasthenia, momentary tremors, shivers, moderate fever. These phenomena diminish rapidly after exposure has ceased.

Exposure to diborane vapours does not appear to have any effect on the skin. Greater concentrations cause a transitory irritation of the ocular mucosae.

No chronic disorders in humans have been reported. The repetition of exposure to low concentrations may be a factor favouring chronic respiratory infections.

Pentaborane and decaborane

In acute poisoning the nervous symptomatology predominates. The disorders may become manifest during work or, especially in cases of exposure to smaller concentrations, they may be delayed for a day or two. The first signs consist in dizziness, vertigo, headache, nausea, hiccup, cramps, somnolence. In more severe cases nervous excitement is added more or less rapidly : fibrillation and spasms of the muscles of the tongue, the face, the neck, the extremities, the abdominal wall; in severe forms, after accentuation of the headache, with or

without mental confusion and coordination disorders, convulsive crises and contractures occur; prostration is then often very marked. The electroencephalogram shows some disturbances (slow- and high-voltage rhythms,tapering waves), which are however transitory.

Biological examinations reveal some disturbances of the renal and hepatic functions.

In the cases reported the outcome was favourable and without sequelae after some inconspicuous and regressive confusional, amnesic, dysarthric or ataxic manifestations.

Prolonged or repeated exposure to low concentrations may cause headaches, tiredness, vertigo, some disorders of behaviour, attention and coordination.

The action on the skin is very slight (sometimes local irritation).

After ocular contact conjunctivitis and keratitis with serpiginous ulcerations of the cornea have been reported.

IV. COMPLEMENTARY RECOMMENDATIONS

The need for maintaining the concentrations to an extremely low (1) non-harmful rate justifies the employment of carefully designed and well maintained technical equipment (sealed apparatus, suction hoods, etc...).

Repeated exposure to atmospheric concentrations which are not discernible by the sense of smell are liable to produce toxic phenomena. Moreover, repetition of exposure probably causes a diminution of the sense of smell.

Delayed phenomena always have to be feared.

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(1) 0.1 ppm for diborane, 0.005 ppm for pentaborane and 0.05 ppm for decaborane according to American hygiene experts.

Respirators are recommended for the protection of the respiratory tract together with overalls and gloves because of the possibility of percutaneous penetration of pentaborane and decaborane.

These preventive measures have to take into account the risk of fire (production of hydrogen by hydrolysis and, moreover, the possible formation of pyrophoric pentaborane.

Any affections of the central nervous system constitute a contra-indication to exposure to boranes and respiratory affections to an exposure to diborane. Renal and hepatic disorders are also undesirable factors.

The biological extent of the exposure has been estimated by the measuring of boric acid in urines, but its level is sometimes inconstant.

Various methods of detection of boranes in the atmosphere have been proposed, but they do not always appear fully satisfactory for low concentrations. Mention may be made of the method of Schrenck (with silver nitrate in amylamine) and that of Kuhn (with triphenyl tetrazonium chloride) usable in portable detectors or automatic detectors.

V. FIRST AID MEASURES

The therapeutics are at present symptomatic. In case of contact with the skin immediate washing with 3 % ammonia water followed by plentiful and prolonged washing with water has been suggested.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 6
ORGANIC CHLORINE, BROMINE AND IODINE COMPOUNDS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE ORGANIC CHLORINE, BROMINE AND IODINE COMPOUNDS

The diseases liable to be caused in the industrial environment by the organic chlorine, bromine and iodine compounds were dealt with in Particulars No. A 17 (Industrial diseases caused by the halogen derivatives of aliphatic and alicyclic hydrocarbons) and No. A 22 (Industrial diseases caused by halogen derivatives of aromatic hydrocarbons) of APPENDIX I.

It has not been considered necessary therefore to draw up a special chapter devoted to these diseases in the present volume.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 7
ALIPHATIC HYDROCARBONS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ALIPHATIC HYDROCARBONS OTHER THAN THOSE REFERRED TO IN APPENDIX I - PARTICULAR NO. A 16

The aliphatic hydrocarbons are made up exclusively of carbon and hydrogen atoms in open (non-cyclic) molecular combinations. Considering them as a whole, all these hydrocarbons are either components of natural gas or petroleum, or else products obtained by the treatment of petroleum. Some of them are obtained by other processes (for example the manufacture of acetylene from calcium carbide). They are all inflammable substances.

Chelically there are two main types :

I. The saturated aliphatic hydrocarbons, of the general formula C_nH_{2n+2}, also called alkanes or paraffins or paraffinic hydrocarbons. At ordinary temperature the substances containing up to 4 carbon atoms are gaseous. They are constituents of natural gases and used as fuel; from 5 to 16 carbons they are liquids used as motor fuel, solvents and, to a lesser extent, refrigerants, etc...; above 16 carbon atoms, they are solids at ordinary temperature entering into the composition of various products, such as e.g. the lubricants.

Methane (CH_4) and ethane (C_2H_6) behave physiologically like inert gases and are harmful in very high concentrations owing to deprivation of oxygen. Higher alkanes have a depressant effect on the central nervous system; propane, for example, is used as a surgical anaesthetic. Active concentrations are high, however (1 % by volume or more) and, furthermore, the volatility diminishes rapidly with the increase in the number of carbon atoms.

The vapours are slight irritants of the mucous membranes.

The contact of the liquid substances of this group with the skin may have a direct effect through destruction of the liposoluble covering.

Tracheal aspiration of liquid is liable to cause pneumonias. In this connection it is important to remember that after an accidental ingestion stomach irrigation may only be practised with extreme prudence.

Finally, the inhalation of certain commercial products containing hexane (for example in France "Essence C") seems to have been at the origin of cases of polyneuritis.

II. The unsaturated aliphatic hydrocarbons

1) Ethylene series

- the olefins or alkenes of general formula C_nH_{2n}, characterized by the presence of a double bond, are products of the cracking of petroleum, raw materials which are used more and more in numerous organic syntheses and as plastic monomers;
- the polyolefins or alkadienes or polyethylenes, characterized by two double bonds; their general formula is C_nH_{2n-2}. They are above all raw materials for synthetic rubber.

The olefins used most (ethene or ethylene C_2H_4, propene or propylene C_3H_6, butenes or butylenes C_4H_8) and several diolefins (such as 1,3-butadiene)are gaseous at ordinary temperature. Isoprene (2-methyl 1,3-butadiene) has a boiling point at 33.5°C.

Their inherent anaesthetic action is not very marked and this effect manifests itself only at high concentrations, that is at concentrations entailing a diminution of oxygen. This inherent anaesthetic power increases however with the molecular weight; by contrast, the volatility diminishes.

2) Acetylene or alkine series

Characterize by a triple bond, of formula C_nH_{2n-2}.

Acetylene (C_2H_2 or HC $\equiv$) has slight anaesthetic effect. It is worth mentioning that acetylene manufactured from calcium carbide contains various impurities, among them phosphuretted hydrogen or phosphine in proportions which may be regarded as noxious.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 8
ALIPHATIC AMINES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ALIPHATIC AMINES

The aliphatic amines may be regarded as resulting from the substitution of one or more hydrogen atoms of ammonia by the same number of aliphatic hydrocarbon radicals. Thus they correspond to the following formulae :

- primary amines : H_2N-R
- secondary amines : $HN\begin{matrix}R\\R'\end{matrix}$
- tertiary amines : $N\begin{matrix}R\\-R'\\R''\end{matrix}$

Furthermore, one or more amino functions may be present in the molecule. Thus monoamines such as methylamine and polyamines such as ethylene diamine are formed.

Finally, the amino-alcohols may be included in this group where the amine function and the alcohol function are on the same chain.

The types of aliphatic amines used in industry multiply rapidly. Any attempt at enumeration would therefore immediately become out of date.

The aliphatic amines are at ordinary temperature volatile liquids, with the exception of the three methylamines which are gaseous and the heavy amines which are solids. The lower amines are soluble in water, the higher amines are soluble in lipids.

The simple amines of low molecular weight give off an ammoniacal odour. The higher amines produce a nauseous smell.

The aliphatic amines all have a pronounced basic character; the primary amines are stronger bases than the secondary ones and these in turn are stronger than the tertiary ones. The basicity of the amines decreases moreover with the number of carbon atoms of the chain.

The presence of several amino functions (diamines and other polyamines) increases the basicity of the molecule. The amino alcohols are in general less strong bases than the corresponding simple amines.

I. SOURCES OF DANGER

The aliphatic amines are used as synthesis agents : they occur in the manufacture of numerous products such as :

- catalysts and hardeners for plastics (polyurethanes, epoxy resins, polyesters);
- corrosion inhibitors;
- antioxidants;
- emulsifying agents;
- surface-active agents;
- vulcanization accelerators;
- synthesis agents in the manufacture of dyestuffs, of pesticides, of deodorants (bactericides);
- additives to certain pharmaceutical products, etc...

The amino alcohols are used in tanning, in the textile fibre industry, in perfumery and as emulsifying agents, anti-freezes, corrosion inhibitors, etc... They are also constituents of cosmetics and of pharmaceutical products.

II. PHYSIOPATHOLOGY

The aliphatic amines have a direct orthoergic action which is a function of their alkalinity. This action is exerted on the skin and on the ocular and respiratory mucosae on contact with

the liquid or dissolved amines or on contact with the vapours.

In addition, certain aliphatic amines may be the cause of a sensitization and bring about at a subsequent exposure phenomena of the type of a cutaneous or respiratory, exceptionally ocular, allergy. The direct action on the skin may sometimes facilitate or even provoke the secondary setting up of a sensitization.

Finally, certain aliphatic amines have a pharmacodynamic effect which is exerted in particular on the sympathetic and parasympathetic systems. This experimentally established notion has rarely been confirmed in industrial environment.

III. CLINICAL SYNDROME AND DIAGNOSIS

1) Direct action

The effects of direct action on the skin range from a simple passing irritation (by vapours or by liquids) to veritable burns (by prolonged contact with liquids). The appearance of the symptoms of such burns is sometimes delayed for several hours.

The projection of liquid into the eyes sometimes causes very severe burns which may leave sequelae (opacification of the cornea). Exposure to concentrated vapours or prolonged exposure to lower concentrations entrains temporary irritation (lacrimation), conjunctivitis, oedema of the cornea.

The inhalation of vapours causes an irritation, particularly of the upper respiratory tracts (nose, throat) and, to a lesser degree, of the broncho-pulmonary tract, healing rapidly and without sequelae.

2) Allergic action

The allergic action manifests itself mainly on the skin. The amines found to be responsible in industrial environment are in particular the ethyleneamines, the polyamines (ethylenediamines, diethylenetriamines, triethylenetetramines, hexamethylenediamines and the ethanolamines).

Evidence of the responsibility of these amines as the cause of these allergic dermatoses is supplied by the positive epicutaneous tests. The negative tests are often without significance. For example, in the cases of dermatoses caused by epoxy resins it is sometimes difficult to share out responsibility between the resin and differentiate between the responsibility of the resin and that of its constituents. The recurrence after resumed exposure represents an argument in favour of the allergic nature of the dermatoses found.

The phenomena of respiratory intolerance of the bronchial asthma type are more rare. They have been reported following repeated exposure to polyamines (ethylenediamines, diethylenetriamine, triethylenetetramine, tetraethylenepentamine). Their allergic nature has been proved by respiratory tests (sensitization, resistance) and by the recurrence on repetition of exposure (see Particular No. C 5 of Appendix I). The induced respiratory tests have to be carried out with great care.

3) Sympathetic or parasympathetic phenomena

Sympathetic or parasympathetic phenomena supervening in humans have only been evoked following exposure to vapours in industrial environment. They manifest themselves by failure of accommodation to distance and to light, by a vision of objects through a bluish cloud and, objectively, by a mydriasis. The association with direct effects on the ocular mucosae (oedema of the cornea) complicates the accuracy of physiopathological diagnosis, the other possible disorders (vasomotoric troubles, or disorders of the respiratory rhythm) being absent. In practice these disorders recede rapidly. The reality of this action has been proved experimentally.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 9a
NITRILES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY NITRILES

The nitriles of the general formula R_ C ≡ N constitute neither chemically nor toxicologically a homogeneous category; from this double point of view they can be considered in three groups :

1°. Ionizable nitriles with liberation of the $_C \equiv N^-$ ion :

- hydrocyanic acid (or formic nitrile or formonitrile) : HCN

$$HCN \rightleftharpoons H^+ + CN^-$$

- cyanides : Na CN $\rightleftharpoons$ $Na^+ + CN^-$

- cyanogen compounds (which form the subject of Particular A 3 c, of Appendix I).

2°. Hydroxynitriles or cyanohydrins or nitriles hydroxylated in position 2, condensation products through the addition of an aldehyde or a ketone to HCN :

- case of aldehyde :

$$R - C(=O)H + HCN \rightleftharpoons R - C(OH)H - CN$$

- case of ketone :

$$R - C(=O) - R + HCN \rightleftharpoons R - C(OH)R - CN$$

In both cases the condensation takes place on carbonyl (=C=O) level common to both types of molecule (aldehyde or ketone.

The formula may be written therefore :

$$R = C(R \text{ (or H)})(OH) - CN$$

The cyanohydrins are stable only in clearly acid medium. In neutral or slightly alkaline medium the original aldehyde or ketone on the one hand and HCN on the other hand are reconstituted. The ionization of this HCN gives rise to the secondary liberation of the CN^- ion.

The fixation in 2 position of the hydroxyl radical thus confers upon these substances very special properties from a point of view of toxicology and makes necessary their separate classification even if their chemical formula allows them to be considered as saturated or unsaturated aliphatic nitriles.

They are liquid substances liable to emit vapours; among those encountered most frequently are :

- acetone cyanohydrin or 2_hydroxy isobutyronitrile : $(CH_3)_2C(OH)-CN$
- acrolein cyanohydrin or 2_hydroxy 3_butene nitrile : $CH_2 = CH - CH(OH) - CN$
- hydroxyacetonitrile : $CH_2(OH)-CN$
- dinitrile of hydroxyglutaric acid : $CN - CH_2 - CH(OH) - CN$

3°. Saturated and unsaturated aliphatic and aromatic nitriles and polynitriles

Alkyl cyanides, also known as carbonitriles, derive from HCN by substitution of the hydrogen with alkyl.

They are also called nitriles of the acid obtained by hydrolysis (the suffix "ic" of the acid being replaced by the suffix "-onitrile"); examples :

- CH_3CN : methyl cyanide or acetonitrile (nitrile of acetic acid)
- CH_3CH_2CN: ethyl cyanide or propionitrile (nitrile of propionic acid).

These compounds have common chemical and toxicological properties. Their toxicity derives only partly from the hydrocyanic part, variable according to the different nitriles, whilst it may be partly due to the non-cyano portion of the molecule.

The dinitriles and the aromatic nitriles appear to be more toxic than the mononitriles.

Those encountered most frequently are in rising order of toxicity in each category :

a) Aliphatic nitriles

1) Saturated mononitriles

- acetonitrile (methyl cyanide) : CH_3CN
- propionitrile : CH_3-CH_2-CN
- butyronitrile : $CH_3-(CH_2)_2-CN$
  isobutyronitrile : $(CH_3)_2-CH-CN$
  azo-bis-butyronitrile : $CN-(CH_2)_2-CH_2-N=N-CH_2-(CH_2)_2-CN$
- valeronitrile : $CH_3-(CH_2)_3-CN$
- capronitrile : $CH_3-(CH_2)_4-CN$

(the higher derivatives are only slightly toxic).

2) Saturated dinitriles

- succinonitrile : $CN-(CH_2)_2-CN$
- adiponitrile : $CN-(CH_2)_4-CN$ (raw material for nylon)
- pimelonitrile : $CN-(CH_2)_5-CN$
- glutaronitrile : $CN-(CH_2)_3-CN$
- malononitrile : $CN-CH_2-CN$

3) Unsaturated mono- and dinitriles

- nitrile of oleic acid : $CH_3-(CH_2)_7-CH=CH-(CH_2)_7-CN$
- dinitrile of fumaric acid : $CN-CH=CH-CN$
- dinitrile of maleic acid (cis isomer of fumaric acid).

b) Alicyclic nitriles

Mononitrile corresponding to cyclohexane : cyclohexane carbonitrile or hexahydrobenzonitrile : $C_6H_{11}CN$.

c) Aromatic nitriles

1) Mononitriles

- benzonitrile (cyanobenzene) : C_6H_5-CN
- methylbenzonitriles (in 2,3 and 4 position) : CH_3-C_6H_4-CN
- 2,5-dimethylbenzonitrile : $(CH_3)_2$-C_6H_3-CN
- 2,6-dichlorobenzonitrile : Cl_2-C_6H_3-CN
- 4-nitrobenzonitrile : NO_2-C_6H_4-CN.

2) Dinitriles

Much used in the manufacture of dyestuffs and of certain polyesters :

- phthalonitrile : CN-C_6H_4CN; this compound only is toxic whereas its meta (isophthalonitrile) and para (terephthalonitrile) isomers have very low toxicity.

These various nitriles and dinitriles occur in various physical forms, as crystalline or finely powdered solids or else as liquids.

d) Special cases

1) Acrylonitrile, an unsaturated aliphatic nitrile CH_2=CH-CN, is a colourless liquid, practically odourless, little soluble in water. Very widely used in industry (synthetic fibres) volatile, inflammable, very toxic from inhalation of its fumes and by skin absorption of the liquid or of the vapours. In slightly acid or alkaline medium its hydrolysis does not liberate HCN but produces acrylic acid and ammonia (provided it is pure acrylonitrile; the industrial products sometimes contain a small amount of HCN). Its toxicity is not of the hydrocyanic order.

Methacrylonitrile, $CH_2 = C(CH_3)CN$, a liquid polymerizable like acrylonitrile, would normally be more toxic than the latter, but may well be less dangerous owing to its lower vapour pressure.

2) The aminonitriles : $R-(NH_2)-CN$. The amino function gives these nitriles the very particular characteristic of having chronic toxicity which is non-hydrocyanic (osteolathyrism). They do not have acute toxicity.

It is not possible to enumerate all nitriles; only those nitriles have been mentioned here which are most currently encountered in industry.

I. SOURCES OF DANGER

Since the great advance in petrochemistry the nitriles have assumed considerable importance in various sectors of the industry as a raw material, as intermediate products or as catalysts, for example, in :

- the manufacture of plastics, synthetic fibres (polyacrylics, polymethacrylics);
- the manufacture of plexiglass (acetone cyanohydrin);
- the manufacture of synthetic rubber (copolymers), of dyestuffs, of pesticides (acrylonitrile);
- the manufacture and utilization of special solvents (acetonitrile) in particular in the petroleum industry;
- the pharmaceutical industry (vitamin B 12).

II. PHYSIOPATHOLOGY

1) The nitriles with hydrocyanic toxicity

The cyanohydrins, nitriles hydroxylated in 2-position, owe their toxicity to the CN groups, the liberation of which is facilitated by alkalinity of the surrounding medium. The penetration occurs via the respiratory (vapours) or percutaneous (projections of liquids) route.

Secondary hydrocyanic poisoning supervenes when the quantity of dissociated cyanohydrin is sufficient for clinical symptoms to appear : the CN^- ion inhibits cellular respiration through blockage of the cytochrome-oxidase enzyme; the blood remains oxygenated owing to the impossibility of the tissue to utilize the oxygen.

The CN^- first excites the respiratory and vasomotory bulbar centres; secondly a paralysis of the respiratory centre is produced which is attributed to cellular anoxaemia.

The detoxication of the CN takes place in the form of thiocyanates which appear in the urine.

Poisoning by cyanohydrins is therefore a secondary hydrocyanic poisoning, frequently retarded by a latent period which may extend over several hours. The presence of this latent period is a common characteristic of these types of poisoning which all comprise :

- a considerable hyperpnoea with characteristic bitter almond smell of the expirated air,
- a progressive diminution of the oxygen consumption,
- a saturation of the arterial blood with oxyhaemoglobin (which distinguishes hydrocyanic anoxaemia from anoxic anoxaemia and poisoning by carbon monoxide or by a methaemoglobinisant).

