Agence nationale de sécurité du médicament et des produits de santé

RÉPUBLIQUE FRANÇAISE

Edition of October 2011
Update May 2016

Piratox sheet n°6

"Yperite and other vesicant mustard agents"

! Key points not to forget

→ The 1st emergency measures are:
- extraction of victims from the hazard area: mucocutaneous and respiratory protection of rescuers is essential.
- emergency decontamination (undressing first and foremost) of victims, possibly followed by in- depth decontamination depending on the context[1] (shower only after elimination of any traces of liquid by adsorption).

→ Yperite is a sufficiently volatile and toxic liquid to constitute a **risk of intoxication** (vapours / liquid) and **of contamination** (liquid).

→ The onset of clinical signs is generally delayed by several hours (insidious poison).

→ In general, the shorter the symptom onset time, the more serious the intoxication and the more severe the symptoms.

→ **Yperite is not very lethal, but highly incapacitating.**

→ Victims should be treated as immunodeficient burn victims and, once decontaminated, their treatment presents no hazard to healthcare workers.

→ Treatment is symptomatic. No antidote has been approved to date.

→ As for any skin affliction, check the victim's vaccination status (tetanus).

→ For additional information concerning the risk, assistance with patient treatment and follow-up, we recommend contacting the military health service, poison control centres, or referring healthcare establishments.

1. Pharmaco-toxicological class of the toxic compound

Yperite (2-2' dichloro diethyl sulphide, CAS number: 505-60-2) is the main representative of the family of vesicant sulphur mustard agents. It possesses a high level of alkylating type chemical reactivity.
It has been referred to as mustard gas since its initial use during the first world war (NATO denomination = agent H or HD for the distilled form). It is still frequently encountered in old, though still active first world war ammunition and accidents have been reported in France. Its high military effectiveness and relative ease of synthesis lead to concerns of military or terrorist use. Other sulphur mustard agents have been vectorised (placed in ammunition), such as agent T.
Nitrogen mustards have been synthesised and vectorised by certain countries, but such ammunition is not to be found in France.
This sheet shall only pertain to yperite as the treatment principles are identical for all these agents, in the absence of specific antidotes.

[1] Decontamination procedures (*cf.* circular french no. 700/SGDN/PSE/PPS of November 7th 2008 and introduction sheet).

2. Physicochemical properties of yperite relevant to treatment

	General	Value and comment(s)
Probable physical state	Volatile liquid	BP* = 227.8°C; MP** = 14°C Volatility 625 mg/m3 at 20°C Oily colourless liquid in pure state, though usually yellow, brown or black, with a garlic or mustard odour.
Vapour density	Heavy colourless gas	5,4
Water-solubility	Low	0.7 g/L at 25°C
Contamination potential	High	Immediately soaks into materials and penetrates the skin. High persistence under cold and temperate climates and on certain materials (*e.g.*: certain types of concrete).

*BP: boiling point = temperature of transition from liquid to vapour state.

**MP: melting point = temperature of transition from solid to liquid state.

3. Main intoxication characteristics

Yperite is known to be an insidious poison, *i.e.* a poison whose symptoms only appear in a delayed manner. The higher the exposure, the shorter this delay.

The volatility of yperite and its smell should probably alert the emergency services. The eye is the organ most rapidly impaired if a face mask is not worn, and this at concentrations barely detectable by smell (approximately 1 $mg.m^{-3}$), the initial irritation type symptoms may appear from circa 1 hour post- exposure.

Asymptomatic victims reporting to have smelt or felt the exposure must be undressed, or even more thoroughly decontaminated. Until undressed, victims able to sit down must not do so to avoid aggravating perineal lesions.

Victims deemed to have been the most highly exposed must be kept under observation for a half-day, enabling physicians to detect exposures of approximately 25-50 $mg.min.m^{3}$ (ocular effects), 180-300 $mg.min.m^{-3}$ (skin effects), 250-1200 $mg.min.m^{-3}$ (respiratory and gastrointestinal effects). The other asymptomatic victims should be advised to consult in the event of appearance of eye irritation, breathing distress or rash.

Immediate mortality is low (less than 5% according to former conflict experience, in open environments). In closed environments, when atmospheric concentrations are higher, we can expect an increase in severe intoxications. A dose of liquid yperite of circa 7 g (approximately 5 mL) is considered as capable to causing death within 24 hours. As medium and long-term effects are likely to appear, patients should be monitored over the long-term.

> *The table on page 4 summarises the expected clinical signs.*

4. Non-specific treatment

Victim decontamination is the most urgent action to perform following extraction from the contaminated area.

Due to the mutagenic and carcinogenic nature of yperite, special precautions must be taken by rescuers (breathing and skin protection).

Moreover, recent experimental studies have show that, after exposure, particularly to concentrated yperite vapours, significant evaporation can be observed during the following hours. Whenever possible, victims should not be placed in poorly ventilated rooms.

5. Antidotes (specific treatments)

No antidote has been approved to date.

