:: Autoimmune myasthenia

- *This document is a translation of the French recommendations drafted by Prof. Christine TRANCHANT, Dr Nicolas WEISS, Hélène Rivière and Dr Gilles BAGOU, reviewed and published by Orphanet in 2010.*
- *Some of the procedures mentioned, particularly drug treatments, may not be validated in the country where you practice.*

Synonyms:

myasthenia gravis, acquired myasthenia

Definition:

Autoimmune disorder of the neuromuscular **junction**, associated with a reduction in the number of functional acetylcholine receptors. It manifests itself in the form of proneness to muscle **fatigue** and of **fluctuating** symptoms as time passes.

Further information:

See the Orphanet abstract

Pre-hospital emergency care recommendations
Call for a patient suffering from autoimmune myasthenia

Synonyms

- myasthenia gravis
- acquired myasthenia

Mechanisms

- Acquired autoimmune disorder affecting the neuromuscular junction that reduces the number of functional acetylcholine receptors. It expresses itself in the form of proneness to varying degrees of muscle fatigue. Clinically, the muscles that are affected to the greatest extent are those that are innervated by the cranial nerves. Congenital myasthenia is due to gene mutations
- (disease is different from myopathy)

Specific risks in emergency situations

- respiratory distress (onset can be very rapid, in a matter of minutes), proneness to muscle fatigue in the diaphragm. It can be exacerbated by bronchial obstruction
- swallowing problems
- cholinergic crisis due to cholinesterase-inhibitor overdose (hypersialorrhoea, miosis, diarrhoea, bronchial hypersecretion)

Commonly used long-term treatments

- oral cholinesterase-inhibitors (pyridostigmine bromide (Mestinon®), etc.)
- sometimes: corticosteroids or immunosuppressant treatment

Complications

- pay close attention to the severity of breathing difficulties. Severe acute respiratory distress can develop in a matter of minutes
- be wary of cholinesterase-inhibitor overdose, causing acetylcholine intoxication which can mimic a flare-up of myasthenia

Specific pre-hospitalisation medical care

- assessment of respiratory mechanics (respiratory rate, amplitude, demand on accessory muscles, obstruction, cough intensity). Cyanosis and sweating are very late signs that develop shortly before a respiratory arrest. A reduction in oxygen saturation is a late sign (be wary of normal saturation)
- outside the hospital environment, treatment is essentially symptomatic for swallowing and ventilatory problems (invasive or non-invasive respiratory support). Non-invasive ventilation should only be contemplated as an interim solution whilst waiting for customised treatment to become effective. There are no solid data that advise non-invasive ventilation in this indication. The presence of severe swallowing problems contraindicates non-invasive ventilation
- in myasthenic patients, even in the absence of flare-ups, be wary of any direct or indirect respiratory depressant drugs (hypnotic agents, curare-type agents, morphine-type products, benzodiazepines)
- in cases of respiratory or swallowing problems and in the absence of signs of cholinesterase-inhibitor overdose, subcutaneous injection of 0.5 mg neostigmine; intravenous administration of neostigmine as used, in particular, in pharmacological decurarisation, can trigger bradycardia, which can sometimes be very severe;

this can be prevented by injecting the patient beforehand with atropine (a ready-to-use syringe of atropine must be kept available)

- direct to an Intensive Care or Resuscitation Unit

Further information

- MGA UK - Myasthenia Gravis Association: www.mga-charity.org
- Please visit www.orpha.net and type the name of the disease → in the summary page click on “Expert centres” on the right tab → select “United Kingdom” in the “Country” field in the Expert centres page.