It should be remembered that the toxicity of the hydrocyanic type of a cyanohydrin may be associated with the inherent toxicity of the rest of the molecule : thus the cyanohydrin of acrolein entrains both the hydrocyanic poisoning as well as poisoning by acrolein which is a violent respiratory vesicant.

2) <u>The nitriles with mixed hydrocyanic and extra-hydrocyanic toxicity</u>

The <u>aliphatic and aromatic nitriles and polynitriles</u> have formed the subject of a variety of experimental work; their very variable toxicity depends upon the speed and the extent of the appearance of CN groups in the organism, upon the speed of detoxication of these CN groups into thiocyanate (thanks to

to the enzyme thiocyanase or transulphurase). The length of molecule of the nitriles and their place in the classification are thus factors of their toxicity; in principle, the toxicity is high for the lower members, low or nil for the higher members.

But the toxicity of these saturated or unsaturated aliphatic or aromatic nitriles depends upon the rest of the molecule as much as upon its cyano portion. These substances are chemically not very reactive and chemical attacks affect more readily the non-cyano portion of their molecule. Although the symptoms of general poisoning by these nitriles call to mind those of hydrocyanic poisoning, they are not absolutely identical with them and in general remain limited. Moreover, isotoxicity does not exist between these nitriles and hydrocyanic acid.

The toxicity of the non-cyano part of the molecule of the aliphatic or aromatic nitriles, variable according to the substance in question, appears certain but its mechanism has not yet been defined.

In the case of acetonitrile (the toxicity is attributed to the detoxication product of the CN^- ions : the thiocyanates accumulating owing to the slow and prolonged liberation of CN groups from the acetonitrile absorbed.

Hexahydrobenzonitrile or cyclohexanecarbonitrile seems to owe its toxicity largely to the liberation of HCN.

The aromatic nitriles, where the CN group is linked to the cyclic carbon atom, do not liberate HCN and will be metabolized to cyanophenol and then benzoic acid.

2,6-Dichlorobenzonitrile has a toxicity near to that of mono- and dichlorobenzene.

4-Nitrobenzonitrile produces a substantial methaemoglobinaemia.

In addition to their general toxicity, certain of these nitriles possess a local toxicity, giving rise to a cutaneous

irritation with erythema and secondary appearance of phlyctenae; this is true in particular for the saturated (adipic) and unsaturated (fumaric) dinitriles.

3) The nitriles of non-hydrocyanic toxicity

Acrylonitrile owes its toxicity to a specific action of the non-cyano fraction of its molecule, but the precise mechanism of this action has not yet been defined. Chemically the non-cyano portion of the acrylonitrile is extremely reactive in respect of multiple functions (alcohol, acid, etc...).

Clinical symptomatology, biochemical symptoms, analyses of the gases in the blood make it possible to eliminate the hydrocyanic mechanism in cases of poisoning by acrylonitrile. Moreover, anticyanide therapy proves ineffective in this case.

Acrylonitrile behaves like an elective poison of the central nervous system and of the peripheral nervous system; locally it acts as a powerful irritant of the mucosae and of the skin. The toxicity of methacrylonitrile is of the same nature but more pronounced.

The aminonitriles : the introduction of an amino function into the nitrile molecule brings with it a particular chronic toxicity which is associated with osteolathyrism, and which is due to an action upon the collagen part of the connective tissue, varying its viscosity. The precise mechanism remains unknown.

III. CLINICAL SYNDROME AND DIAGNOSIS

1) Secondary hydrocyanic poisoning

This intoxication is brought about by nitriles generating HCN, that is to say the hydroxynitriles (cyanohydrins), and to a lesser degree by the aliphatic and aromatic nitriles for which the hydrocyanic poisoning syndrome is very often incomplete, mitigated by and associated with a symptomatology of other origin.

The poisoning develops in several phases :

- after the silent, latent phase, the duration of which depends upon the mode of penetration of the poison (from a few minutes to several hours),
- supervenes the initial phase of discomfort with vertigo, dizziness, nausea, intense headache, pharyngeal and tracheal burning,
- then a phase of nervous excitation with convulsions, mydriasis, tetaniform contraction of the jaws, thoracic tightness, thirst for air and frequently loss of consciousness. This phase is generally short,
- finally, a phase of suffocation and coma which becomes accentuated progressively to a coma with irregularity of pulse, chilling of extremities, pallor.

According to the extent of intoxication, the development may remain limited to the first and second phase (this is the case most frequently with aliphatic or aromatic nitriles). Owing to its low volatility, acetone cyanohydrin is particularly dangerous through cutaneous penetration : this product practically does not evaporate and penetrates the skin; similarly, the intoxication process will continue if clothing impregnated with the poison is not removed.

It is important to note that :

- in the event of cutaneous or mucous projection, the asymptomatic latent phase, which corresponds to the absorption of the poison through the skin or the mucosa and its decomposition in the blood, provides some time, even if very limited, during which it is possible to intervene,
- the period of premonitory general feeling of discomfort should really raise the alarm and cause specific treatment to be instituted,
- the terminal coma phase is brief : when the concentration of CN^- ions in the blood reaches a sufficient level, the process is rapidly fatal.

2) Poisoning by acrylonitrile

This intoxication may follow inhalation of acrylonitrile vapours. The poison readily passes through the skin and the mucosae, especially in its liquid form, and this way of penetration may be the origin of general intoxications.

Acrylonitrile in liquid or vapour form locally irritates the skin causing the appearance of erythema, cutaneous oedema and phlyctenae. It also irritates the mucosae, in particular the conjunctivae and may injure the cornea.

In its acute form, the general intoxication develops in four phases :

- according to the mode of poisoning a latent phase may exist but this is always very short : 5 to 10 minutes after inhalation, a little longer after projection onto the skin;
- phase of commencement of nausea, vomiting, headache, vertigo, abdominal pain, pronounced asthma;
- phase of nervous manifestations with excitation, trembling, convulsions or localized paralyses, even epileptiform convulsive crises;
- terminal phase, characterized by a state of irreversible shock.

In the most frequently occurring subacute form the symptoms are less severe; it is above all a matter of asthenia and anorexia. Cases of gastritis and benign icterus have been reported.

Methacrylonitrile gives the same manifestations.

3) The osteolathyrism of aminonitriles

Chronic poisoning by aminonitriles results in loss of weight, deformation of the skeleton with fragilitas ossium, radiological appearances of osseous rarefaction and zones of condensation at the level of the long bones; aneurysms of the aorta have been reported. The syndrome recalls that of lathyrism or osteolathyrism.

IV. FIRST AID MEASURES

1) Secondary hydrocyanic poisoning (hydroxynitriles and aliphatic or aromatic nitriles) reacts remarkably to anti-cyanide treatments. It is necessary to insist particularly on the need and urgency of the complete undressing and washing down of any subject contaminated by a liquid cyanohydrin. Treatment must be put in hand immediately even if the subject does not yet experience any feeling of discomfort (phase of deceptive latency).

- Benign cases : patient conscious, spontaneous breathing, cardio-vascular condition normal :
  - simple oxygen therapy,
  - medical supervision for one to two hours.

- Serious cases: loss of consciousness but respiration normal, cardio-vascular condition good, blood pressure above 70 mm Hg :
  - pure oxygen by inhalation,
  - slow intravenous injection of sodium nitrite (10 ml at 3%) and of sodium hyposulphite (50 ml at 25%),
  - possibly hypertonic glucose serum with vitamine B, B_2, C, B_6, PP.

- Severe cases : loss of consciousness, apnoea or irregular respiratory rhythm, blood pressure above 70 mm Hg :
  - to the above treatment is added the intravenous injection of cobalt chelate (Co-EDTA), 2 ampoules of 20 ml at 1.5 % that is 600 mg altogether or of hydroxocobalamine (4 g in sodium hyposulphite solution).

V. SPECIAL RECOMMENDATIONS

If respiration stops, artificial respiration must be applied immediately, associated with oxygen therapy (the mouth-to-mouth method should not be applied because of possible risks to the rescuer).

Heart stimulants and adrenaline (risk of fibrillation) are to be proscribed.

In case of poisoning by an aliphatic or aromatic nitrile, where the exact influence of the cyano part of the molecule is not known, it is prudent to add to the symptomatic treatment the intravenous injection of sodium nitrite with sodium hyposulphite.

Poisoning by acrylonitrile

In addition to washing and removal of clothing in :

- benign cases : most frequently :
  - oxygentherapy,
  - intravenous injection of sodium,hyposulphite (50 ml at 25 %),
  - intramuscular or intravenous administration of thyroxine (1 ml),
  - hypertonic glucose serum with vitamins B_1, B_2, B_6, PP.
- severe cases : with nervous symptoms, add to the above treatment :
  - tranquillizers for the nervous system : Gardenal intramuscular, possibly Reserpine (Serpasil),
  - cardio-respiratory analeptics : Micorene (1 amp) intramuscular.

The caustic character of acrylonitrile shows up locally by the appearance, frequently delayed for 24 hours, of extensive blisters. These should be treated like all burns, careful and immediate washing of any cutaneous projection being given as first aid.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 9b
ORGANIC ISOCYANATES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ORGANIC ISOCYANATES

The isocyanates are organic compounds characterized by the function -NCO. Various monoisocyanates are used in industry in particular as intermediate products. It is the polyisocyanates, however (molecules containing several -NCO groups), whose use has widely developed in recent years. The -NCO functions combine by addition onto the mobile hydrogens of other molecules to form macromolecules; in particular, the isocyanates form polyurethanes through addition with the hydroxyl groups of polyols or polyglycols.

It is above all the noxious effects of the diisocyanates, the substances which have been used longest and most widely (for example under the name of "Desmodur") which are well known, that is to say :

- tolylene diisocyanate : $H_3C-C_6H_3-(NCO)_2$ or TDI
- diphenylmethane diisocyanate : $H_2C-(C_6H_4-NCO)_2$,

and to a lesser extent :

- triphenylmethane triisocyanate : $HC-(C_6H_4-NCO)_3$,
- hexamethylene diisocyanate : $OCN-C-(CH_2)_6-NCO$ or HDI
- naphthylene diisocyanate : $H_3C-C_{10}H_7-(NCO)_2$ or NDI.

I. SOURCES OF DANGER

The main industrial sources of danger are :

for the monoisocyanates :

- their manufacture,
- their utilization as organic synthesis intermediates in the pharmaceutical industry.

for the diisocyanates :

- their manufacture,
- their utilization as raw materials for rigid polyurethanes, rigid, semi-rigid and flexible foams, coatings, varnishes, paints, glues, etc...

The technical characteristics of these polyurethanes have resulted in many applications, such as sealing, insulation, etc..., which sometimes require the use in situ of monomers and adjuvants according to various technical processes such as atomization or application by spray gun.

The harmful effects of the isocyanates are among the major reasons why suppliers of raw materials for polyurethanes endeavour, in so far as the applications allow it, to present these products in the form of prepolymers in which free diisocyanates appear in amounts of less than 1 % or possibly 0,5 %; it appears that up to now the use of such preparations has not been the cause of any trouble at the consumers.

As a finished product the polyurethanes are inert and non-harmful; however, very small amounts of free isocyanates may still be given off for some time after the start of the polymerization.

II. PHYSIOPATHOLOGY

The -N=C=O radical is very reactive. All the products of this group have irritating properties on the organism, but they do not equally pronounced for all of them; moreover, the sensi-

tization reactions which form an essential noxious factor are probably not a feature of all isocyanates.

In particular the volatility of each of these compounds has to be taken into account. For example, the volatility of totylene diisocyanate is considerable and it is in connection with this substance that the first, the most frequent and the most serious cases have been reported. The volatility of the naphthylene diisocyanate is low and it seems that its use at low temperature limits the danger.

The conditions of use may well alter these physical factors, for example, if such products are used at elevated temperatures or when they are used by atomization with the product in a state of fine division which penetrate into the respiratory tract. It should also be borne in mind that the reaction giving rise to the formation of polyurethanes is exothermic and that at this moment the liberation of isocyanate not yet converted is facilitated.

Finally, the constitution of the polyurethanes necessitates the addition before or during the polycondensation of auxiliary or adjuvant products (catalysts, hardeners, stabilizers, fire-proofing agents, swelling agents, etc...) which vary according to final presentation and according to commercial brands. Certain of these products have harmful properties and may cause trouble on their own account (aliphatic or aromatic amines for example).

The studies on the pathology of isocyanates relate above all to tolylene diisocyanate which will be taken as typical.

In experiments it was found that, as for humans in cases of substantial exposure to vapours or mists, the attack is characterized by direct irritative effects on the mucosae, notably on the respiratory mucosae; this direct attack of the type of tracheitis or obstructive bronchiolites may be accompanied by the temporary or definitive, partial or total formation of granular tissue. In a very large number of cases the effects in humans of an exposure to relatively moderate doses are of the bronchospasm type and become manifest after a certain period of exposure.

The reaction of isocyanates with the proteins of the respiratory mucosae, in particular with the amino groups, may bring about the formation of antigens and a veritable sensitization, this intolerance frequently follows an acute attack; it may also appear however without any initial period of irritation having been evident.

Although the appearance of such an intolerance is frequent, it is by no means constant even after an acute incident.

The diisocyanates are primary irritants for the ocular mucosae. They are also primary irritants for the skin. Experimentally it was possible to reproduce cutaneous sensitization effects in animals; such effects are rarely found in humans.

III. CLINICAL SYNDROME

The major risk for personnel exposed to vapours or aerosols of tolylene diisocyanate is of a respiratory nature, owing to primary irritation and sensitization.

An exposure to substantial quantities causes acute chemical broncho-pneumopathies, acute pulmonary oedema and other sequelae. Fatal cases have been reported during an acute phase or through supervening respiratory diseases.

After exposure to moderate concentrations disorders generally set in progressively. After a period of work without incidents of 2 to 8 days, sometimes even several months, attention is required in respect of signs of ocular and in particular respiratory irritation (laryngeal prickling, dry cough predominantly at night and sometimes a slight rise in temperature). Stoppage of exposure causes these signs to disappear. Otherwise more serious disorders will appear : more and more pronounced cough, dyspnoea, possibly asthmatiform phenomena.

When as a result of the elimination of exposure the disorders have disappeared, a new exposure frequently induces recurrence of the respiratory phenomena; they are often more pronounced than during the first manifestations. These recurrences follow exposures which are sometimes of very short duration or very low concentrations, considerably lower than those which have brought about the first phenomena. Once such sensitization has become established a change of employment becomes imperative.

After each of these primary or secondary acute phases some respiratory insufficiency may remain.

The ocular and cutaneous disorders of the irritative type are generally not very pronounced and clear rapidly.

Among the other isocyanates used more frequently in industry in recent years the following may be quoted :

- the diisocyanate of diphenylmethane or MDI is a crystalline product of low volatility available in the form of a powder; when used at low temperatures it does not appear to have given rise to any incident. The release of vapours by heating has produced some respiratory irritation phenomena. Its use by atomization which causes inhalation of fine droplets has given rise to acute, sometimes asthmatiform bronchitis; however, recurrence in the event of a renewed exposure through sensitization is rare. Contact with the product in liquid form has produced cases of irritation of the conjunctiva or of the mucosae. Some exceptional dermatoses which seem to be allergic have been reported.

- polymethylene polyphenylisocyanate (PAPI), the dimer or polymer of MDI, a liquid product, possesses toxicological characteristics which are very close to those of MDI.

- hexamethylene diisocyanate or HDI, whose volatility is fairly pronounced, has produced some respiratory irritation effects. At direct contact it is an irritant of the ocular mucosae and of the skin. It does not appear to provoke sensitization.

- naphthylene diisocyanate or NDI, solid at ordinary temperature, has induced respiratory disorders in some persons after heating. It appears liable to cause a sensitization.

- dicyclohexyl diisocyanate has a low vapour pressure; it is nonetheless an irritant and lacrymatory product when used hot or by atomization. No cases of sensitization have been reported.

- methyl isocyanate is a volatile product, highly irritant for the mucosae and for the skin. It also induces sensitization of respiratory form and cases of cross-sensitization with tolylene diisocyanate, not yet fully explained, have been reported in humans.

IV. COMPLEMENTARY RECOMMENDATIONS

It follows from the above that isocyanates as a whole must be regarded as irritant products; moreover, several of them have a definite power of sensitization. Correct preventive measures allow an effective protection against the irritant character. However, an exposure to very small quantities of the product is liable to cause a sensitization, the setting of which is sometimes insidious. It is very important therefore that by such preventive measures exposure is kept at very low levels from the start so as to avoid the setting in of such a sensitization. In fact, once sensitization has become established, the inhalation of minimal quantities is sufficient to release acute respiratory phenomena in persons thus sensitized. The threshold of olfactory perception cannot constitute a sign of alarm because this is above the level of concentrations liable to prevent the setting in of sensitization.

Healing of accidents is usually free of sequelae, but functional manifestations of respiratory insufficiency have occurred subsequent to simple or repeated acute episodes. The possibility of respiratory insufficiency following exposure which brought about catarrhal pulmonary irritation without acute episode has also been mentioned. This respiratory insufficiency has been confirmed by functional t

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO.A 10a
VINYLBENZENE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY VINYLBENZENE (STYRENE)

Vinylbenzene, better known under the name of styrene (or styrene monomer, styrol, phenyl ethylene), formula $C_6H_5CH = CH_2$, is a colourless liquid of penetrant odour, slightly volatile and little soluble in water. Its boiling point is at 145°C and its vapours are heavy (density : 3,6).

I. SOURCES OF DANGER

The main industrial uses of styrene are :

- the manufacture of plastics (of the polyester type) and of synthetic rubbers (one type of which is butadiene-styrene) where styrene may be at the same time raw material (monomer) and polymerizable solvent;
- other organic syntheses;
- perfumery, pharmacy.

II. PHYSIOPATHOLOGY

Styrene has an irritant action on the skin, the ocular and respiratory mucosae. These irritation effects are useful warning signs, rendering difficult a further sojourn of the worker in the polluted atmosphere. Prolonged exposures to notable concentrations entrain a certain degree of functional depression of the central nervous system.

In industry styrene is absorbed by inhalation of the vapours and by slow penetration through healthy skin.

It was found in experiments that with increasing levels of concentration the exposure causes :

- an irritation of the eyes and of the upper respiratory tracts;
- a depression of the central nervous system;
- a coma with pulmonary complications, sometimes fatal.

No effects consequent upon a prolonged or repeated exposure to low concentrations have been reported.

It has been found that styrene inhaled in the form of vapours is metabolized to benzoic acid and excreted in the urine in the form of hippuric acid or mandelic acid (50 to 90 % of the quantity absorbed). A portion is rejected, unchanged into the expelled air.

III. CLINICAL SYNDROME AND DIAGNOSIS

Exposure to styrene vapours causes :

- an irritation of the eyes, the nose, the throat; these effects rapidly retrocede, without sequelae, at the end of exposure to the hazard;
- some transitory digestive troubles : nausea, diarrhoea;
- in high concentrations, some neurological manifestations such as headache, vertigo, tiredness, drunkenness and depressive tendency; cases of retrobulbar neuritis and polyneuritis have been reported.

No effects of the benzene type on the haematopoietic organs have been observed after prolonged exposure to styrene.

No other long-term pathological manifestations in humans have been reported. The disorders observed disappear on cessation of noxious exposure.

Direct contact with liquid styrene causes a transitory irritation of the eyes without sequelae.

Repeated or prolonged cutaneous contact brings about dermatoses of the orthoergic type (dry, cracked skin) liable to secondary infection.

IV. COMPLEMENTARY RECOMMENDATIONS

As styrene does not give rise to the haematological anomalies of the benzene type, no formal indication of exposure to styrene is supplied in the systematic haematological examinations.