6. Symptomatic treatments

Treatment is that of a burn, symptomatic only due to the lack of antidote and the main details are given in the table. Skin grafts may be indicated.

7. Laboratory support

No yperite exposure markers are routinely assayed or available to help treat victims. A certain number of markers have been reported to confirm exposure to this poison and are available in a very small number of laboratories belonging to the Piratox network. Urine samples must be frozen and blood samples simply refrigerated.

YPERITE: CLINICAL PRESENTATION ACCORDING TO SYMPTOM APPEARANCE & TREATMENTS TO INITIATE

Symptom ranking		Treatments
In ophthalmic terms	**Low-level intoxication in 4 to 12h:** *- conjunctival irritation,* *- photophobia,* *- increasing eye pain,* *- intense lacrimation,* *- blurred vision.* **High-level intoxication in 3 to 6 hours:** *- blepharospasm,* *- intense pain,* *- conjunctival haemorrhage,* *- purulent lacrimation,* *- palpebral oedema followed by blistering,* *- possible corneal ulceration,* *- possible blindness in the event of contact of liquid yperite with the eye.*	**Occlusive dressings must not be used before washing the eyes.** **Prolonged eye washing** with physiological saline, after oxybuprocaine hydrochloride infusion followed by clinical examination. **Prevent eyelid adherence** by applying sterile Vaseline. **Dark glasses should be worn** to limit photophobia. **Direct victims to an ophthalmologist:** to monitor the condition of the cornea and to prescribe antibiotic or anti-inflammatory eye drops when necessary.
In respiratory terms	**Low-level intoxication in 12 h and above:** *- signs of **irritation** (rhinitis, pharyngitis, laryngitis, unpleasant dry cough) with non-specific upper respiratory tract congestion,* *- followed by productive tracheobronchitis.* **High-level intoxication between 4 and 8 h:** *- extensive oedema leading to dyspnoea and dysphonia,* *- epithelial necrosis of the bronchial mucosa with mechanical obstruction (pseudo-membranes),* *- signs of atelectasis and bronchopneumopathy with purulent sputum.* **The most serious forms appear during the 1st days:** *- pulmonary oedema,* *- acute respiratory failure.*	**Measures to adapt to the type of affliction** **Oxygen therapy.** β**2 mimetic aerosol** in the event of bronchospasm. **Respiratory physiotherapy.** **Curative antibiotic therapy.** **For serious forms** Respiratory intensive care is that of lesional pulmonary oedema **Oxygen therapy.** **Intubation and controlled positive pressure ventilation.** **Antibiotic therapy** (according to bacteriological sample results).

Symptom ranking		Treatments
At the skin level (according to exposure dose and type, liquid vs. vapours)	**Search for lesions, particularly in areas of thin and moist skin.** **Between 2 and 12h:** *- painful erythema,* *- pruritus,* *- followed by subcutaneous oedema.* **Between 12 and 48h:** *- vesicles,* *- phlyctenules,* *- high risk of superinfection.* **Healing:** *- very slow (several weeks or months).*	**Decontamination** - *If possible using fuller's earth, or any other means failing this; remove any liquid present by adsorption (the very low water-solubility of yperite reduces the effectiveness of showering and, in the event of high-level contamination, spreading the poison over the body could actually be detrimental).* - *Abundant water and mild soap.* **Rapid cooling of lesions has been shown experimentally to reduce their severity.** **Analgesics,** due to the highly painful nature of yperite-induced lesions. Ex: *morphine, buprenorphine.* **Burn disinfection according to protocols appropriate for burn victims.** **In the hospital environment only,flattening of the largest phlyctenules that could burst, and treatment of necrotic areas.** **Dressing with** silver sulfadiazine ointment (such as Flammazine®) applied as a thick coat (500 g for 15% area), with emphasis on folds. **As for burns, general treatment** involves the correction of initial hydro-electrolytic loss (reported as minor compared to heat burns of similar area and depth) according to burnt area and control of denutrition. Laser detersion and hydrodissection techniques, used for heat burns, have demonstrated their usefulness in the case of yperite burns. Dermabrasion now appears to be less used. Skin grafts may be indicated.

Symptom ranking		Treatments
Systemic effects	**Digestive signs (ingestion or very severe intoxication):** *- nausea, vomiting, abdominal pains, bloody diarrhoea.* **General signs:** *- asthenia,* *- fever,* *- neuromuscular impairment,* *- psychological disorders.* **Haematological signs:** *- transient hyperleukocytosis,* *- from the 5th day: leukocytopaenia,* *- occasionally thrombocytopaenia,* *- less frequent anaemia.*	**Antibiotic therapy** of infectious complications according to bacteriological documentation. In the event of bone marrow impairment, the treatment shall combine probabilistic antibiotic therapy and packed red blood cell and platelet transfusions. For severe impairments, several animal studies have reported a probable advantage to using hematopoietic growth factor G-CSF. In primates, a 10 µg/day treatment for 21 days led to a decrease in the duration of aplasia. No GM-CSF studies have been published.