Recommendations for hospital emergency departments

Emergency issues

- There are two situations that need to be contemplated:
  - **Acute decompensation of myasthenia**
  - **Management of an intercurrent disorder in a patient suffering from myasthenia**

The same precautions need to be taken in both cases, since any intercurrent disorder, along with the use of certain drugs (cf. below), is likely to decompensate for myasthenia

Emergency recommendations

- **Emergency diagnostics:**
  - Assess severity:
    - Assess the presence of:
      - Severity criteria:
        - ◊ respiratory condition
        - ◊ swallowing problems
        - ◊ chewing problems
        - ◊ speech problems
        - ◊ condition affecting palpebral muscles
        - ◊ limb deficit
      - Complications:
        - ◊ respiratory arrest
        - ◊ **pulmonary infection** secondary to respiratory or swallowing problems
        - ◊ signs of **cholinesterase-inhibitor overdose** (hypersalivation, miosis, diarrhoea, bronchial hypersecretion)
  - Emergency investigations:
    - Clinical investigations
      - **assess respiratory status**: chest expansion, cough efficacy, respiratory rate (polypnoea), involvement of accessory respiratory muscles, apnoea count. Signs of hypercapnea (sweating, headaches) and cyanosis develop very late and are very serious.
      - **muscle strength score** (/100) (see Table in the Annex)
    - paraclinical investigations where there are respiratory or swallowing problems
      - vital capacity (clinical approximation of apnoea count)
      - blood gases (hypercapnea is a sign of exhaustion)
      - saturation (this remains normal for a very long time and can be falsely reassuring)

- **Immediate therapeutic measures**
  - **In the absence of signs of cholinesterase-inhibitor overdose and where cholinesterase-inhibitor dosage** (pyridostigmine bromide (Mestinon®)) **is less than 8 tablets per day**:
  - **Combine analgesic-antipyrexial drugs (e.g. paracetamol) with nonsteroidal anti-inflammatory drugs**:
    - **1 ampoule of neostigmine** s.c. to alleviate respiratory or swallowing problems quickly: this injection requires **strict clinical observation**
    - **increase the daily dosage** (without exceeding 8 tablets per day)
  - where there are swallowing problems, pass a nasogastric tube
  - **in the event of respiratory problems**: **oxygen therapy**, discuss transfer to an Intensive Care or Resuscitation Unit quickly for observation and to allow assisted ventilation to be provided
  - where there are signs of cholinesterase-inhibitor overdose:
    - dose-reduction
    - **1 ampoule of neostigmine** s.c. can be **helpful** where a cholinesterase-inhibitor overdose is suspected. This injection requires strict clinical observation

Orientation

- **Where?**
  - transfer to a **Neurology Department**, if possible, at an establishment where there is an **Intensive or Continuous Care Unit and a Resuscitation Unit**
  - **in cases of swallowing or respiratory problems: Continuous or Intensive Care Unit, giving preference to a Resuscitation Unit if there is the slightest doubt**
- **When?** As soon as the patient is fit to be transported
- **How?** Via the emergency services if there are swallowing or respiratory problems or if there is the slightest doubt (respiratory exacerbation can develop extremely fast, in a matter of minutes)

Drug interactions

Drug class	Formally contraindicated substances	Substances to be used with caution
Antibiotics	Parenteral aminoglycosides Colistin Injectable cyclines Telithromycin	Topically-applied aminosides and polyamines Lincomycin Clindamycin Fluoroquinolones
Cardiovascular drugs	Quinidine Procainamide Beta-blockers	Intravenous lidocaine
Anaesthetics	Curare-type agents	Volatile anaesthetics i.m. or i.v. barbiturates Ketamine Propanidid
Central nervous system drugs	Trimethadione Diphenylhydantoin Dantrolene	Carbamazepine Chlorpromazine Lithium
Miscellaneous	D-penicillamine i.v. magnesium Quinine and chloroquinine Halofantrine Mefloquine Beta-blocker drops Oxybutynin	Benzodiazepines Phenothiazine Quinquina Oral magnesium Interferon alpha Nicotine patch

Precautions for anaesthesia

- The use of **curare-type agents** is not recommended: the curare effect will be very long-lasting, over an unpredictable period. If such agents have to be used for intubation, give preference to non-depolarising curare-type agents
- **volatile anaesthetics**, **i.m. or i.v. barbiturates** and **ketamine** must be used with **caution** (cf. above)
- i.v. administration of neostigmine as used, in particular, in pharmacological decurarisation, can trigger bradycardia, which can sometimes be very severe; this can be prevented by injecting the patient beforehand with atropine (a ready-to-use syringe of atropine must be kept available)
- in cases of anaesthesia, the patient will need to be **kept under observation in Recovery for a lengthy period**