The possibility of estimating the extent of exposure to the hazard from the increase in urinary excretion of the metabolites is disputed. Some believe that this excretion is augmented and in particular is made evident by the increase in the ratio mandelic acid/creatinin in the hours following exposure : this would represent the most sensitive biological exposure control test. Others claim that hippuric acid constitutes the main metabolite excreted by the urine (50 to 90 % of the quantity of styrene inhaled); but the usual concentrations of styrene in the atmosphere of industrial media would not bring about a perceptible or sufficiently significant increase of this excretion.

The ocular or respiratory irritation phenomena which may follow exposures to strong concentrations are generally transitory without any sequelae.

Cutaneous contact with liquid diphenyl may produce in some cases a slight local irritation. The action of diphenyl has been associated with the origin of rare cases of cutaneous allergy.

Projection into the eye causes slight conjunctivitis with prickling and burning sensation after a few minutes. Recovery is rapid and without sequelae.

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APPENDIX II - PARTICULAR NO. A 10c
DECALINE AND TETRALINE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY DECALINE AND TETRALINE

Tetraline and decaline are tetra- and decahydrogenated compounds of naphthalene.

The formula of tetraline or tetrahydronaphthalene is $C_{10}H_{12}$ and that of decaline or decahydronaphthalene is $C_{10}H_{18}$.

They are colourless liquids, fairly volatile, emitting heavy vapours at ordinary temperature. Their boiling points are high at 207°C and 184°C to 195°C respectively.

I. SOURCES OF DANGER

These two products are used mainly as solvents for rubber, resins, bitumen, asphalts, greases, etc...; as such they are constituents of floor and furniture polishes, oil paints and varnishes.

Furthermore, tetraline is included in the composition of certain wetting, derusting and insecticide agents, and decaline in the composition of certain benzene motor fuels.

II. PHYSIOPATHOLOGY

Tetraline and decaline have an irritant action on the skin and the mucosae and a depressive action on the central nervous system.

Animal experiment with large doses has produced evidence of hepatic and renal troubles, a cataract and some blood anomalies. These troubles follow ingestion, inhalation of vapour, but

also penetration of liquid through the healthy skin. These products do not appear to have the same haemolytic effect as naphthalene.

The glycuronic compounds which are metabolites of these products are eliminated through the urine to which they impart a green or brown colour which does not necessarily indicate a renal, blood or hepatic lesion.

Tetraline appears to be somewhat less noxious than decaline.

III. CLINICAL SYNDROME AND DIAGNOSIS

Exposure to vapours produces :

- some general disorders : headache, vertigo, asthemia, etc...
- some digestive disorders : nausea, vomiting, diarrhoea;
- irritation of ocular and upper respiratory mucosae.

The urine is green or brown coloured. This coloration is due solely to the presence of metabolites.

Cases of this type have been reported after a more or less prolonged residence in a room freshly painted with a paint including tetraline as a solvent.

Prolonged cutaneous contact entrains a pruriginous vesicular eczema. The occurrence of urobilinuria and proteinuria associated with this dermatosis has sometimes been reported.

IV. COMPLEMENTARY RECOMMENDATIONS

Patet tests may have been positive in cases of dermatoses.

The green or brown coloration of the urine is a sign of exposure. It will only appear, however, after substantial exposure.

After a substantial or prolonged exposure it is advisable carry out a haematological examination and to watch the renal system and the hepatic functioning.

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APPENDIX II - PARTICULAR NO. A 11
AROMATIC ACIDS AND ANHYDRIDES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY AROMATIC CARBOXYLIC ACIDS AND ANHYDRIDES (1)

The aromatic acids are organic acids where the carboxyl groups (-COOH) are fixed directly to an aromatic or aryl radical (phenyl, naphthyl, anthracyl, etc...).

The anhydrides of aromatic acids which are generally converted to the corresponding acids on contact with water, do not for this reason present any difference to the acids from the point of view of toxicology; phthalic acid is an exception in this respect (see later).

The most important compounds of this group are the following :

- benzoic acid : C_6H_5-COOH
- toluic acid : H_3C-C_6H_4-COOH
- chlorobenzoic acid : Cl-C_6H_4-COOH
- the nitrobenzoic acids (and in particular paranitrobenzoic acid) : NO_2-C_6H_4-COOH
- the dinitrobenzoic acids : $(NO_2)_2$-C_6H_3-COOH
- the aminobenzoic acids (ortho and para) : NH_2-C_6H_4-COOH
- salicylic acid : HO-C_6H_4-COOH
- acetylsalicylic acid (aspirin) : H_3C-CO-O-C_6H_4-COOH

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(1) Other aromatic compounds with acid function also exist : the inorganic acids such as aryl-sulphonic acids and the aromatic compounds with acid reaction such as the phenols (see Appendix I - Particular No. A 23).

and para-aminosalicylic acid : $HO-C_6H_3(NH_2)-COOH$

- the dihydroxy benzoic acids : $(HO)_2-C_6H_3-COOH$
  and the trihydroxybenzoic acids, among them the gallic acid : $(HO)_3-C_6H_2-COOH$
- phthalic acid : $C_6H_4(COOH)_2$
  and phthalic anhydride : $C_6H_4(CO)_2O$
- anisic acid : $H_3CO-C_6H_4-COOH$
- the naphthoic acids : $C_{10}H_7-COOH$

I. SOURCES OF DANGER

The aromatic acids and their halogen derivatives are widely used in the chemical industry as raw material for syntheses of all kinds, as explosives (because of their richness in oxygen atoms), as auxiliary products in the textile industry and as insecticides and fungicides, etc...

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

Most of the substances in this group are liable to cause allergic and orthoergic dermatoses; these cutaneous affections may be accompanied by lesions of the ocular and respiratory mucosae. Practically no other noxious effects, which might result from an industrial exposure, are known in humans.

Mention may be made here of the ear buzzing, vertigo, etc..., and the effects on the gastric mucosae (notably occult haemorrhages) following exaggerated consumption of acetyl salicylic acid or its derivatives.

Methaemoglobinemia which might be foreseen in connection with the aminobenzoic and nitrobenzoic acids has practically never been found. In this context reference should be made to the large group of aromatic amino and nitro compounds which formed the subject of Paragraphs A 24 and A 25 of Appendix I.

Phthalic acid and especially phthalic anhydride are irritants for the skin and the respiratory tracts, notably the upper respiratory tracts. Through direct contact or through inhalation of the vapours an atrophy of the nasal mucosae may be produced with anosmia and, more rarely, a perforation of the septum. To this comes frequently a laryngitis and a bronchitis which may develop into a chronic complaint. Cases of intolerance at cutaneous or respiratory level have been reported; it has been suggested that impurities may play a part in this connection.

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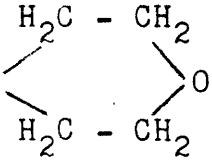
APPENDIX II - PARTICULAR NO. A 12 a
DIOXANE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY DIOXANE

Dioxane or diethylene dioxide ($C_4H_8O_2$) or  is a colourless, inflammable liquid with a weak smell.

Its boiling point is 101°C and its vapour density is 3.03. In the presence of moist air it may give rise to the formation of peroxides which form explosive mixtures with air.

I. SOURCES OF DANGER

The main industrial sources of danger are found in the use of dioxane as :

- solvent for greases, waxes, paints and varnishes, natural and synthetic resins (polyvinyls) nitrocelluloses and cellulose acetates, synthetic rubbers, etc...
- agents in organic syntheses.

II. PHYSIOPATHOLOGY

Dioxane in liquid form or through its vapours exerts a direct irritant action on the eyes and on the upper respiratory tracts.

It penetrates into the organism by ingestion, by inhalation of the vapour and, to a minor degree, through the skin.

The metabolism of dioxane is not well known. Its decomposition in the organism is rapid, but its degradation products are badly defined. Its transformation to diglycolic acid and to oxalic acid has been disputed.

Dioxane when it is administered experimentally in substantial doses by the various routes including percutaneous absorption, produces beside narcosis phenomena, a glomerulo-nephritis. Repeated ingestion induces hepatic lesions.

Repeated exposure to low concentrations of vapours has produced in animals degenerative and congestive lesions of the renal tubes.

In humans, renal and hepatic lesions of the same type have been reported in an observation of collective acute intoxication through inhalation.

III. CLINICAL SYNDROME

In the industrial environment exposure to relatively low concentrations produces irritation phenomena. The severe collective intoxication quoted earlier appears to have been due to an exposure to substantial concentrations of vapours.

After exposure to vapours in relatively low concentration, the ocular irritation manifests itself by a sensation of burning and watering of the eyes.

At higher concentrations a laryngeal burning sensation, coughing, a nasal catarrh and dyspnoea are added; frequently epigastric pains occur.

The severe cases reported following the inhalation of substantial quantities were characterized by nausea, vomiting, abdominal pain; sometimes a hepatomegaly is detectable; in some case icterus has been reported. Azotemic and frequently haematuric nephritis is the most serious element and several cases with fatal outcome have occurred.

Repeated contact with liquid dioxane has been associated with the origin of erythema, sometimes with eczema.

Cases of chronic intoxication in humans have apparently not been reported; sporadic haematological anomalies which have sometimes been reported do not appear to be characteristic.

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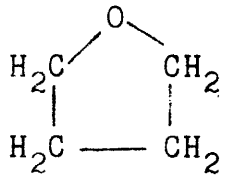
APPENDIX II - PARTICULAR NO. A 12 b
TETRAHYDROFURANE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY TETRAHYDROFURANE

Tetrahydrofurane (C_4H_8O) or  is a colourless liquid (boiling point 65°C) of ethereal odour, inflammable, which in contact with air gives rise to the formation of explosive peroxides.

I. SOURCES OF DANGER

The main source of danger in an industrial environment is the use of tetrahydrofurane as a solvent, in particular as a solvent of certain plastics (polyvinyl chloride, polyvinylidene chloride); it is also used as a solvent for varnishes, glues and inks.

II. PHYSIOPATHOLOGY

It has been found experimentally that tetrahydrofurane produces a transitory conjunctivitis when the liquid product comes into contact with the eye, and that its vapours produce :

- an irritation of the ocular and respiratory mucosae,
- a depression of the central nervous system with coma after exposure to large concentrations,
- renal and hepatic lesions.

The effects on the central nervous system, the liver and the kidneys may also be consequent upon a prolonged cutaneous contact.

The irritative effects and the lesions of liver and kidneys have been attributed to impurities or to secondarily formed peroxides.

III. CLINICAL SYNDROME

In the industrial environment tetrahydrofurane has been responsible for very few cases of disorders.

Nausea, headache and vertigo may follow exposure to notable concentrations. After cessation of exposure they subside rapidly.

Phenomena of ocular or cutaneous irritation are also transitory.

Manifestations of cutaneous sensitization have not been confirmed. Here again the impurities may in reality prove to be the responsible agent.

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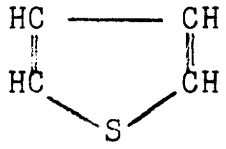
APPENDIX II - PARTICULAR NO. A 13
THIOPHENE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THIOPHENE



Thiophene, also called thiofurane, thiol or divinyl sulphide is a clear liquid which boils at 84°C. It is insoluble in water but very easily soluble in alcohol, ether and benzene.

It is a derivative of coal-tar and browncoal-tar and it is consequently always obtained when benzene is extracted from these tars.

I. SOURCES OF DANGER

The main industrial sources of danger are :

- all places of work where benzene is extracted from coal-tar in the distillation process when, through heating, there may be a formation of toxic sulphurous anhydride;
- utilization of thiophene and its derivatives as pesticides;
- manufacture of pharmaceutical products (analgesics, anti-histamins) synthetic resins, dyestuffs, etc...

II. CLINICAL SYNDROME

The knowledge of the pathology of thiophene rests upon the results of animal experimentation.

Thiophene induces oedematic and haemorrhagic reactions of the skin and of the mucosae. A certain quantity is absorbed through the skin; more substantial contacts with the palmo-plantar cutaneous surfaces produce cramps and haematurias in

rats.

Inhalation of thiophene provokes an irritation of the mucosae and acute neurological troubles analogous to those brought about by benzene.

An ataxia may appear under conditions of acute poisoning as well as under those of a chronic poisoning.

Experiments carried out on animals did not produce any findings of haematological dyscrasias.

III. DIAGNOSIS

Incipient ataxia which can be discovered only by a particularly careful neurological examination.

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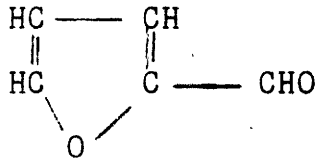
APPENDIX II - PARTICULAR NO.A 14
FURFURAL

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY FURFURAL



Furfural or 2-furfuraldehyde (C_4H_3O-CHO) or "furfurol" according to an obsolete denomination (1), is an oily liquid which turns brown-red on exposure to light. In strong concentrations it has a disagreeable, pungent smell.

Its high boiling point (161°C) together with its low vapour pressure considerably reduce the hazard of exposure in industrial environment. Technical accidents, however, may lead to projections or inhalation of vapours when strongly heated.

I. SOURCES OF DANGER

Furfural is used mainly :

- as a solvent and in particular as a solvent for cellulose products and also in the petroleum industry for the extraction of olefins and of butadiene
- as insecticide and fungicide.

II. PHYSIOPATHOLOGY

Furfural penetrates into the organism substantially through the respiratory tract (inhalation of vapours). Furthermore, experiments have revealed a certain degree of skin absorption of the liquid.

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(1) The denomination "furfurol" according to present nomenclature, is reserved to the furfuryl alcohol.

Furfural is an irritant for the skin and for the mucosae. Moreover, it possesses convulsivant and depressive action on the central and peripheral nervous system. The latter action has been discovered above all in experimental work, but such effects are rare in humans.

III. CLINICAL SYNDROME AND DIAGNOSIS

Irritation of the mucosae by vapour manifests itself by a rhinitis, cheitis and conjunctivitis.

Inhalation of vapour in strong concentrations may provoke headaches and vertigo. Convulsions occurring hours and days following prolonged but single inhalation and cutaneous contact, has been quoted in humans.

The splashing of liquid into the eyes produces pain and an oedema of the conjunctiva. These troubles heal rapidly without sequelae.

After prolonged or repeated exposure to vapour an irritation of the throat and of the eyes (watering of the eyes, conjunctivitis) has been reported together with fatigue, headache, vertigo and a tendency towards depression. A possible prolonged exposure to furfural has also been associated with some cases of tremor of the fingers and of the tongue, polyneuritis and nystagmus.

Cutaneous disorders : furfural is a primary cutaneous irritant. Prolonged or repeated exposure produces erythema with possible secondary eczematisation. Cases of sensitization dermatosis have also been quoted.

IV. COMPLEMENTARY RECOMMENDATIONS

In view of the disorders caused by furfural, exposure to this product is not recommended for persons suffering from neurological disorders and chronic dermatological disorders.

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APPENDIX II - PARTICULAR NO.A 15
THE TERPENES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE TERPENES AND TERPENIC DERIVATIVES AND ESPECIALLY TURPENTINE.

The terpenes are naturally occurring aliphatic or alicyclic unsaturated hydrocarbons of general formula $(C_5H_8)_n$. They are found in oils extracted from numerous plants (in particular coniferae and rutaceae) in the form of their hydrogenated derivatives, as alcohols, ketones, acids, etc... The most important compounds derive from the actual terpenes ($C_{10}H_{16}$) and the sesquiterpenes ($C_{15}H_{24}$).

The pure forms are seldom isolated or used in industry; the products used are more often complex products, mixtures of several terpenes. Most of them are insoluble in water but soluble in solvents and oils. Several of them are inflammable and can form explosive mixtures with air.

Chemically the following distinctions are made :

- the terpenes proper ($C_{10}H_{16}$) : aliphatic, monocyclic (such as limonene) or bicyclic (such as camphene or the pinenes);
- the sesquiterpene ($C_{15}H_{24}$) : mono or polycyclic, such as zingiberine from ginger, cadinene from Spanish juniper oil, santalene from sandelwood oil;
- the diterpenes ($C_{20}H_{32}$) such as colphene;
- the higher polyterpenes such as ambrine, the carotenes, etc...
- the high-molecular polyterpenes are found above all in certain resinous products such as natural rubber.

The most important product from a point of view of industrial hazard is turpentine, whose composition varies according to its source but which consists largely of and pinene and, in so far as turpentine from certain origins is concerned, of 3- carene, which might be the allergizing agent; it may also contain additives (adulteration). It is to be distinguished from "turpentine substitute" which is a mixture of petroleum and tar products.

I. SOURCES OF DANGER

The main areas of exposure to terpenes and their derivatives are :

- the extraction of turpentine by distillation of the resins of certain pines or of the pulp of their woods and its utilization as a diluent for certain paints, lacquers and varnishes or as a scouring agent for materials;
- the utilization as a solvent for greases and oils, for iodine and the manufacture of certain maintenance products (waxes and polishes);
- the decoloration of ivory, cleaning in the printing industry;
- in the chemical industry for organic syntheses and notably in the manufacture of synthetic camphor and its utilization as plasticizer in the manufacture of celluloid;
- in the manufacture of photographic films;
- in the pharmaceutical industry (notably the synthesis of vitamin A);
- in the perfumery industry (manufacture of essential oils).

II. PHYSIOPATHOLOGY

The terpenes are essentially irritants of the skin and of the mucosae.

Turpentines of certain origin may also exert an allergic action, with sensitization sometimes supervening only after several years of exposure. Moreover, the possible effect of certain impurities such as formic acid, formaldehyde and phenols must not be excluded.

In the industrial environment absorption occurs mainly through inhalation of vapour. Experimentally, a certain absorption through the skin has also been observed. Absorption through the digestive tracts in man is accidental (children). In high concentrations, the terpenes have an action on the central nervous system (excitation, depression) and on the digestive and renal systems.

A part of the terpenes absorbed is rejected in the expired air, another part is excreted through the sweat glands, but the bulk is excreted in the urine, unchanged or in the form of glycuro-conjugates. In this case the smell of the urine is peculiar and recalls that of violets.

III. CLINICAL SYNDROME

In the industrial environment the disorders encountered most frequently are dermatoses provoked by direct contact of the product with the skin.

The cutaneous lesions are polymorphous. After being pruriginous and erythematous at the start, they easily become vesiculo-oedematous and then tend to develop towards lichenified eczema. They remain essentially on the hands, on the rear of the phalanges, at the finger tips and around the nails. They appear at the end of several weeks of work. Variations in supplies may give rise to collective dermatoses. These sensitization dermatoses may appear only after several years of exposure to the hazard (see Particular B2 of Appendix I).

Repeated exposure to low concentrations of vapour may cause some respiratory, digestive and renal disorders.

Exposure to strong concentrations of vapour provokes immediate irritation of the ocular and respiratory mucosae (cough, dyspnoea, ocular prickling) together with neurological troubles (headache, vertigo, somnolence) which may go as far as a certain

degree of prostration. When this passes digestive disorders (nausea, vomiting, diarrhoea) and urinary disorders (albuminuria and haematuria) set in. If the exposure was of short duration recovery is usually without sequelae at the end of a few weeks.

Exposure to massive concentrations of vapour or the accidental absorption through the digestive tract are liable to produce hyperthermia and substantial neurological disorders (agitation, mental confusion, convulsive crises) which may lead to coma. After regression of the shock, digestive disorders (nausea, vomiting, diarrhoea) or urinary disorders (haematuria, albuminuria) may appear. Disturbances of the electroencephalogram may sometimes persist for 2 to 3 weeks.

Recovery without sequelae is the rule.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A 16
ACRYLAMIDE - METHACRYLAMIDE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ACRYLAMIDE AND METHACRYLAMIDE

Acrylamide of formula $CH_2=CO-NH_2$, also known as propeneamide, is a crystalline product obtained in the form of white pellets (melting point 84°C) soluble in water, in alcohol and in ether. It is synthesized from acrylonitrile by hydrolysis in acid medium. Its only use is as a monomer for polyacrylamide plastics.

The polymer, polyacrylamide, of formula $(-CH_2-CH-CO-NH_2)_n$ is a white powder, odourless, soluble in water.

Methacrylamide, of formula $H_2C=C(CH_3)-CONH_2$ may be regarded as approx. ten times less noxious than acrylamide.

I. SOURCES OF DANGER

Acrylamide is used in industry essentially as a monomer of polyacrylamide plastics. The latter are constituents of glues and adhesives, thickeners for paints, etc... They are also used in paper-making, the photographic industry, the leather industry and for the preparation of viscose regeneration products. Finally, they are used in building for sealing work.

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

The cases observed in the industrial environment have been consequent upon skin penetration, the physical condition of the product rendering absorption through the respiratory tract less likely.

After prolonged exposure, acrylamide exerts a neurotoxic action both on the central nervous system and on the peripheral nerves. The lesions become manifest through polyneurites which are associated with central disorders, positional tremors, disturbed gait, visual and auditive hallucinations, muscular atrophies.

Emaciation is practically constant and early, thus constituting a warning sign.

The cessation of exposure to the risk allows a regression of these symptoms. In severe cases, however, this regression is slow and several years are sometimes required for the symptoms to disappear. An increased sensitivity in case of new exposure always persists.

Single exposure to large doses does not provoke the disorders of the type described; these appear to result from repeated exposure to moderate concentrations.

Acrylamide has irritative effects on the skin. It is liable to produce a palmar hyperhidrosis, even erosive palmar dyshidrosis, developing towards desquamation.

Certain authors have reported positive cutaneous tests.

If acrylamide makes direct contact with the ocular mucosae conjunctivitis will result.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A a 1
MOTHER OF PEARL DUST

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE DUST FROM MOTHER OF PEARL

Mother of pearl is the inside part of the shells of gasteropodous and lamellibranchiate molluscs. It is constituted of superimposed layers of calcium carbonate (97 %) and organic films of conchioline (3 %) presenting a smooth and iridescent surface.

I. SOURCES OF DANGER

The main industrial sources of danger are essentially all types of work involving exposure to the dust from mother of pearl and notably the sawing, grinding, trimming, polishing, burring and carving of the shells.

The main use of mother of pearl remains, however, the manufacture of buttons. It is also employed in making fork, knife and penknife handles and fancy articles and insets in wood and lacquer.

At present the manufacture of buttons is carried out more and more in industrial plants and preventive measures, in particular work under water, have considerably reduced the risk. Nevertheless, work on mother of pearl is still frequently done by craftsmen and in many cases the antiquated methods used cause the generation of very considerable amounts of dust.

II. PHYSIOPATHOLOGY, CLINICAL SYNDROME AND DIAGNOSIS

1. Osseous affections

The longest known of the diseases caused by the dusts from mother of pearl is an osteitis known under the name of conchiolinic osteomyelitis or osteomyelitis of the mother of pearl workers.

The pathogeny is not well defined; it has been attributed either to conchioline itself or to pathogenic germs deriving from the remains of the mollusc bodies on badly cleaned empty shells, or again to mother of pearl dust embolisms in the bones. The disease appears to have become extremely rare, however, and it affects essentially young persons in whom ossification is not yet complete.

At the outset violent pains are felt spontaneously, made worse by pressure, situated at the distal extremities of the diaphyses of the long bones (cubitus, radius), rarely at the level of the flat bones. However, cases of affection of the maxillaries with osseous necroses and deformation of the rising branch have been reported.

Progressively the pain reaches the medium portion of the bone. Sometimes a slight swelling of the overlying soft parts is noted.

After a few days or even weeks a febrile reaction is frequently seen. Suppuration, however, is exceptional. Neighbouring joints nearly always remain undamaged. Radiography shows a picture of osteitis with periostitis confirming the diagnosis of subacute osteomyelitis. The pains and the swelling diminish spontaneously little by little. Recovery is generally complete without sequelae.

2. Irritative affections of the respiratory system

It is largely a matter of an irritation of the upper respiratory tracts; rhinitis, pharyngitis and sinusitis frequently accompanied by a conjunctivitis. The disorders, which are not particularly serious, affect primarily persons fairly recently exposed and as a rule progressive adaptation takes place. Affection of the bronchial tracts is more rare and more delayed. The symptomatology is non-specific : dyspnoea, cough, expectoration.

If exposure to the dusts continues, the affection may develop slowly towards a non-specific chronic respiratory syndrome.

3. Manifestations of allergic character

Cutaneous and respiratory manifestations of an allergic character have been described which have been attributed to dusts consisting either of the actual mother of pearl, or of organic residues of the mollusc bodies, or, and more likely, of conchioline.

4. Febrile manifestations

Finally, some cases of pyrexia of short duration have been reported for which several pathological mechanisms have been postulated.

III. COMPLEMENTARY RECOMMENDATIONS

The pathological manifestations described do not present any specific character. The diagnosis will rest solely on the knowledge of the industrial hazard involved.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A a 2
HORMONAL SUBSTANCES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY HORMONAL SUBSTANCES

The hormones are products of internal secretion; they pass directly into the blood stream or into tissue fluids so exerting their action on other cellular groups of the organism.

The only hormonal substance which has attracted attention from a point of view of industrial toxicology is folliculin; this hormone is encountered most frequently in various synthetic forms; among these synthetic "oestrogens", the most frequently used are stilboestrol and oestrostilbene D and their derivatives.

The chemical structures of these substances differ from that of folliculin whilst retaining one or more of the physiological characteristics of the same.

I. SOURCES OF DANGER

The disorders reported were observed in the pharmaceutical industry during the manufacture and conditioning of hormonal substances.

In addition the utilization of synthetic oestrogens in the cosmetic industry and in the breeding of cattle and of chickens has to be mentioned.

II. CLINICAL SYNDROME

The oestrogens exercise their harmful action mostly in the form of dusts; the absorption of these by inhalation and by skin absorption forms the basis of any poisoning.

In pharmaceutical workers exposed to oestrogens gynaecomastias sometimes accompanied by mastitis and in fairly rare cases a sometimes very pronounced diminution of the libido have been noticed.

Among female personnel menstrual disorders essentially menorrhagias, sometimes metrorrhagias have been observed. In most cases these troubles cease very rapidly after cessation of the exposure to risk.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. A a 3
ENZYMES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY PROTEOLYTIC ENZYMES

The enzymes are substances of biological origin which exercise in the organism the role of specific catalysts liable to promote, to accelerate and to render possible all sorts of chemical reactions. Outside the organism they can exercise their action only under certain particular physico-chemical conditions (temperature, pH, etc...) and in the absence of inhibiting factors.

Within the framework of industrial pathology, the enzymes which have attracted particular attention form part of the group of proteolytic enzymes.

I. SOURCES OF DANGER

The main industrial sources of danger are :

- the extraction and utilization of pancreatic trypsin, an enzyme which is extracted in the slaughter-houses and is used in the pharmaceutical industry;
- the extraction and purification of enzymes of vegetal origin; bromelin (from pineapple juice), papain (from paw-paw juice), ficin (encountered in the latex of certain fig-trees cultivated in South America). The above mentioned extracts from fruits are used in the manufacture of "fruit juices";
- the preparation of certain proteolytic enzymes and their incorporation in so-called "biological" washing. These proteases and alpha-amylase are extracted from micro-organism cultures, notably of "bacillus subtilis" and "aspergillus orysae". The personnel of cleaning and laundering establishments is particularly exposed to this risk.

Certain observations have suggested that the mixture of these substances with the other ingredients entering into the composition of products delivered for consumption might in certain stages of the manufacture be even more aggressive than the enzymes themselves.

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

The pathological phenomena caused by the proteolytic enzymes are of two orders : essentially orthoergic or allergic cutaneous manifestations, and principally pulmonary allergic phenomena.

a) The cutaneous manifestations arise on direct contact of dusts containing proteolytic enzymes with the skin, the ocular mucosae and the upper respiratory tracts; the disorders may be of the orthoergic or allergic type. Thus, trypsin, papain, bromelin and ficin may provoke dermatoses of the orthoergic type : prickling, erythema, excoriation; subsequently, painful superficial erosions and even deep fissures of the hand (trypsin), which bleed on contact, may be observed. Likewise, it has been observed that bromelin is liable to produce erosions of the buccal mucosa. The disorders clear up more or less rapidly after exposure to the risk has ceased.

The orthoergic forms may be complicated by eczematous lesions of the allergic type, recurring on any new contact with the noxious agents; the tests with products manipulated are frequently positive. Not infrequently the preventive measures are not enough to avoid relapses and it is necessary to arrange for a change in employment.

For more extensive information in respect of cutaneous manifestations, see Particular B 1 of Appendix I.

b) The respiratory manifestations involve mainly the lungs. They are of the orthoergic or allergic type, whilst it is not always possible, especially at the beginning, to distinguish between them. Rhinitis resisting treatment, frequently tenacious dry irritative coughs, rarely accompanied by sputum, can be observed.

Manifestations of the asthmatic type are observed in the industrial environment, mainly in the manufacture or use of detergents based on proteolytic enzyme. They are of the allergic or orthoergic asthma type (see Particular C 5 of Appendix I) or of the hyperergic allergic asthma type. The symptomatology of the latter form is often very mild at the start and may remain unnoticed. In such cases, the cough, dyspnoea or thoracic pains do not appear characteristic; the more serious conditions, however, are characterized by a combination of the more significant symptoms. Frequently, and notably in severe cases, the skin tests (intradermic or by scarification) are positive.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. B 1 a
COAL, CARBON, GRAPHITE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE DUSTS FROM COAL, CARBON AND GRAPHITE

The dusts from coal are largely constituted of carbon particles, but these may be associated with other mineral particles such as quartz, feldspar, mica, clay, etc... The association of siliceous particles is responsible for the clinical syndromes commonly called "anthracosilicoses" (see Particular C 1 of Appendix I).

The pulmonary affections provoked by the dusts from graphite will be taken as typical in the description. They are not the most frequently occurring, but graphite itself is made up predominantly, if not exclusively of carbon.

Graphite is a powdery substance of greyish black colour with metallic reflexions, soft to the touch and soiling. It is an amorphous substance. It is found in abundance in the natural state where it occurs with other crystalline rock such as schist, gneiss, quartz and marble. It is also found in oil-bearing muds. A graphite practically free of silica also exists which is obtained electrically from coke.

It is used essentially for its plastic qualities, its resistance to high temperatures, its electrical conductivity, its inert property in relation to numerous reagents and its miscibility with numerous solid and liquid substances.

I. SOURCES OF DANGER

The main sources of danger are :

- the extraction and the treatment of the ore and the extraction from oil-bearing muds;
- the powdery residue deriving from the manufacture of cast-iron and steel;
- the manufacture of brake linings, pencils, waxes and polishes, electrolytic anodes, electrodes and electric contacts, electric batteries;
- the utilization as lining for furnaces;
- the mixing in as additive to certain oils and petrols;
- the manufacture of moderators for nuclear reactors.

II. PHYSIOPATHOLOGY, CLINICAL SYNDROME AND DIAGNOSIS

The individuality of a specific pneumoconiosis caused by the repeated inhalation of graphite free of any other noxious particles (so-called graphitosis) has been disputed. It is rather a matter of a pneumoconiosis from mixed dusts caused by the joint action of the dusts from graphite and from dusts of other kinds. The evolutive character and the seriousness of the affection depend above all on the proportion of siliceous dusts associated with the graphite dusts.

When the dust coverage is very abundant and persistent, clinical signs such as a cough with expectoration may appear.

The radiological images are of the fuzzy nodule type. In the case of exposure to mixed dusts of high silica content, the images may assume the aspect of pseudotumoral formations. These may excavate themselves and give rise to a blackish expectoration.

III. SPECIAL RECOMMENDATIONS

The aetiological diagnosis is based substantially on the occupational history.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. B 1 b
BARIUM SULPHATE

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE INHALATION OF BARIUM SULPHATE DUSTS

Barium sulphate or baryte ($BaSO_4$) is very widely distributed in the natural state. It is frequently very pure, but sometimes associated with small quantities of strontium and calcium. It is of very high density (4.5) and presents itself in the form of transparent and colourless crystals. The slight blue, brown or green coloration, which is frequently observed, is due to the presence of iron, lead or silver ores. It is practically insoluble in water.

I. SOURCES OF DANGER

The main risks of industrial exposure are :

- the extraction of barium sulphate and the production of barium and its compounds;
- the utilization in the petroleum industry for well drilling (drilling muds);
- the manufacture and the conditioning as a contrast substance in radiology;
- the utilization as a filler in gramophone records, linoleum, soap, synthetic leather, rubber and paper-making (glossy paper) industries as well as in certain lacquers and stains;
- the utilization as a pigment in the manufacture of certain paints, such as blanc-fixe or lithopone (mixture of 70 % barium sulphate and 30 % zinc sulphide).

The workers occupied in the crushing and packaging of barium sulphate are particularly exposed to risk.

II. PHYSIOPATHOLOGY

The inhalation of fine dusts of barium sulphate causes essentially a benign pneumoconiosis called barytosis. This pneumoconiosis may assume a sclerotic character which is due to free silica particles when these are present in a certain concentration as impurities in the barium sulphate (mixed dusts).

III. CLINICAL SYNDROME AND DIAGNOSIS

The clinical signs of barytosis are : cough, expectoration, dyspnoea. Functional tests showed only very inconspicuous disorders.

Radiography is the essential diagnostic element. At the start a reticulation with fuzzy micronodules of 1 to 1.5 mm (deposits of barium sulphate) appear which subsequently expand to 1 to 3 mm. This development is more or less rapid according to the extent of the dust coverage, but the opacities are not confluent and do not give rise to proximity reactions.

If the worker is withdrawn from the risk, and if the barium sulphate inhaled was in pure condition, the few clinical disorders disappear rapidly and the radiological aspect becomes normal again after a few years. However, if the evolution was relatively long, some clinical and radiological signs of bronchial irritation may persist.

The possible presence of free silica particles in the barium sulphate inhaled may provoke a pneumoconiosis syndrome with all the radiological and functional characteristics of pneumoconioses from mixed dusts.

IV. SPECIAL RECOMMENDATIONS

In the occupational anamnesis it is particularly important to search for and to measure the particles of free silica in the dusts inhaled. Barytosis provoked by barium sulphate free of silica does not cause disablement.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. B 1 c
TIN OXIDES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY THE INHALATION OF TIN OXIDE DUSTS

The main tin mineral is cassiterite (SnO_2) which occurs in the form of crystals with an enamel-like shine, of brown or black colour. In the course of industrial processes the tin oxides (SnO, SnO_2, SnO_3) are encountered in the form of dusts, of vapours, or of fumes.

I. SOURCES OF DANGER

The main risks of industrial exposure are :

- the extraction of tin from cassiterite, notably the separations by screening and the roasting and electrolytic refining of cassiterite;
- the industrial preparation of oxides from powdered tin;
- the preparation of tin alloys;
  white metal : tin - antimony - copper
  tin bronze : tin - copper
  printing types : tin - lead - antimony;
- the manufacture of tin objects such as certain household utensils and tin-covered sheets for the wrapping of tea, chocolate, tobacco, etc...
- the tin-plating of metals used for the manufacture of preserve cans;
- the utilization for welding of lead-tin-cadmium rods;
- the preparation of certain anti-corrosive coatings and their applications in the electronic industry as in radio and television;

- the operations of the mixing of tin into steel in order to increase its hardness and anti-corrosive strength (e.g. for the manufacture of engine blocks);
- the ceramic industry and the manufacture of certain enamels.

II. PHYSIOPATHOLOGY

The inhalation of dusts or fumes of tin metal or tin oxides provokes pneumoconiosis with inconspicuous non-evolutive tissue reactions, called stannosis.

The tin oxides are non-toxic but they deposit in the lungs, the liver, the spleen and the lymphatic glands. At autopsy the lungs pleurae show a black pigmentation as do the glands and vessels, as well as of the perivascular and peribronchial spaces; this pigmentation is due to local deposits of tin or of its oxides. After an exposure of more than twenty years the tin content in the pulmonary tissue may attain 20 000 times the normal content.

III. CLINICAL SYNDROME AND DIAGNOSIS

The inhalation of dusts or of fumes of tin, being frequently associated with the inhalation of other metallic fumes (zinc, antimony, cadmium), may bring about feverish attacks, calling to mind the symptomatological syndrome of "metal fume fever".

In so far as the stannosis described above is concerned, its clinical symptoms are always very inconspicuous : sometimes there may be slight effort dyspnoea, minimal sputum, but general health is well maintained. Functional tests are normal; but, when the exposure has been of long duration, the ventilatory tests may be disturbed.

In most cases stannosis is only discovered during systematic radiological examinations. The intense shadows contrast with the absence of clinical symptoms. These opacities sometimes

appear as early as the sixth month, but more generally they only appear after long years of exposure.

At the start the X-ray picture reveals the existence of isolated and dense, scattered, micronodules and a pronounced accentuation of the hilar regions. Subsequently, giant nodules form, first seen in the central third of the lung and extending progressively over the whole of the two pulmonary areas. They may look like small droplets of lipodol. The hila are then enlarged with very opaque glands effacing the broncho-vascular pedicle. These appearances persist in spite of the cessation of exposure.

IV. SPECIAL RECOMMENDATIONS

Concern regarding the presence of associated free silica need only be felt during the operations of extraction and treatment of cassiterite. This silica may then provoke a simple pneumoconiosis from mixed dusts. In such cases it is appropriate in the occupational anamnesis to search for and measure in particular the particles of free silica in the dust content of the working place.

Stannosis proper is a rare occupational disease; it is a benign, non-sclerogenous pneumoconiosis; but in view of the extent of the radiological images, occupational anamnesis is essential to differentiate it from other less benign pneumoconioses.

Moreover, it has to be remembered that in the industry the risk of lead-poisoning is very frequently associated with work using tin.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. B 2
METAL DUSTS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY METAL DUSTS OF METALS NOT MENTIONED ELSEWHERE

The action of the following metals has been studied in the Particulars of the European schedules "Appendix I" and "Appendix II" as follows :

Aluminium	App.	I	- Particular	C 2	Manganese	App.	I	- Particular	A 7
Arsenic	"	I	"	A 1	Mercury	"	I	"	A 6
Barium	"	II	"	B 1b	Nickel	"	I	"	A 9
Beryllium	"	I	"	A 2	Thallium	"	I	"	A 13
Cadmium	"	I	"	A 4	Tin	"	II	"	B 1c
Chromium	"	I	"	A 5	Tungsten	"	I	"	C 3
Cobalt	"	I	"	C 3	Vanadium	"	I	"	A 14
Iron	"	I	"	C 1c	Zinc	"	II	"	A 4
Lead	"	I	"	A 11					

Bismuth, boron, cerium, cesium, colombium, gallium, germanium, indium, lanthanum, lithium, molybdenum, osmium, palladium, rhenium, rhodium, rubidium, ruthenium, selenium, strontium, tellurium, zirconium are metals for which no cases of pulmonary fibrosis following industrial operations liable to produce dusts have been reported.

In the present complementary Particular only antimony, silver, copper, magnesium, platinum, tantalum and titanium will be studied, the inhalation of the dusts of which is liable to bring about a more or less substantial affection of the respiratory tracts.

A. ANTIMONY

Antimony (Sb) is encountered very rarely in pure state in the nature. Its most widely distributed mineral is stibnite (Sb_2S_3) or antimony sulphite. It is a bright metal, silvery white with bluish reflections. It is of crystalline structure and very powdery. It melts at 630°C, evaporates at 1 380°C but burns in contact with air at 900°C, liberating fumes of Sb_2O_3 and of Sb_2O_5 of alliaceous odour.