Preventive measures

- Nasogastric tube, special diet where there are swallowing problems (also be wary of chewing problems)
- Respiratory physiotherapy where there is superinfection

Additional therapeutic measures and hospitalisation

- When managing intercurrent disorders, **make sure that the usual treatment** for myasthenia continues (cholinesterase-inhibitors, corticosteroids, immunosuppressants, etc.)
- If a myasthenia-linked emergency develops, do not forget to administer treatments linked to any other diseases that the patient may have (diabetes, heart problems, hypertension, thyroid problems, etc.)
- During stays in hospital, **adapt the patient's environment and positioning in line with any motor problems that may exist**:
  - risks of falls, grasping difficulties, difficulty with limb movements (make sure that the bell is within easy reach, give drinks and food, etc.
  - diplopia, ophthalmoplegia: place useful objects within the field of vision, etc.
  - swallowing problems: adapt the texture of foodstuffs, move the chin back to swallow, be careful with tablets that have to be swallowed, etc.
- People suffering from myasthenia are prone to fatigue: **avoid repeated and/or prolonged muscle exertion** (including whilst chewing meals or speaking)

– NB: Be careful in recently-diagnosed cases: not all people have had experience of a disabling myasthenic crisis. It is, therefore, helpful to anticipate myasthenic crises and to prevent motor paralysis (**check regularly** to make sure that the bell can be reached, that people can eat or drink alone, swallow their medicines, go to the toilet, etc.). Education is essential.

- In cases of severe, acute flare-ups, intravenous plasmapheresis or immunoglobulin treatment may be indicated. Call to a Centre used to dealing with myasthenia (a Neurology Department or Resuscitation Unit that specialises in myasthenia can help in directing the patient).

Organ donation

- No contraindication to organ donation

Emergency telephone numbers

- Please visit www.orpha.net and type the name of the disease → in the summary page click on "Expert centres" on the right tab → select "United Kingdom" in the "Country" field in the Expert centres page.

Documentary resources

- Jani-Acsadi A, Lisak RP: **Myasthenic crisis: guidelines for prevention and treatment.** *J of Neurol Sci* 2007, 261: 127-33.
- Smulowitz PB, Zeller J, Sanchez LD, Edlow J: **Myasthenia gravis: lessons for emergency physician.** *Eur J Emerg Med* 2005, 12:324-6.
- Tranchant C**: Therapeutic strategy in myasthenia gravis.** *Rev Neurol* 2009, 165:149-54.

Annex

Table: Myasthenic muscle score (Gajdos et al, 1997)

Function		Score
Keeping upper limbs in the horizontal position	maximum (1) minimum (1)	15 0
Putting the lower limbs in Mingazzini's position	maximum (1) minimum (1)	15 0
Raising the head whilst lying down	Against resistance With no resistance Impossible	10 5 0
Sitting up from a lying-down position	Without assistance from the hands Impossible	10 0
Extrinsic ocular musculature	Normal Ptosis Diplopia	10 5 0
Eye closure	Complete Incomplete, cornea covered Incomplete, cornea uncovered	10 5 0
Mastication	Normal Reduced Impossible	10 5 0
Swallowing	Normal Malfunction without aspiration Aspiration	10 5 0
Speech	Normal Nasal Dysarthria	10 5 0

(I) 1 point for 10 seconds

(2) 1 point for 5 seconds

These recommendations have been compiled in collaboration with Professor Christine Tranchant - Reference Centre for Neuromuscular Diseases, Strasbourg Hospital Group-; Dr Nicolas Weiss - Georges Pompidou European Hospital, Paris-; Hélène Rivière - Association Française contre les Myopathies- and Dr Gilles BAGOU - SAMU-69, Lyon.

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