It is not used industrially in its pure state; its compounds, on the other hand, are very widely used in industry in the form of :

- antimony trioxide Sb_2O_3
- " pentoxide Sb_2O_5
- " trisulphide Sb_2S_3
- " pentasulphide Sb_2S_5

I. SOURCES OF DANGER

The main industrial circumstances of exposure to the risk are :

- the extraction of the metal from its ores, mainly the trisulphide, by melting or by electrolysis;
- the utilization in the manufacture of certain alloys to make use of its power as a hardener and for its anti-corrosive qualities
  - . with lead in the manufacture of electric accumulator electrodes (5 to 18 % of antimony),
  - . with tin, lead and copper in the production of anti-friction alloys (10 to 18 % antimony),
  - . with tin and lead in the manufacture of printing types (linotype and stereotype) (13 % of Sb),
  - . with tin for the manufacture of decorative objects such as statuettes, candle-sticks, etc... (5 to 20 % of Sb),
  - . with tin and lead for the manufacture of certain welding rods, its presence in the alloy lowering the melting point,
  - . with aluminium for the manufacture of transistorized elements.
- the manufacture of fire-resisting textiles;

- the utilization of antimony trioxide notably as a pigment in dyeing, in the blueing of the metals, in certain paints;
- in pyrotechnics as a producer of fumes;
- the vulcanization of rubber;
- the glass and enamel industry as an opacifying agent.

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

The general action of antimony and its compounds may be regarded as similar to that of arsenic and its compounds of the same chemical structure.

The effects of the inhalation in appreciable concentrations of antimony or its compounds in the form of vapours, dusts or fumes are those of the classical "foundryman's fever" without special characteristics. Recovery from the attack is without sequelae.

Repeated inhalation of small concentrations causes at all an irritation of the upper respiratory tracts (laryngitis and tracheitis) notably in foundrymen. However, there is no formal evidence that repetition of these effects may bring about the occurrence of an evolutive fibrosis of the pulmonary parenchyma.

Antimony chloride ($SbCl_3$) is a respiratory irritant.

B. SILVER

Silver (Ag) is fairly widely distributed in the nature, both in pure state and in the form of numerous minerals, the main one of which is argentite (Ag_2S). It is a bright metal, somewhat less malleable than gold, resistant to the majority of organic acids and to oxidation, but it is attacked by most sulphur compounds.

I. SOURCES OF DANGER

The main industrial exposures are :

- the extraction of the metal or of its ores and their purification;
- the manufacture of alloys with other metals for numerous purposes because of its resistance to oxidation :
  - . with copper for the manufacture of electrical contact relays,
  - . with aluminium in the manufacture of scientific instruments,
  - . with magnesium and nickel in the manufacture of electrical instruments operating at high temperatures,
  - . with cadmium and copper in the motor car industry,
  - . with chromium and nickel in the formulation of certain special steels,
  - . with cadmium in the manufacture of welding rods.
- the use of silver ink for the printing of printed circuits;
- the manufacture of coins, silver-ware and jewellery;
- the manufacture of tubes, valves, etc... for pasteurization in the milk industry, cider-making and in breweries;
- the application of metallic films in the glass and ceramic industries;
- the chemical, pharmaceutical and photographic industries;
- the use as a bactericide in the sterilization of water, fruit juices, vinegar, etc...

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

Silver may be absorbed by the gastro-intestinal tract and by inhalation of its dusts. Excretion is essentially fecal. If absorption is excessive it produces argyria which is a local or general overloading of the tissues with silver (gingival line and permanent cutaneous coloration).

Argyrosis, whether or not associated with local or general argyria, is caused by the deposition of inhaled metallic particles in the walls of the bronchi and the bronchioles and along the lymphatic vessels of the pulmonary parenchyma. This impregnation by silver does not involve the risk of pulmonary fibrosis.

C. COPPER

Copper (Cu) is widely distributed in the world, both in its natural state and in the form of numerous minerals such as malachite, cuprite or chalcopyrite. It is a malleable metal of red-brown colour. Its thermal and electrical conductivity is among the highest of all the metals with the exception of silver. Its melting point is at 1 083°C.

I. SOURCES OF DANGER

The main industrial exposures to risk are :

- the extraction of copper and its ores;
- the manufacture of numerous alloys which have numerous applications in a multitude of industrial and domestic fields with zinc, tin, aluminium, iron, manganese and nickel, notably with tin for the manufacture of bronze which sometimes also comprises zinc, lead, phosphorus and nickel;
- the electrical industry in the form of resistance wire, high-conductivity tubes, switch blades, etc...
- the manufacture of tubing;
- the manufacture of bronze paints.

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

The effects of the inhalation of notable concentrations of copper and its compounds in the form of dusts, vapours or fumes are those of the classical "metal fume fever" without special copper characteristics. Rapid recovery is the rule.

A setting-in of pulmonary fibrosis has not been observed either after repetition of these feverish attacks or after the frequent inhalation of low concentrations of fumes, vapours or dusts of copper.

D. MAGNESIUM

Magnesium (Mg) is widely distributed in the earth crust in the form of carbonate (magnesite and dolomite) of silicate (olivine, serpentine, talc, asbestos) of sulphate and of chloride (sea water).

It is a light metal, silvery white, stable in ordinary air but rapidly corroding in saline atmosphere. It is highly resistant to hydrofluoric acid and a little harder than aluminium. It reacts violently in the presence of oxiding agents and the molten metal burns with an explosive effect in the presence of an excess of moisture. Its melting point is 650°C.

I. SOURCES OF DANGER

The main industrial circumstances of exposure to risk are :

- the manufacture of alloys used in the aeronautics, astronautics and motor-car industries;
- the manufacture of industrial machines and radio and television sets; the main metals used in these alloys are manganese, aluminium and zinc, and more recently cerium, thorium and zirconium;
- the use as antioxidant in the copper, nickel and steel industry;
- pyrotechnics;
- the manufacture of incendiary bombs, tracer bullets, flares by the utilization of magnesium in powder form.

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

Apart from the risk of accidental burns and ulcerations caused by the physical effects of magnesium under certain conditions, the inhalation of concentrated vapours of nascent magnesium oxide may cause a characteristic attack of "metal fume fever". In workers exposed to this risk a febrile reaction with cough, thoracic oppression and pronounced leuco-,

cytosis has been observed analogous to that found on exposure to zinc oxide vapours.

The effects of asbestos and of magnesium silicate have been studied in Particular No. C 1 b, C 1 c of Appendix I.

E. PLATINUM

Platinum (Pt) belongs to the class of heavy metals which also comprises palladium, iridium, osmium and rhodium. It is found in pure state in nature, alloyed with the other metals of the group. It is a white, fairly malleable metal; its melting point is 1 769°C.

I. SOURCES OF DANGER

The main industrial circumstances of exposure to risk are :

- the use in electrical, electronic and telecommunication equipment (pure or in alloys with high platinum content);
- the chemical industry for the manufacture of platinum anodes and catalysts;
- the metallurgical, glass-making and ceramic industries (platinum-rhodium alloy);
- the aeronautics industry (platinum-tungsten alloy);
- the manufacture of laboratory equipment;
- jewellery industry;
- the electro-galvanization with solutions of complex platinum salts (platinates);
- the photographic industry (potassium chloroplatinate);
- the manufacture of fluorescent screens (barium platinocyanate).

II. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

Platinosis is a complex syndrome, respiratory as well as cutaneous, which can be ascribed to an allergy to soluble platinates.

The cutaneous effects have been studied in Particular No. B 2 of Appendix I and the respiratory effects (immediate asthmatiform syndrome) in Particular No. C 5 of Appendix I and No. B 4 of Appendix II.

It appears, however, that the repeated inhalation of small concentrations of dusts, vapours or fumes of platinum or of its salts may bring about a chronic irritation of the respiratory tract.

F. TANTALUM

Tantalum (Ta) is a silvery white metal which is found in the form of an ore in combination with colombium, essentially as ferrous colombium-tantalum Fe $(Nb\ Ta\ O_3)_2$, called tantalite when tantalum is present in a larger quantity, and columbite in the reverse case.

Tantalum is attacked solely by hydrofluoric acid and by concentrated alkalis. Its melting point is 3 000°C.

I. SOURCES OF DANGER

The main industrial circumstances of exposure to risk are :

- the extraction of the mineral;
- the radiophonic and electrical industry for the manufacture of lamps;
- the chemical industry for equipment for acid tests;
- the rubber industry as a catalyst in the butadiene synthesis;
- numerous uses in the form of alloys, mainly with tungsten, titanium and cobalt, notably in the production of calcined metallic carbides;
- the manufacture of material for surgical prostheses.

The action of tantalum was discussed in the pathology of hard metals - Particular No. C 3 of Appendix I.

G. TITANIUM

Titanium (Ti) is widely distributed in the nature in the form of its minerals; it is a dark grey metal. When pure, it is relatively malleable at ordinary temperature; it is non-magnetic and highly resistant to corrosion. Its melting point is 1 820°C.

I. SOURCES OF DANGER

The main industrial circumstances of exposure to risk are :

- the extraction of minerals;
- the manufacture and utilization in the form of alloys with aluminium, tin and vanadium and in the form of ferro-titanium in the production of certain special steels;
- the glass-making and ceramics industry;
- the utilization as white pigment in certain paints;
- the manufacture of material for surgical prostheses;
- the manufacture of electrodes and lamp filaments together with carbon and tungsten.

II. PHYSIOPATHOLOGY

Observations of workers who had been exposed for fairly long periods to titanium dusts showed the appearance of a measure of radiographic reticulosis.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. B 3-4-5
ANIMAL AND VEGETABLE DUSTS

RESPIRATORY DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ORGANIC DUSTS OF ANIMAL AND VEGETABLE ORIGIN.

The inhalation of organic dusts of animal or vegetable origin may provoke various types of respiratory affections which may be classified differently according to whether the criteria adopted are :

- anatomo-clinical,
- physiopathological or
- aetiological (agents responsible).

The anatomo-clinical aspects differ according to whether the reactive manifestations predominate on the alveolar level on the level of the bronchi or on these two levels at the same time.

In accordance with the immunological state of the subject, the hypersensitivity reactions of the pulmonary parenchyma will :

- sometimes be retarded and then with alveolar and interstitial predominance; this is the case in non-atopical subjects;
- sometimes acute and then preferably with bronchial predominance; this is the case, in particular, in atopical subjects.

The different physiopathological processes allow classification of these affections into three groups :

a) the affections where the antigens of animal or vegetable origin provoke the production in the plasm of specific precipitating antibodies, generally of group IgG (immunoglobulin G). These phenomena can be attributed to hypersensitivity of type III of

the classification of Gell and Cooms (antigen - precipitating antibody complex) and possibly to cellular mediator hypersensitivity (type IV of the classification of Gell and Cooms). Histologically, these affections are characterized most frequently by an alveolitis.

The following are typical of this group :

- farmer's lung,
- bird-handlers' lung,
- bagassosis.

b) the affections of the asthmatic type, which can be attributed to the hyperergic-allergic form, caused by certain antigens of animal or vegetable origin, involve the production of antibodies intimately linked to certain cells (notably tissue mastocytes). These antibodies belong to the group IgE immunoglobins. At the time of the antigen-antibody reaction, histamine and other active substances are released which provoke oedema of the bronchial mucosae and bronchospasm. According to Gell and Cooms, this whole mechanism can be attributed to the immunological type I. To this type belongs baker's asthma.

c) the affections for which various inductor mechanisms have been proposed (orthoergic mechanical action, presence of an histamine liberator, role of micro-organisms or their toxins, allergic sensitization, etc...). They are characterized on the anatomo-pathological level by broncho-alveolitis. To this type belong the respiratory affections consequent upon inhalation of the dusts of cotton, flax, hemp, jute and sisal.

Byssinosis has been chosen as a typical example for the description.

These various affections have also been classified according to the nature of the agents responsible (whose constitution and origin may be very varied).

The following diseases will be dealt with successively in this Particular :

A. - FARMER'S LUNG,

B. - BAGASSOSIS,

C. - BIRD-FANCIER'S LUNG,

D. - BRONCHIAL ASTHMA DUE TO INHALATION OF ORGANIC DUSTS,

E. - THE RESPIRATORY AFFECTIONS CAUSED BY THE INHALATION OF DUSTS FROM COTTON (BYSSINOSIS), FLAX, HEMP, JUTE AND SISAL.

A. - FARMER'S LUNG

This disease is observed after inhalation of mildewed vegetable remains of hay, straw, grains. It is caused by the spores of mildews of the family of the actinomycetes thermophiles, the most frequent of the micropolyspora foeni.

I. SOURCES OF DANGER

This disease rages especially in humid regions after wet summers; it appears at the end of autumn and at the beginning of spring. It may be induced by all work exposing to vegetable dust and notably by the handling of mildewed hay.

II. PHYSIOPATHOLOGY

The inhaled particles act at the same time as irritants of the respiratory system through the dusts and as antigen through the spores with the production of specific precipitating antibodies leading to hypersensitivity reactions.

The disease is marked by the appearance of granulomatous micronodules with giant cells and lymphocytic reaction. Later the appearance of a diffuse interstitial fibrosis may be observed.

III. CLINICAL SYNDROME

a) Acute form

Five to ten hours after exposure to the dust symptoms of acute bronchopneumopathy appear with sensation of cold, shivers, sweating, diffuse stiffness, headaches and fever. Dyspnoea, sometimes very intense, is the major symptom; auscultation reveals crepitant rales, frequently disseminated but sometimes very inconspicuous.

Chest X-ray frequently shows finely disseminated and frequently hardly visible, bilateral nodular shadows.

Recovery is the rule, the acute phenomena subsiding in two or three days, sometimes overnight.

In case of new exposure, the crises repeat themselves and may become more serious, leading to persistant respiratory disorders with loss of weight and affection of the general condition.

Immediate complications are very rare (spontaneous pneumothorax, haemoptysis, acute respiratory insufficiency). Lethal forms are exceptional at this stage.

b) Chronic form

This may follow one or more acute episodes or it may set in directly in an insiduous manner. It progresses towards a condition of respiratory insufficiency. Dyspnoea is in the forefront of clinical symptoms; it first appears on exertion, later becomes permanent with cough, expectoration, thoracic pains, asthenia and emaciation. The development is sometimes interspersed with acute episodes of respiratory insufficiency.

Radiography shows reticulo-nodular images with retraction; if development is prolonged areolar images are sometimes found.

The respiratory function tests remain normal for a long time. Later a restrictive syndrome is observed which may become complicated subsequently by an obstructive syndrome; to this is sometimes later added a drop in the transfer factor.

IV. DIAGNOSIS

The immunological investigations constitute one of the essential elements of the diagnosis. The search for serous specific antibodies is positive for the micropolyspora foeni, more seldom for other actinomycetes of mildewed hay. To be regarded as significant these reactions must be clearly positive. In case of doubt, or if they remain negative, they will have to be repeated. On the other hand, these tests may be positive in 20 % of subjects apparently not affected by the disease.

In general the skin test remain negative. The tests of specific antigen inhalation may reproduce the symptoms of the disease.

If the individuum is removed from the contaminating atmosphere, the development is mostly favourable. However, a new contact may bring about a relapse. Moreover, in severe cases a syndrome of chronic respiratory insufficiency with emphysema supervenes possibly leading later to the syndrome of chronic cor pulmonale.

V. COMPLEMENTARY RECOMMENDATIONS

The history of the handling of mildewed hay before the onset of the disorders and the specific biological examinations allow a positive diagnosis to be made and certain differentiation from other chest conditions with a similar clinical picture (asthmatic crisis, granulitis, etc...).

In a rural environment, moreover, other interstitial pneumopathies, immunitary or not, of vegetable or animal origin, mycosic or bacterial, are observed.

Specific treatments for this affection are, at present, not known.

When the disease is confirmed or merely suspected, the subject should be removed from any risk of an inhalation of mildewed vegetable fragments. The wearing of a mask is recommended.

B. - BAGASSOSIS

The bagasse consists of the remains of sugar-cans after their passage through the mill where the sugar has been extracted. A portion of these remains is subjected to a fermentation and used for the preparation of tafia (rum); the dry refuse from this operation may serve as a fuel or as a fertilizer.

The bagasse refuse consists in the main of cellulose but contains 20 % of proteins; it has been found to harbour various micro-organisms.

I. SOURCES OF DANGER

The main industrial sources of danger are situated at the places of work most exposed to the inhalation of dusts deriving from dried and powdered bagasse products. These products are used in the manufacture of sound-proofing and insulating materials, as starting material in paper-making, the manufacture of rayon, feedstuffs for cattle, fertilizers and the extraction of furfural.

II. PHYSIOPATHOLOGY

Bagassosis is a bronchiolo-alveolitis which has been the subject of various theories with regard to its aetiopathogeny. Among these the role of micro-organisms (bacteria, fungi, spores of fungi) has been singled out mainly because of the abundant presence of spores in the bagasse refuse. Other authors have mentioned the presence in the serum of specific anti-bagasse and anti-actinomycetes thermophiles precipitins.

III. CLINICAL SYNDROME

Bagassosis appears after some weeks or some months of exposure to the risk. The start is usually fairly rapid. After a few days of cough, of dyspnoea of effort and subfebrile condition, the symptoms worsen rapidly.

A persistent cough with blood-stained sputum (haemoptysis is rare), a continuous dyspnoea with cyanosis, asthenia, loss of weight in a febrile patient are the essential elements of the clinical syndrome at this stage.

The chest X-ray frequently shows micronodules distributed in the two pulmonary areas. Sometimes hilar and perihilar opacities exist as well as bronchopulmonary infiltrates. The respiratory function tests reveal disorders of ventilation.

Even when exposure is stopped, recovery is slow and does not become complete for several weeks or even months. However, sometimes the lesions do not subside and death may supervene in a syndrome of acute cor pulmonale. In other cases broncho-pulmonary sequelae may persist.

IV. SPECIAL RECOMMENDATIONS

Occupational history takes prime importance in making the diagnosis and for the possible removal of workers from risk.

C. - BIRD HANDLER'S LUNG

The disease affects the handlers of pigeons, budgerigars and turtle-doves.

Moreover, in recent years cases have been observed in fowl handlers and bird handlers in general. The danger appears to affect mainly those working in small establishments where working conditions and hygiene are inadequate.

The agents responsible for this disease appear to be undoubtedly the antigens present in the excreta, the plumage and the serum of the animals.

The clinical syndrome of the disease does not differ appreciably from that described for farmer's lung. The search for antibodies precipitating the aviary antigens constitutes an essential element of diagnosis.

I. SPECIAL RECOMMENDATIONS

It is necessary to eliminate first the diagnosis of ornithosis the aetiology of which is viral.

It should be pointed out that fowl handlers may be exposed to other antigens and notably to those from mildewed hay.

Beside the affections caused by mildewed hay, bagasse, the excreta and remains of birds, a whole series of affections have been described which are listed in the following table drawn up according to the German medical review "Deutsche Medizinische Wochenschrift" (No. 50 December 1971).

DISEASE	DUST INVOLVED	ANTIGEN FOR WHICH PRECIPITINS HAVE BEEN IDENTIFIED
Bird handler's lung	Excrements of pigeons and parrots	Antigen of serous proteins of birds
Mushroom-worker's lung	Mushrooms, compost	Actinomycete thermophile ?
Malt-worker's lung	Mildewed barley and malt	Aspergillus fumigatus and clavatus
Cheese-worker's lung	Cheese mildew	Penicillum casei
Lung of workers manipulating flour infested with parasites	Parasite-infested flour	Sitophilus granarius
Forester's lung	Sawdust from the oak, cedar, etc...	Sawdust extracts ?
Pneumopathy of maplewood	Mapletree bark	Coniosporium corticale
Sequoiosis	Mildewed sawdust from the sequoia tree	Aureobasidium pullulens
New-Guinea lung	Dust from mildewed straw	Straw extract
Suberosis	Bark of the oak, cork	Mildewed bark
Red-pepper maker's lung	Red-pepper	?
Coffee-worker's lung	Dust of coffee grains	Extract of coffee-grains

D. - BRONCHIAL ASTHMA THROUGH INHALATION OF ORGANIC DUSTS

The affections of this type have formed the subject of Particular C 5 of Appendix I in which not only a certain number of chemical agents were mentioned but also products of animal or vegetable origin. It is considered appropriate to present here supplementary examples of antigens of animal and vegetable origin which may be encountered in the industrial environment. The enumeration given below must not be considered exhaustive. The various allergens may be encountered in widely differing occupations, the agent responsible sometimes not being immediately apparent.

Furthermore, the phenomena observed are often of a clearly asthmatic nature; but in numerous cases the physio-pathological process appears to be of a complex nature.

Among the dusts of animal origin liable to give rise to affections of this nature mention should be made of the hair and furs as well as of the skins deriving from sloughing. The dusts may also be of animal origin : horses, cattle, sheep, dogs, cats, goats, rabbits, guinea-pigs, rats, mice, hamsters, game, ermine, mink, marten, beaver and other fur animals (untreated, undyed skin). Likewise, the venom of serpents, the dejections of ascaris, the dusts and the dejections of insects (bees, acarids, tinea, tenebrios, domestic flies, drosophilae, etc..., silkworm moth, cockroaches, grasshoppers, bugs) are liable to give rise to pathological phenomena of this type.

Among the dusts of vegetable origin which may be responsible for identical affections, we may mention : the dusts of cereals, lucerne, the flours and brans (rye, wheat, corn, buckwheat, rice, tapioca, soya), the cocoa nibs (untreated), rapeseeds, the dusts

of indigenous woods (oaks, firs, beaches, walnuts, etc...), the dusts from exotic woods (limawood, limba, obeche, ako, teak, mansonia, kumus, afrormosia, mangrove, Brazilian rosewood, etc...), the narcissi, tulips (bulb essence, volatile odoriferous substances, pollen), the pollens, the powder of lycopodium, the fungi (spores), gum arabic, essential oils (cosmetics, perfumes).

E. - THE RESPIRATORY AFFECTIONS CAUSED BY THE INHALATION OF DUSTS FROM COTTON (BYSSINOSIS), FLAX, HEMP, JUTE AND SISAL

These are essentially pulmonary affections caused by the inhalation of organic vegetable dusts. The agents responsible are notably textile materials derived from plants (cotton, flax, hemp, jute, sisal).

COTTON, cultivated in a number of tropical and sub-tropical countries consists of fibres forming a flock. This is the fleecy, white, soft-feeling material which surrounds the seed of the cotton plant. The unicellular fibre is formed of concentric layers of cellulose. The length of the fibres varies between 2 and 8 cm and their thickness is a few microns. Their whole forms the tow or raw cotton and contains 1 to 2 % of impurities (dusts from the soil, vegetable dusts such as remains of leaves or of seed capsules, micro-organisms).

After harvesting, the cotton is compressed into bales and moved to the textile factories. On arrival at the "mill", the bales are opened and the cotton is unpacked. It is then sent to the "blowing room" where it is subjected to air blasting which removes the dust and the short fibres. It is then sent to the carding room where the fibres are combed and prepared for spinning.

a series of machines which draw it out into a thin strand ready for spinning.

The fibres contained in this pulvurent mass then pass to a card-room where a sliver is formed which is then subjected to various manipulations (stretching, spinning, combing, winding) to be finally woven into cloths of crude cotton. The bulk of this crude cotton is treated by passing it through alkali and acid baths to free it from its final impurities (natural greases and waxes) and is subjected to bleaching.

FLAX is a textile plant cultivated in temperate and sub-tropical zones; its stalk consists of long fibres holding together small bundles of cellulose filaments. The extraction of the "bast" comprises the following operations :

- the retting of the stalks which eliminates the gummy matter surrounding the fibres; it is done by soaking either in river water for several weeks or in a bath containing certain microbic cultures;
- the bleaching which may be carried out on grass in the open air or by chemical processes; the flax straw so obtained is dried in hot air tunnels;
- the hackling which by reducing the wood of the stalks to small fragments facilitates the separation of the textile fibre proper;
- the swingling, the removal of these remains of crushed woods is still often done by hand; although mechanical means (Flemish mill) are used more and more, dust continues to be produced;
- the fibres so produced are packed into bales and transported to the textile mills. They are subjected to the same operations as the cotton fibres (stretching, combing, spinning, etc...). The cellular remains from the hackling are used for the manufacture of cigarette paper.

HEMP cultivated in temperate and sub-tropical zones yields a long strong fibre extracted from the stalk; these fibres are subjected to the same operations as the cotton and flax fibres.

JUTE is cultivated in India and China. The stalk consisting of long fibres is subjected in the first place to a retting in water, then to a stripping. The fibres are then impregnated with oil by spraying and thus acquire a certain suppleness. This operation is called "oiling". They are then hackled and converted to "tow". The latter is spun and woven to a coarse jute cloth usable for packaging and making into sacks. The jute which is combed before spinning gives a finer cloth suitable for the manufacture of carpets, dyed cloth, waxed cloth and a special cloth used for the protection of underground electric cable. The cellulose remains are crushed and serve for the manufacture of paper pulp and artificial leather.

SISAL, tropical agave, cultivated in Mexico and eastern Africa, gives long textile fibres, white and strong, of a length of one to one and a half metres. After treatment they are used primarily for the making of strings and ropes.

I. SOURCES OF DANGER

The main industrial sources of danger are situated at the places of work most exposed to the inhalation of dusts deriving from the manipulation of dry, powdery products, both in the textile industries and in the industries utilizing the waste.

The operations preceding the spinning of the long and medium length cotton fibres - particularly the carding operations actually inside the buildings and around the machines used for this purpose - are those during which the greatest amount of dust is given off and consequently which create a risk of byssinosis.But the use of new machines running at high speed tends to propagate the dust towards the spinning rooms and particularly the spooling rooms, while there is practically no risk of byssinosis in the weaving rooms.

to the later processes, including weaving, which are free from this disease.

In so far as the jute dusts are concerned, they seem to be less noxious because of the more or less intensive oiling to which these fibres are subjected.

II. PHYSIOPATHOLOGY

These affections are due essentially to the inhalation of organic vegetable dusts deriving from the various manipulations of these products or of their dusty waste. Associated with these dusts are numerous widely differing agents such as cellulose, sap, chlorophyll, pollen, spores, fungi, bacteria and even animal parasites such as mites.

The pathogeny of the affection is still disputed and various theories have been put forward :

- the orthoergic mechanical action of irritation of the air passages bringing about a bronchiolar fibroplastic reaction enwrapping the vegetable fibres;
- the role of micro-organisms (bacteria and fungi) or of their toxins;
- the allergic sensitiveness in respect of the protein fraction of the fibre itself or in respect of other allergens that may possibly be present (the presence of serous precipitins for the cotton extracts has been reported by some authors);
- the presence of a liberator of histamine either of vegetable origin or of bacterial origin.

III. CLINICAL SYNDROME AND DIAGNOSIS

Byssinosis is a specific respiratory affection which occurs among the employees of the cotton and linen industry. It seems that a certain level of dust concentration and a certain duration of exposure are necessary in general for the production of this disease.

At the beginning - usually not less than 2 years after starting work in the card room -, the symptomatology is transitory. On resumption of work after the week-end rest, chest tightness and slight dyspnoea ("Monday feeling") become evident. The symptoms disappear in the course of the afternoon or evening and do not recur when work is resumed in the morning, but only after a new stoppage of one or two days (stage I).

The disease can develop progressively over the years and the symptoms will then persist beyond the first day of work and later still perhaps during the whole period of contact and disappear only after a definite stoppage of work (stage II).

Finally, in certain cases and progressively, the pathology develops towards the clinical syndrome of emphysema with respiratory insufficiency, with or without chronic bronchitis (stage III).

IV. SPECIAL RECOMMENDATIONS

The aetiological diagnosis rests essentially on the occupational history and a clear account of the symptoms and their timing.

Many workers suffering from incipient "byssinosis" are capable of working and leading normal lives for many years. However, the only possible solution for certain workers who have reached the irreversible stage of the illness is to give up the work which exposes them to the risk. The factory doctor will take action when it is clear that the worker is suffering from developing byssinosis which justifies his removal from the job which exposes him to risk.(1)

(i) Byssinosis is totally different from "mill fever". In mill fever, a few hours after the inhalation of vegetable dusts of various kinds, violent headaches and a general feeling of discomfort, sometimes accompanied by feverish outbreaks occur. The symptoms disappear after a few hours or a day and do not recur when exposure to the dust is repeated. This acute syndrome occurs in many people exposed for the first time to dusts from cotton, flax, hemp or other amylaceous and cellulosic dusts under certain conditions of temperature and humidity. These phenomena are secondary to the inhalation of vegetable proteins.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 1
OCCUPATIONAL CRAMPS

THE OCCUPATIONAL CRAMPS

The occupational cramp is a form of dyskenesia characterized by a very localized disturbance of the motor functions intervening in a particular manipulation whilst other movements remain unaffected.

I. SOURCES OF DANGER

The occupational cramps, known for a long time and sometimes referred to as functional spasms, are observed generally in persons whose work comprises repeated specific movements accompanied by an effort localized in a particular group of muscles. Writer's cramp is the most frequently occurring and the best known; however, such cramps have also been observed in a very large number of occupations, notably in telegraph operators, ropemakers, dressmakers, ironers, blacksmiths, engravers, goldbeaters, painters, shoemakers, saddlers, post-office workers (letter sorters), cigar-makers, diamond-cutters, polishers, grinders, cafe waiters, newspaper folders, typists and copying machine operators, cow-milkers, etc... They may also affect various artistic activities, for example, pianists, violinists, harpists, flutists, trumpeters, dancers, etc..., or professional sportsmen such as cyclists or fencers.

These diseases are fairly rare at present, thanks to the mechanization of a lot of work previously carried out by hand, and also owing to a better adaptation to the tools, the machines or the techniques.

II. PATHOGENESIS

The origin of the disease is not well known and has called forth a number of theories. Writer's cramp was for a long time regarded as a neurosis more or less close to hysteria or pithiatism. However, persuasive therapies proved to have little effect. The psychological concept was pushed further and a psychoanalytical explanation was attempted, in which the occupational cramps were looked on as a conversion or frustration syndrome; other suggestions included in certain cases psychic traumatism of the Freudian or Adlerian order, or even more or less substantial and recent affective shocks which would relate the functional disorder closely to the so-called reactive states in Swiss psychopathology.

A purely psychological pathogenesis or mechanism appears hardly acceptable however in the majority of cases if the customarily belated appearance of the syndrome (at the age of forty or fifty) is taken into account, together with the poor results achieved by psychoanalytical or psychotherapeutical treatments.

A concept derived from the conditioning theory of Pavlov seems more satisfactory with regard to the mechanism of the functional muscular dyskenesia. This is said to be due to a loss of coordination of the muscles or muscular bundles participating in a complex stereotyped movement; writing or playing a musical instrument requires a narrow synergy of segmented movements combining in the elaboration and the execution of the automatic act, repeated and variable in its adaptations. The dyskenesia results from a break in the stereotype of movement inscribed in the connections of the nervous elements concerned, a break caused either by a prolonged excessive effort of these elements (fatigue), or by endogenous or exegenous antagonistic factors (psychic disorders, infections, endocrinous or vascular disorders, etc...).

Strictly speaking we have here a number of general and rather unprecise factors which partake of the eatiology rather than of the pathogenesis. What is more important is the dis-

covery, if one takes the trouble of investigating the symptoms, of the quasi-constancy of a neuro-psychic picture of asthenia with difficulty of effort, disturbed sleep, moroseness of temper, hypochondriac uneasiness giving support to the functional cramp process. Another pathological factor to which insufficient attention is given is the existence of small manifestations of vertebral or scapular arthrosis, the action of which on the nervous relays is not without importance.

III. CLINICAL SYNDROME AND DIAGNOSIS

The disorders become evident through the loss in precision of certain movements associated with a deficiency in motor coordination. They consist of a spasmodic contraction of the extremities. The most current form of occupational dyskenesia is the writer's cramp which has here been chosen as typical.

The disease strikes generally in a progressive manner towards the age of 40 to 50. The subjects affected feel awkward when writing. They are obliged to clench their fingers around the pen and change the position of their hand; they tire rapidly, lose the speed and flexibility of movement and their writing deteriorates.

At a later stage involuntary positions of the hand and cramps in certain fingers appear which render writing impossible. These symptoms are accompanied by muscular tension at the level of the forearm spreading to the arm, the shoulder and sometimes even the muscles of the neck and of the face.

By contrast, all the other movements of the hand and of the fingers can be executed without difficulty. This is the most frequent, spasmodic form.

There is also a paretic form with a weakening of the muscles of the wrist during writing. Forms with tremor have also been described, and neuralgic forms where the fact of

writing provokes uncoordinated agitation of the fingers or acute pain. Quite frequently combinations of several of these clinical forms are encountered.

The clinical examination is mostly negative; disturbances of sensation are rare; there is no limitation of passive or active movements on the level of the hand or of the fingers.

Electromyographic studies frequently, but not always, show a diminution of responses to stimulation tests.

The prognosis is serious: writer's cramp is a frequently irreversible dyskenesia and those affected by it are compelled to stop writing by hand. The capacity to write with the other hand or with the help of a typewriter cannot be regarded as fully compensatory because prolonged work might bring about the same symptoms. In general, a change of occupation will be necessary.

Writer's cramp, which has been chosen as typical because it is by far the most frequent, is not the only one. Other muscular groups may be affected, notably on the level of the leg and of the foot in dancers, dressmakers working on a sewing machine, cyclists, etc..., sometimes on the level of the lips or the tongue in the case of musicians, clarinettists, trumpeters, etc...

IV. SPECIAL RECOMMENDATIONS

Occupational cramps may be avoided by training, starting from apprenticeship, in the correct way of doing the various movements, of holding tools, including a pen.

The shape of tools, especially their handles, the material they are made of, the correct posture to be adopted when using them, are important elements.

Finally, it is of some interest to perform biological examinations on workers who display such symptoms (notably in order to investigate a possible disturbance of the calcium or magnesium metabolism).

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 2
WORK UNDER HOT CONDITIONS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY HEAT

The immediate effects of heat (such as burns for example) come normally under the heading of work accidents. Other effects however only become evident after prolonged exposure or with some delay. This is why, without prejudging the question of responsibility, it seemed important to mention here the main elements of disorders brought about by work under hot conditions.

I. DEFINITION

The thermal environment is characterized by the combination of the following four factors :

- air temperature,
- heat radiation,
- air humidity,
- air movement.

It is also possible to regard as "hot" any environment in which the evaporation of sweat becomes an important means of elimination of the heat from the organism.

Equipment and measuring units (1)

- air temperature measured in degree centigrade : liquid thermometers, resistance thermometers, etc...
- heat radiation measured in degrees of the resulting temperature: black-bulb thermometer, etc...

(1) For further details reference should be made to the list of climatic measuring instruments of the EEC.

- air humidity measured in % relative humidity on the basis of information furnished by a psychrometric device in degrees of humid temperature,
- air velocity expressed in metres per second (m/s) by the anemometer.

II. MODE OF ACTION

The four factors, as they attain certain levels and in various combinations, generate thermal stress.

If a subject is exposed to heat, he must eliminate at the same time the calories produced by his metabolism and the calories he receives from the ambient surroundings. This elimination occurs normally through two physiological mechanisms : the increase in peripheral circulation and the production of sweat. These two mechanisms involve four physical properties : convection, conduction, radiation, evaporation. When the thermal load exceeds a certain level, perspiration becomes the predominant factor in the defence of the organism. The evaporation of sweat reduces the thermal charge since one litre of sweat which evaporates eliminates 580 kilocalories. However, the organisms can mobilize these means of regulation only within certain limits and under certain conditions.

In a hot and very dry atmosphere the physiological regulating mechanisms are exercised freely during a space of time which varies according to the magnitude of the thermal stress.

In hot and very humid atmosphere the thermal stress will increase with the rise in ambient temperature on the one hand and the rise in humidity on the other hand. The thermal stress will be all the greater as the humidity approaches saturation. The difficulty of the evaporation of sweat in hot and very humid atmospheres must therefore be taken into account. The more humid an atmosphere becomes, the more calories accumulate in the organism because of the difficulties of regulation. A small accumu-

lation provokes a moderate elevation of the internal body temperature (possibly attaining 38° at the end of work). On the other hand, a substantial accumulation brings about an accumulation of the internal body temperature up to 39°, 40° or even higher. The organism now moves from the stress zone to the danger zone (heat-stroke sometimes leading to death).

Air movement generally improves tolerance to climatic stresses. This favourable effect does not make itself felt when the air is superheated and close to saturation with moisture.

The intensity of physical work also plays a major part in thermal stress.

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In view of the number of parameters involved in the assessment of thermal environments, studies have been made for assessing them in an overall manner.

To achieve this object, the synthetic measure of the climatic environment is most frequently expressed according to the "American effective temperature" and the "French resulting temperature" (1) which can readily be determined with the help of nomograms and formulae containing as parameters the dry temperature, the humid temperature and the velocity of the air.

To assess the effective temperature the thermal stress index of Belding and Hatch has also been used, which is determined by means of a nomogram and which is a function of the same factors and also of the intensity of work; the index 0 (zero) corresponds to situations in which the thermal equilibrium is maintained without notable perspiration; the index 100 corresponds to cases where the perspiration attains the maximum possible.

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(1) Formula allowing to establish the "resultant temperature (T°R)" : T°R = 0.3 T° dry + 0.7 T° humid - V air
where V air is the air velocity expressed in metres per second.

It is necessary to take into consideration the whole of the working conditions (nature and situation of heat sources, posture and movements of worker, etc...) and the individual reactions which will be dealt with later.

III. SOURCES OF DANGER

The main industrial sources of danger are to be found in all work liable to bring about a thermal stress; more specifically :

- glass-works;
- metallurgical industry (blast furnaces, ironworks, steel mills, hot rolling mills, foundries, etc...);
- mining industry, certain coal mines (humid), potash mines (dry);
- repair and maintenance of furnaces (refractory brick setters);
- steam generating stations;
- agricultural work under certain conditions, for example, work in greenhouses;
- work in hot regions;
- work exposing to intensive solar radiation;
- certain occupations in the rubber and textile industries;
- etc...

IV. PHYSIOLOGY AND PHYSIOPATHOLOGY

The two regulating mechanisms mentioned above, the increase in peripheral circulation and in perspiration, produce a series of phenomena, in particularly dehydration, disturbances of the electrolytic equilibrium, increase in cardiac frequency, rise in internal temperature, diminution of physical and mental efficiency.

The intensity of physical work, the individual factors and the capacity of adaptation considerably influence the effects of thermal stress; they do not only depend upon climatic

factors but also on individual factors, such as the morphology, the general state of health, obesity, age, sex, psychic factors, dress, alimentary habits (consumption of alcoholic drinks) etc...

Naturally, the intensity of physical work and the duration of exposure to the heat play an important role.

- Influence of adaptation

Certain persons adapt badly to heat. By contrast in persons who do adapt themselves, a favourable evolution of physiological reactions is observed at the end of a certain number of days of work in a hot environment (acclimatization) most frequently between 7 and 10 days : less accentuated tachycardia, internal temperature closer to normal, more abundant sweating with renewed ability to carry out normal work.

- Dehydration

Very abundant perspiration without compensation by drinking may lead to dehydration which interfers with the osmotic equilibrium of the tissues.

It should be noted that the maximum quantities of sweat liable to be produced experimentally in cases of extreme stress are :

2.1 litres in one half hour,
7 litres in 2 hours
14 litres in 4 hours.

In the usual working situations, however, the quantities excreted will be considerably below this level.

- Disturbance of the electrolytic equilibrium

The excretion of sodium chloride in the case of heavy sweating may produce a deficiency of salt in the body, especially if there is no absorption of salted beverages. Persons not

adapted to work in hot surroundings are more sensitive to this deficiency.

Thermal stress may lead to changes in the serum content of potassium, calcium and sodium, especially when there is abundant absorption of water.

Variations in concentration of these salts appear to have an influence on the activity of certain enzymes and on endocrine activity.

- Increase of cardiac frequency

An increase in pulse rate follows increased peripheral circulation and sweating. The measurement of the pulse is therefore one of the signs which helps in the assessment of thermal stress (telemetric method).

- Increase of pulmonary ventilation

- Increase of internal temperature

The increase of internal body temperature occurs when the thermal equilibrium cannot be fully maintained. In still more unfavourable circumstances a complete breakdown of the regulators takes place with serious hyperthermia.

- Diminution of efficiency

At certain levels of thermal stress a diminution of physical efficiency as well as of mental performance (attention tests, etc...) is observed.

V. CLINICAL MANIFESTATIONS OF THERMAL STRESS

Thermal stress may bring about clinical manifestations of various frequency and gravity which may appear in isolation or combined.

1) Cramps

Cramps may be observed in cases where the blood level of sodium chloride falls to a certain level. Tetanoid phenomena of asymmetrical localization result, affecting above all the muscles which are heavily used in the course of the work. These phenomena may be preceded by muscular fibrillations. Nausea and anorexia may aggravate the predisposition to cramps, the risk of these disorders being in fact greater when the diet is low in sodium chloride.

2) Lipothymic manifestations

Lipothymic manifestations have been observed to follow not very substantial exposures, for example, in cases of a prolonged stay in a moderately hot atmosphere, without appreciable rise in internal temperature or deficit in water or sodium chloride. When the circulatory system and the thermal regulation are overstressed, circulatory collapse may occur. Rise in internal temperature and dehydration favour even more such lipothymic manifestations and the occurrence of a collapse.

Beside non-specific symptoms (headaches, vertigo, nausea, etc...), this condition is characterized by a tachycardia accompanied by a drop in blood pressure (especially the systolic values). The skin is hot and covered with sweat, then becoming pale and moist with cold sweat.

3) Dehydration

The disorders appear generally when the drop in the water-level exceeds 2 % of the bodyweight. The condition is heralded by tachycardia and, in cases of more intensive dehydration, by incoordination of movements, somnolence and various non-specific symptoms. When in desert regions people

cannot make up the deficit by drinking, delirium sets in, followed by coma the development of which may be fatal in less than 24 hours.

4) Heat-stroke

Heat stroke is the clinical expression of an appreciable rise in internal body temperature. It becomes evident by nausea, vomiting, meningeal reactions, hyperaesthesia, delirium and coma. The skin is burning and dry. The risk of a fatal outcome increases with the body temperature. In many cases sun-stroke becomes identified with heat-stroke.

5) Secondary manifestations

- Cutaneous lesions : certain skin affections, such as sudamina, mycosism, intertrigo are observed more often in persons working in a hot environment.
- Digestive troubles : The long recognized manifestations are favoured by an injudicious diet (vomiting, epigastric pains, diarrhoea, etc...).

Beside these relatively well defined clinical forms, other forms of mixed symptomatology exist which have sometimes been regarded as separate affections. It is for this reason that such divergences exist between the various clinical classifications of affections related to thermal stresses.

VI. INDICATIONS FOR DIAGNOSIS AND PROGNOSIS

Climatic factors, intensity of work, manner of dress, training, individual factors, and above all characteristics of the place of work have to be taken into account.

The following subjects should be excluded from work under hot conditions :

- persons subject to disturbances of the water metabolism,
- persons subject to variations in blood pressure,
- persons suffering from organic diseases (diabetes, high blood pressure, arteriosclerosis, acute rheumatism, pulmonary tuberculosis, ichthyosis, cystic fibrosis of the pancreas),
- persons subject to chronic orthostatic troubles,
- older persons newly recruited.

Hygienic measures (suitable clothing, food and drink adapted to conditions) render work under hot conditions more tolerable. Fresh drinking water (avoid iced drinks) or non-alcoholic beverages (danger of becoming accustomed to alcohol) should be available in sufficient quantities and at readily accessible places. If daily food provisions are adequate the level of sodium chloride in the blood remains sufficient in spite of increased excretion of salt by perspiration. The prophylactic administration of salted drinks or of salt pills does not appear to be necessary in general under these conditions. In certain regions of Italy it has been observed, however, that some of the prepared food (bread for example) is very low in salt. It is advisable then to provide salt prophylactically either in the form of saline drinks or in the form of sodium chloride tablets which would be taken with an amount of liquid : 250 g of water per gram of salt.

It is clear that an improvement in working conditions and the introduction of suitable technical arrangements (mechanizations of certain manipulations, heat insulation, screens, ventilation, air conditioning, etc...) are liable appreciably to reduce the thermal stress.

If the worker is exposed at the same time to heat and to toxic agents, a particularly rigorous system of prevention is imperative, as working in hot surroundings increases the sensitivity of the organism towards poisons.

VII. FIRST AID MEASURES

The treatment of circulatory collapse caused by thermal stress aims at combating the disequilibrium existing between the quantity of blood present and the excess vascular capacity owing to the dilatation of the vessels. It is wise to give fluids, to make them rest in a cool place, possibly apply cold compresses and fan the moistened skin. These measures are generally sufficient to bring about prompt recovery. If necessary, cardiovascular analeptics will be administered.

In the event of heat-stroke the treatment should aim essentially at lowering the body temperature. This lowering may be realized by subjecting the moistened skin to the action of a fan or compressed air. The saving action of cold baths (certain authors make reservations, however, because of the peripheral vasoconstriction they provoke) has been reported in grave cases provided that the rectal temperature checked every 10 minutes does not drop at first to below 38°C. It has to be remembered that the thermo-regulator system will subsequently remain disturbed for some time and premature return to work should be avoided.

The treatment of fluid loss should aim at replacing the water lost and at lowering the body temperature if the same has risen following the relatively large losses of water. Equilibrium is re-established by the frequent administration of small quantities of fluid by mouth or by the intravenous administration of 5 % glucose solutions. If the clinical syndrome is complicated by a loss of salt, it is advisable also to administer intravenously an isotonic solution of sodium chloride. It is important at this juncture to check the body weight and the kidney function.

In case of loss by the organism of excess sodium chloride, the saline equilibrium is re-established by oral

administration of salted meat broth or of a physiological serum solution (if necessary, solutions with higher concentrations of sodium chloride).

In case of cramps, sedatives are ineffective. Sometimes the administration by intravenous route of 5 % sodium chloride solutions has been advocated. Even after the cramps have disappeared, the giving of salt per os should be continued for a few days whilst the patient is confined to bed, until the urine again contains a minimum of 2 to 3 g of chloride per litre.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 a_1
RADIATIONS - GENERAL

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY CORPUSCULAR AND ELECTROMAGNETIC RADIATIONS.

The absorption by the organism of corpuscular and electromagnetic radiations evokes physical and chemical effects liable to produce pathological effects. The nature of the physiopathological processes and the clinical syndrome of the disease are determined by the nature of the radiation.

I. CORPUSCULAR RADIATIONS

The corpuscular radiations consist of flows of particles which as a general rule are constitutive parts of the atom and which, with the exception of neutrons, carry an electric charge. The corpuscular radiations which occur in industrial, technical and medical applications are the following :

a) electrons,

b) positrons,

c) protons,

d) deuterons,

e) particles,

f) heavy nuclei and fragments of nuclei

g) neutrons.

II. ELECTROMAGNETIC RADIATIONS

The spectrum of the electromagnetic waves is illustrated by Chart I appended to this Particular. It ranges from the gamma rays and ultrahard X-rays of frequency 10^{21}Hz and over to long-wave radio-waves (kilohertz range). By taking into account the energy of the photons and the mode of interaction with matter, it is possible to distinguish several spectral zones, though their frontiers are not always clearly delimited.

a) X-rays and gamma rays (ionizing radiations)

The range of frequencies extends between approx. 3.10^{16}Hz and 10^{21}Hz (and sometimes over), corresponding to a wave-length comprised generally between 10^{-8}m and 10^{-13}m or to an energy of photons generally comprised between 200 eV and 10^{7}eV.

When X-rays or gamma rays are absorbed by matter, their energy becomes essentially exhausted through ionization of the neighbouring atoms and molecules.

The induced electronic excitations, together with the ionizations, finally lead to non-specific radiochemical reactions. These non-specific reactions are at the origin of secondary biological reactions of a generally unfavourable character. The heat release by the absorption of radiations, as well as the thermal epiphenomena of the radiochemical reactions are biologically negligible.

b) Ultraviolet rays

The wavelength of the ultra-violet radiations lies between 10 nm and approx. 0.39 µm, which corresponds to frequencies of 3.10^{16} Hz to $7.8.10^{14}$ Hz and to energies extending from 200 eV to 2.6 eV.

In fact, the energies encountered in practice lie between 10 eV and 2.6 eV. The absorption of photons belonging to this

range entrains more or less specific excitations on the level of the external electronic layer of the atoms and molecules with corresponding photochemical reactions. The photobiological effects, notably those which entrain acute and chronic clinical lesions to be considered as industrial diseases, are a consequence of these photochemical reactions. The heat produced by the absorption of ultra-violet rays, as well as the thermal effects of the photochemical reactions are biologically of very secondary importance.

c) Visible light

The spectrum of the visible light ranges from approx. $7.8.0^{14}$ Hz to approx. $4.0.10^{14}$ Hz which corresponds to wavelengths in vacuum from 0.39/um to 0.76/um or to a photonic energy range between 2.6 eV and 1.7 eV. In this spectral fields the photochemical reactions have a very specific character (vision, photosynthesis). In humans a large portion of the luminous energy absorbed by the skin is converted to heat and it is necessary consequently to include in the effects of the visible light specific biological effects (dazzle, photosensitization) and purely thermal effects (burning of the skin or of the retina).

d) Infra-red radiations

The spectrum of the infra-red radiations ranges from $4.0.10^{14}$ Hz to approx. $3.0.10^{12}$ Hz, which corresponds to a wavelength in vacuum from 0.76/um to 0.1 mm and to an energy range from 1.7 eV to 0.022 eV. The absorption of infra-red radiations by biological tissues causes simply an excitation on the vibrational and rotational levels. In the course of this absorption process, only the thermal energy of the substance subjected to infra-red radiation increases. The production of heat is the only biological effect of this absorption.

e) Microwaves

The spectrum of microwaves ranges from 3.10^{11} Hz (0.e THz) to 3.10^{8} Hz (300 MHz) which corresponds to wavelengths between 0.1 mm and 1 metre. The absorption of microwaves causes excitation on some vibrational levels, but it is essentially the rotational levels which are excited. Moreover, these high-frequency fields generate electric currents. All these effects result in a production of heat through dielectric losses and the Joule effect.

The non-thermic effects appear to play only a very subordinate role.

f) Radio waves

The spectrum of radio waves varies from approx. 300 MHz to a few KHz, which corresponds to wavelengths ranging from 1 m to a few hundreds of km. The absorption has the effect of creating in the cells and tissues electric currents which produce heat through dielectric losses and the Joule effect. At frequencies below approx. 300 KHz, and for certain electric field strengths, the cells and the tissues may undergo a certain excitation without its being accompanied by other effects.

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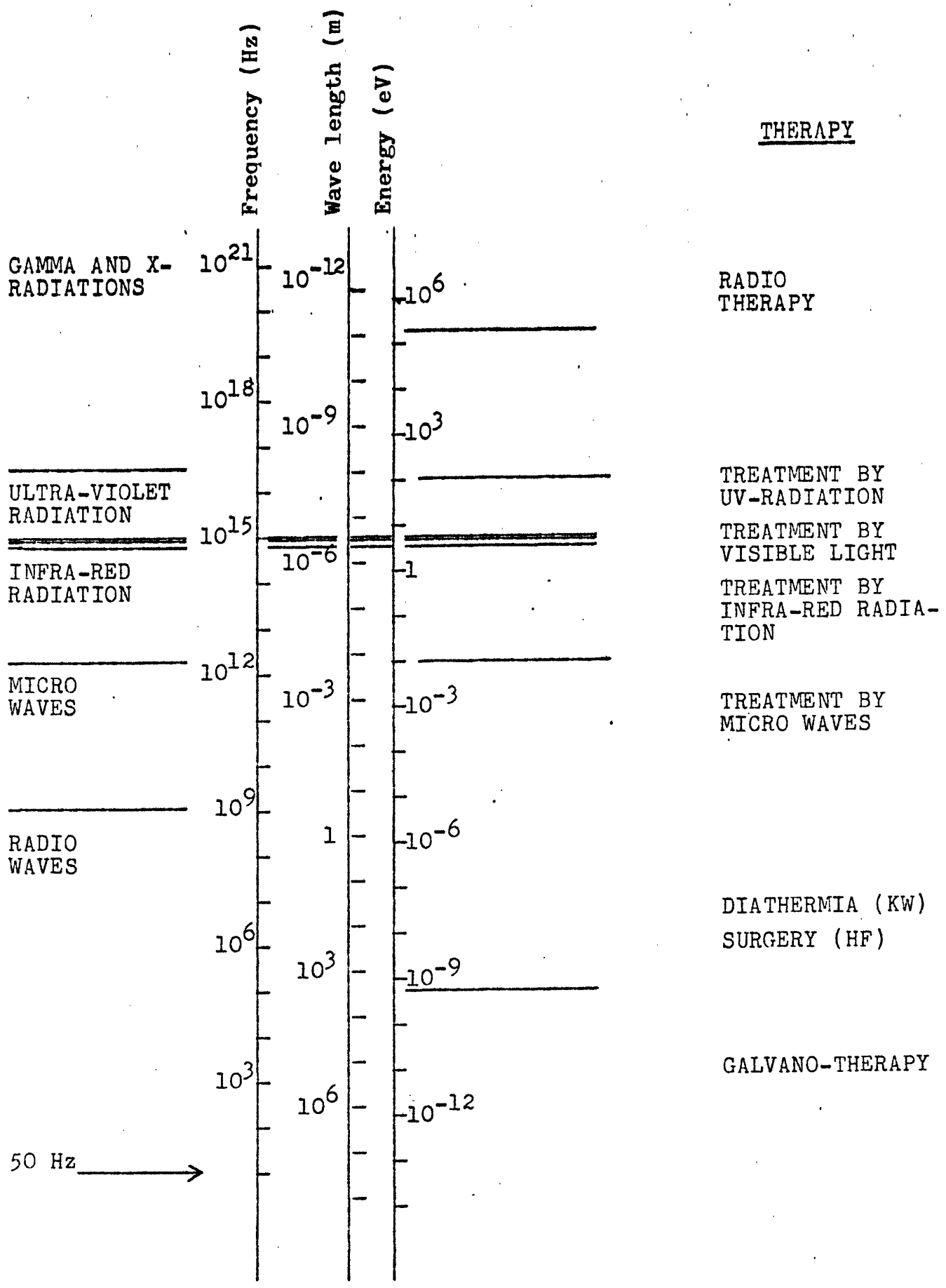
1) Industrial diseases caused by ionizing radiations	See Appendix I - Particular No. E 1
2) Diseases liable to be caused in industrial environment by ultra-violet radiations	See Appendix II- Particular No. $C3a_2$
3) Diseases liable to be caused in industrial environment by the visible light	See Appendix II- Particular No. $C3a_3$
4) Diseases liable to be caused in industrial environment by the handling of laser beams	See Appendix II- Particular No. C3b
5) Diseases liable to be caused in industrial environment by infra-red radiations	See Appendix II- Particular No. $C3a_4$ and Appendix I - Particular No. E 2
6) Diseases liable to be caused in industrial environment by microwaves	See Appendix II- Particular No. $C3a_5$
7) Diseases liable to be caused in industrial environment by radio waves	See Appendix II- Particular No. $C3a_6$

TABLE I


Frequency (Hz)
Wave length (m)
Energy (eV)
THERAPY
GAMMA AND X-RADIATIONS
ULTRA-VIOLET RADIATION
INFRA-RED RADIATION
MICRO WAVES
RADIO WAVES
50 Hz
10^{21}
10^{18}
10^{15}
10^{12}
10^{9}
10^{6}
10^{3}
10^{-12}
10^{-9}
10^{-6}
10^{-3}
1
10^{6}
10^{3}
1
10^{-3}
10^{-6}
10^{-9}
10^{-12}
RADIO THERAPY
TREATMENT BY UV-RADIATION
TREATMENT BY VISIBLE LIGHT
TREATMENT BY INFRA-RED RADIATION
TREATMENT BY MICRO WAVES
DIATHERMIA (KW)
SURGERY (HF)
GALVANO-THERAPY

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C $3a_2$
ULTRA-VIOLET RAYS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY ULTRA-VIOLET RADIATIONS

The ultra-violet radiations are the electromagnetic waves with wavelengths varying between approx. 0.39 µm and approx. 10 mm, which corresponds to frequencies ranging from $7.8.10^{14}$ Hz to $3.0.10^{16}$ Hz and to photonic energies comprised between 2.6 eV and 200 eV. The ultra-violet rays which are situated in the zone of the spectrum close to the soft X-rays (ultra-violet rays in vacuum), are so strongly absorbed in air that they are of no practical interest. The only range that is of practical interest extends from 0.39 µm to approx. 0.20 µm, which corresponds to a photonic energy of 2.6 eV to 10 eV.

The most important source of ultra-violet rays is the sun. Ultra-violet rays are also emitted by the high-temperatures plasmas, for example, the electric arc or discharge lamp.

I. PHYSIOPATHOLOGY AND MODE OF ACTION

The ultra-violet radiations are very strongly absorbed by the cells and the tissues. The depth of penetration, on cornea and conjunctiva level is only approx. 0.1 mm. The absorption results in more or less specific photochemical reactions.

The heat created by absorption of ultra-violet rays is biologically negligible. By contrast, the photochemical reactions cause congestive phenomena (sun-stroke, kerato-conjunctivitis).

II. SOURCES OF DANGER

In industrial environment, an exposure may occur in the following cases :

a) Solar ultra-violet radiations

- road construction,
- agricultural work,
- work at sea (fishing)
- work in the high mountains,

b) Artificial ultra-violet radiations

- glass-making,
- iron smelting and casting,
- metallurgy (rolling),
- checking of metal moulds,
- arc welding and cutting,
- manufacture of incandescent mantles,
- manufacture and checking of ultra-violet lamps and discharge tubes,
- litography, photogravure,
- luminous irradiation of foodstuff, medicines and tobacco,
- medical treatment and beauty care by ultra-violet rays.

III. CLINICAL SYNDROME

Over-exposure to ultra-violet rays causes lesions of an acute or chronic character. The most frequent acute lesion is sun-stroke and actinic erythema. Light skins are particularly endangered. The consequence of sun-stroke and that of local or general symptoms accompanying it depends on the extent of the epidermic surface irradiated and on the quantity of ultra-violet energy absorbed. Clinically sun-stroke is comparable to a first-degree burn.

A prolonged or too intense exposure of the eyes to ultra-violet rays is liable to produce a painful kerato-conjunctivitis, the healing of which is rapid however and without sequelae. Such over-exposures occur frequently when new welding processes are used (for example, in a protective gas atmosphere or with electric arcs emitting a particularly intense ultra-violet radiation).

After prolonged or repeated exposure, permanent cutaneous changes may result. The skin becomes brown and dry, it wrinkles and loses its elasticity. Telangiectases may then appear. On the nape of the neck, movements of the head result in the formation of oblique cutaneous folds. This dermatosis is also called "fisherman's skin", "farmer's skin" or "sailor's skin". These disorders are hardly ever serious. However, keratoses and epitheliomas may eventually be found on the site of this dermatosis.

A certain number of photo-sensitizing agents have the effect of reinforcing the action of ultra-violet rays. Thus, coal-tar is liable to favour the appearance of melanoses. The increased frequency of skin cancer in workers exposed to tar is undoubtedly not only the consequence of the presence of carcinogenic substances. Photo-sensitization phenomena certainly also play a part in this affection.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 a_3
VISIBLE LIGHT

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY VISIBLE LIGHT

To a lesser degree the effects of visible light on the organism are qualitatively analogous to those of the ultra-violet rays (see Particular No. C 3 a_2 - Appendix II). Moreover, a prolonged exposure is equivalent to an exposure to heat (see Particular No. C 2 - Appendix II).

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 a_4
INFRA-RED RAYS

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY INFRA-RED RADIATIONS.

The infra-red radiations are electromagnetic waves with frequencies from $3.0.10^{12}$ Hz to $4.0.10^{14}$ Hz, which corresponds to wave-lengths extending from 0.1 mm to 0.76 µm.

All matter is liable to emit infra-red rays, whether it is in solid, liquid or gaseous state. The higher the temperature, the more intense will be the infra-red radiation emitted.

I. PHYSIOPATHOLOGY AND MODE OF ACTION

In humans the depth of penetration of the infra-red radiation through the skin or the other organs is approx. 1 mm for wave-lengths close to those of the visible light. However, an infra-red radiation of a wave-length between 10 µm and 0.1 mm has only a depth of penetration of about 0.1 mm. The energy absorbed is converted to heat at the place of impact. In view of the feeble penetration, the only organs that can be affected in humans are the skin and the eyes.

According to the density of energetic flow of the infra-red radiation absorbed by the skin, either a slight local hyperthermia, or burns, or a generalized more or less serious hyperthermia is observed.

If large surfaces of skin are exposed to infra-red radiations a generalized hyperthermia may result. If the organism does not succeed in eliminating this surplus of thermal energy,

and in particular in case of prolonged exposure, a combination of general symptoms known under the name of "insolation syndrome" may be observed.

The classical ocular lesion, apart from burns of an acute character, is the cataract which most frequently only appears several years after exposure to infra-red radiations (see Appendix I - Particular No. E 2).

II. SOURCES OF DANGER

In the industrial environment, over-exposure to infra-red radiations threatens persons who work in the vicinity of furnaces or on bodies or objects taken to high temperature, blast furnaces, cupola furnaces, furnaces for the manufacture of alloys on steel basis, rolling mills, foundries, furnaces for glass and for the manufacture of glass objects, electric power stations, reaction furnaces in the chemical industry, combustion plants, fire-brigades, welding work, handling of infra-red lasers.

III. CLINICAL SYNDROME

The cataracts from infra-red radiations were dealt with in Particular No. E 2 of Appendix I. Burns and heat-strokes formed the subject of Particular No. C 2 of Appendix II.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 a5
MICROWAVES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY MICROWAVES.

The microwaves are electromagnetic waves the frequency of which lies between 300 MHz and 0.3 THz, which corresponds to wavelengths extending from 1 m to 0.1 mm. They are produced in radar installations, television transmitters, relay stations, microwave furnaces and various apparatuses used for therapeutical purposes. Moreover, they are used in space research and transmissions. They are emitted both in the form of a continuous radiation and in the form of a pulsing radiation.

I. PHYSIOPATHOLOGY AND CLINICAL SYNDROME

The depth of penetration of the microwaves absorbed by the organism depends upon the frequency, the height of the subject and also the thickness of the panniculus adiposus. At a frequency of approx. 3 GHz (wavelength of 10 cm in vacuum), a fairly commonly used frequency, one half of the energy will be absorbed in a thickness of tissue of approx. 1 cm. The microwaves of a lower frequency penetrate more deeply into the human organism. The microwaves of a higher frequency are practically absorbed by the skin. The absorbed energy is completely converted to heat. The rise in temperature at a given point of the human organism depends upon :

a) the quantity of microwave energy absorbed,

b) the thermal conductivity of the tissue and the thermal transport through the medium of the blood circulation.

The physiological and pathological effects are a consequence of the local rise in the temperature and in the thermal charge of the whole organism (thermal effect).

This is the reason why high intensities may give rise to localized burns for example of the skin or of the subjacent tissues. Given the absence of vascularization of the crystalline lens, the rise in temperature in the lens may become sufficient to produce an opacity of the lens, most frequently after a certain delay. An increase in temperature in extensive regions of the organism would be liable to give rise to a lethal hyperthermia.

All the same, until now no cases of death caused by microwaves have been reported in civilian life.

The generalized hyperthermia brought about by microwaves is to be considered in the same manner as a hyperthermia induced by other means. Local hyperthermias, for example, of the skin, should be treated like serious burns. It should be noted that the tissues situated at greater depth may be disturbed as a result of the overheating (risk of necroses).

The cataract produced by microwaves becomes manifest generally only after a latent period of several months; it is comparable to the cataract produced by infra-red waves.

The microwaves are liable to disturb the operation of the cardiac stimulators. Likewise metallic objects inserted in the organism (for example metallic prostheses and internal electrodes) may function as a receiver antenna sensitive to microwaves and provoke local overheating. Persons wearing a metallic object inserted in their body should not enter within fields of microwaves. This is why, for reasons of safety, in the technical or medical applications of microwaves, the densities of energy flow in the peripheral zones of the aerials should be identified.

The zones in which such densities are high should be marked out and their access subjected to regulations.

Lesions have also been reported which were due to ionizing radiations generated by high-power radar installations (X-rays), but these are parasitic radiations.

II. DANGER RISK

Owing to the existence of a wide-spread network of television everybody is exposed to microwaves. However, the density of energy flow - outside the zone adjoining the aerial - is so weak that no biological effect need be expected.

A substantial risk of exposure exists in the following professions :

- flying personnel or airport ground personnel;
- maritime personnel;
- radar mechanics and personnel working in radar stations;
- personnel working in space research stations;
- personnel exposed around high-frequency furnaces;
- personnel working with lasers;
- persons using medical microwave apparatuses;
- persons assigned to dosimetric checking;
- persons using microwave ovens (kitchens);
- persons engaged in the sterilization of foodstuffs and pharmaceutical products;
- workers in the manufacture of plywood.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 a6
RADIO WAVES

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY RADIO WAVES

The radio waves are electromagnetic vibrations having a frequency comprised between 30 KHz and 300 MHz and a wave length in vacuum extending from 10 km to 1 m. They are transmitted by aerials. It is in the immediate neighbourhood of these powerful transmitters that the greatest field intensities are encountered. Suitable transmitters are used in industry for the purpose of drying and heating of various materials and objects. In medicine high-frequency transmitters are used in diathermy and in surgery.

The dimensions of the human body are small in relation to the wave length of radio waves and, in general, it is simple to calculate the intensity of the surrounding field. In general, the intensity of the body field is much weaker than that of the surrounding field. For a frequency of 1 MHz the body field intensity is 10^4 times weaker and for 1 KHz it is 10^6 times weaker.

The electric fields generate electric currents in the tissues; their intensity depends on the field, the frequency and the electric conductivity. These electric currents cause a rise in the temperature of the tissues, an effect which is utilized in diathermy as well as in surgery.

In general, the radio waves used industrially induce in the organism intensities which are so weak that no biological effects result. However, in the case of certain industrial installations neuro-vegetative manifestations, fatigue, asthenia have been observed. These symptoms disappear without sequelae after cessation of the exposure.

Recomm. 1962 - Ind. diseases
APPENDIX II - PARTICULAR NO. C 3 b
LASER

DISEASES LIABLE TO BE CAUSED IN INDUSTRIAL ENVIRONMENT BY LASER RADIATION (1)

The effects of laser radiations known at present are burns, However, particularly in so far as the ocular effects are concerned, they may be discovered a long time after the causal event and thus lose their acute characteristics.

Lasers are emitters of strongly collimated luminous beams whose energy density and power density can be considerable. These luminous beams are coherent at the same time in space and in time :

- in space, because all the spatially distinct emitter-oscillators in a laser source, vibrate at any moment in phase,
- in time, because of the phase intensity of all the elementary waves which constitute the plane wave issued from a laser source.

These beams are monochromatic, the ranges of emission extending from ultra-violet to infra-red passing through the visible region.

Lasers are used in increasing manner in the fields of research, of medicine, of material processing, of meteorological technique, of telecommunications, etc..., and it is very likely that their use will expand in future.

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(1) LASER = Light Amplification by Stimulated Emission of Radiation

I. PRINCIPLE OF THE LASER

The laser effect is obtained by stimulating the return to the normal state of a certain number of atoms which have an electron population previously inverted from the atomic level. In such atoms the distribution of a population is said to be "normal" if the density of population diminishes progressively as one moves away from the base level. It is possible under certain conditions to "invert" this population, that is to say, arrange for the upper level to be more populated than the level immediately below. A corpuscular population returns to the normal state spontaneously with incoherent emission of radiation. The laser amplifies and coordinates this return. To create a laser effect it is necessary to have available :

- an atomic material, the electronic population of which can be inverted (the first one used consisted of chromium atoms dispersed in a monocrystal of aluminium oxide : ruby with 0.05 % of chromium);
- a means for inverting this population (for example with ruby lasers, the optical pumping realized by a flash tube);
- a means for stimulating the return to normal state with the help of an optical resonator.

The energy of the beam can be regulated by acting upon the intensity of pumping, upon the rate of reflection of mirrors and upon the temperature. The pulse duration of the laser depends essentially upon the mode of operation. The following are distinguished :

- continuously operating lasers,
- normal-pulsed lasers (pulse duration approx. 1 millisecond)
- released or giant-pulsed lasers (pulse duration approx. 1 nanosecond).

Pulsed lasers reach high power within necessarily very short times especially when they operate with giant pulses

(example : 1 gigawatt in less than 30 nanoseconds). The continuously operating lasers emit radiations extending from e few milliwatt to 500 watt.

From a technological point of view the following are distinguished :

- crystal and amorphous solids laser,
- gas lasers,
- semiconductor lasers,
- liquid lasers.

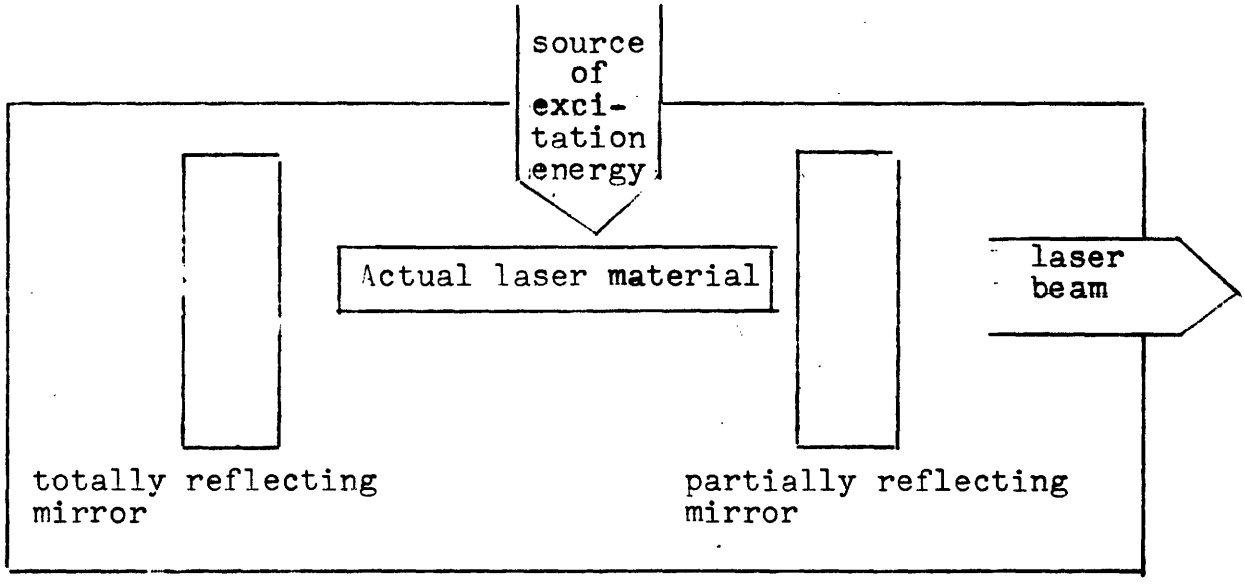
These different laser types have some points in common :

a) the actual material of the laser,

b) an optical device consisting of two mirrors placed at either end of a "resonance cavity" (Pero Fabry cavity). One of these two mirrors is semi-reflecting, the other is totally reflecting,

c) a source of excitation energy so as to realize the "optical pumping" of the energies.

BASIC LASER SCHEME



II. SOURCES OF DANGER

The laser allows considerable electromagnetic power to be concentrated in a linear beam and thus to obtain at the point of impact extremely high temperatures capable of causing the most refractory materials to melt and of destroying the tissues.

Thus different types of laser radiations have found numerous uses :

- surgical : ophthalmological interventions (detachment of the retina, for example), destruction of naevous tumours, etc...
  The laser radiation, when it is used, ensures instantaneous cauterization and brings about an excellent haemostasis;
- industrial and technical :
  - micro-welding,
  - micro machining of metals,
  - drilling and cutting,
  - level determination in building work,
  - photochemistry,
  - applied optics (holography),
  - metrology (extraordinary precision of measuring techniques),
  - telemetry (telemetry - Lidar : "Light Detection and Ranging" - equipment operating on the same principle as radar and allowing extremely precise measuring);
- telecommunications : it is here that the laser will probably have more and more uses owing to the multiplicity of channels and to the fact that the coherence of laser renders the same an oscillator with a directivity that cannot be attained with the same accuracy by micro-waves;
- scientific : the laser will certainly continue more and more to be the subject of much research work in the universities and laboratories.

III. PHYSIOPATHOLOGY

The physical damages liable to be caused by laser radiation may be due to the action of direct radiation but also to that of reflected radiation.

The laser radiation has a triple biological effect :

a) Thermal effect

The thermal effect depends upon the type and the power of the laser and upon the structure of the biological specimen exposed. In particular, the heterogeneity of biological media may result in irregular distribution of heat and certain differences in action according to the nature of the tissue.

b) Electrical effect

The laser oscillator disturbs the electronic array of the atoms of the irradiated matter. Disturbances follow which may be the start of various chemical effects (liberation of free radicals, orientation of anisotropic molecules, etc...) which in turn may have biological consequences.

c) Mechanical effect

The laser beam induces in the medium which it traverses stimulated phonons (the phonon is the elementary quantity of elastic energy) carrying a very high energy which are called hypersons (Brillouin effect). This is a depth effect on the subject of which some uncertainties persist.

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The most exposed organ is the eye. The skin comes in second place. The main danger to the eye, as well as to the skin, is that of burning.

The factors conditioning the ocular lesions are as follows :

1) Focusing on the retina

The laser rays traversing the eye are focused on the retina by the crystalline lens, which brings about a strong increase of energy density. In drawing up savety instructions it is necessary to take into account the most unfavourable case where a beam of parallel rays is focused on the level of the retina on a surface having the diameter of a diffraction disc, the diameter of which depends on the following factors :

a) radius of aperture of the pupil,
b) wavelength of the radiation,
c) possible aberrations of the crystalline lens.

The order of magnitude of the disc diameter is 10 μ; the focusing on the retina multiplies the density of energy by a factor of 10^5 or 10^6.

2) Transmission through the eye

The region of the eye situated in front of the retina is transparent to the range of wavelengths extending from 0.4 to 1.4 μ and to two other ranges in the infra-red. When the laser beam traverses the regions of the eye situated in front of the retina, a portion of the energy is absorbed by the more superficial tissues and the density of energy reaching the retina is diminished. These superficial tissues may be damaged, but the absence of focusing reduces some of the damage of the radiation.

3) Absorption and reflection by the retina

Absorption and reflection by the retina depend upon the wavelength. Furthermore, absorption is very strongly linked to pigmentation and hence to ethnic characteristics.

4) Duration of radiation

In the case of pulsed lasers or lasers with giant pulses, it has been found experimentally that the density of energy that can be tolerated diminishes with the duration of the pulses. In fact, when the input of energy is slow, the heat effect may dissipate, raising the critical threshold of lesion accordingly. Furthermore, the frequency of repetition of the pulses plays a certain part in this respect.

Not much is known as yet about delayed damage, which may result from the summation of minor doses to doses liable to cause lesions which are evident and are distributed over a long period of time.

5) Size of image

Experimental work has shown that the density of energy required to cause the appearance of a lesion increases as the surface of the irradiated region becomes smaller.

d) Other effects

1) Risk of the production of ionizing radiations

The lasers operating at voltages greater than 15 kV are liable to generate X-rays. This emission is very limited, however, and its effect appears negligible in relation to the effects proper of the laser radiation.

2) Other risks associated with chemical agents or materials used jointly with the laser radiation

In this connection mention has to be made of the conventional risks involved in the use of electricity (high voltage) or the refrigerant of the laser heads. The high energy density present under some parts of the laser head may bring about on this level incidents of an explosive nature. Finally, and notably in the case of a high pulse rate, the laser beam may cause the liberation or the for-

mation of irritant or toxic gases (ozone, nitrous gases, gases emitted through the evaporation of targets, etc...).

IV. CLINICAL SYNDROME

A. OCULAR EFFECTS

All the tissues of the ocular globe may be affected, the damages extending from minimal lesions to lacerations of the explosive type.

Whilst minor lesions of the cornea generally tend to heal, all the lesions of the retina are definite.

The lesions of the retina vary in their seriousness according to their location :

- a lesion affecting the emergence of the optic nerve may result in total loss of vision;
- a lesion located on the level of the macula may considerably reduce the quality of visual acuity;
- the lesions of other regions of the retina are often punctiform, very localized and remarkably well tolerated. Sometimes these lesional images are distributed in a highly characteristic rectilinear manner. In the majority of cases, the victim is unaware of these lesions at the moment when he is struck by the laser beam because they are painless and well compensated. If the irradiation is weak, the only changes of the retina may be such as to be difficult to detect in the clinical examination.

In more serious cases a diminution of visual acuity and even a loss of vision may be observed.

A certain number of unknown factors remain in the matter of ocular effects relating to :

- the effect of the summation of low-energy beams;
- the effect of the summation of peripheral punctiform effects;
- the long-term effects of laser radiation after cessation of exposure to risk;
- the depth effect (Brillouin effect).

B. CUTANEOUS EFFECTS

The incidence on the skin of a laser radiation may provoke an immediate burn with local coagulation entraining a rapid cicatrization.

The cutaneous reaction depends upon several factors which are :

- the wavelength of the beam,
- the duration of exposure,
- the "optical qualities" of the skin in the matter of absorption, of transmission and of reflection characteristics. Thus the absorption of laser energy is facilitated by a greater local density of pigmentation. In general and in accordance with what is known at present, it can be said that light skin constitutes a better protective barrier against radiation than pigmented skins.

Little is known as yet about chronic cutaneous exposure to laser radiation.

V. SPECIAL RECOMMENDATIONS

The operation of a source of laser radiation demands the adoption of a certain number of protection standards which depend both on the nature of the work carried out and on the type of laser used.

Technical prevention necessitates special equipment of the premises; furthermore, contrary to observations made in the matter of protection against ionizing radiations, the loss of energy in space is very small and distance from the source

hardly reduces the danger. Fire hazards also have to be taken into consideration. Finally, it is necessary by means of an adequate ventilation to prevent damage by vapours or gases.

Personnel must be warned of the hazards and receive the necessary training. Above all the wearing of suitable protective goggles and, if necessary, of insulating clothing must be accepted.

The goggles against laser radiations must be adjusted to the power and the wavelength of the latter. On their frame the manufacturer has to indicate in a clearly visible manner the optical density of the glass used as a function of the wavelength.

The medical supervision of the personnel exposed to the risk should include a medical examination on employment and periodical medical examinations which include an ophthalmological examination comprising :

- an examination of visual acuity,
- an examination of the external appendages of the eye (eye-lids, conjunctiva, etc...),
- an examination of the different refractive media,
- an examination of the fundus of the eye with dilatation of the pupil,
- an examination of the binocular vision,
- an examination of the visual field.

An identical examination should be carried out when the worker ceases to be exposed to laser radiation.

All the information should be recorded on a document which may be a chart of the different elements of the condition of each eye.

Similarly, it is necessary to carry out an examination of the skin.

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ALPHABETIC LIST OF THE CONTENTS OF THE INDUSTRIAL DISEASES NOTICES

This index has been compiled to show the agents causing diseases both under their own names and under the synonyms used in the notices.

On the other hand diseases or symptoms have only been included when they have characteristics which relate specifically to industrial diseases.

In the same way professions and jobs have only been mentioned when they have a particular occupational risk attached to them.