:: Type IV Ehlers-Danlos Syndrome

- *This document is a translation of the French recommendations drafted by Dr Michael Frank and Dr Gilles Bagou, reviewed and published by Orphanet in 2009.*
- *Some of the procedures mentioned, particularly drug treatments, may not be validated in the country where you practice.*

Synonyms:

Ehlers-Danlos syndrome, vascular type (EDSv), EDS IV, Sack-Barabas syndrome

Definition:

Genetic disorder exhibiting autosomal dominant transmission, secondary to a mutation in the *COL3A1* gene that codes for type III collagen. It results in structural **fragility in organs that are rich in type III collagen: arteries, veins, bowels, lungs, skin, liver and spleen**.

Further information:

See the Orphanet abstract

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Pre-hospital emergency care recommendations
Call for a patient suffering from Type IV Ehlers-Danlos Syndrome

Synonyms

- Ehlers-Danlos syndrome, vascular type (EDSv), EDS IV, Sack-Barabas syndrome

Mechanisms

- autosomal dominant genetic disorder that results in a structural abnormality in type III collagen and causes fragility in certain tissues: arteries, veins, bowels, lungs, skin, liver, spleen, etc.

Specific risks in emergency situations

- spontaneous arterial rupture or dissection (primary cause of mortality)
- pneumothorax, pneumomediastinum: spontaneous or iatrogenic, linked to mechanical ventilation or to the central superior vena cava approach
- bowel rupture
- pulsating exophthalmos due to formation of a carotid-cavernous fistula
- uterine rupture during pregnancy, delivery or the post-partum period

Commonly used long-term treatments

- beta-blockers
- preventive treatment currently undergoing validation: celiprolol

Complications

- be wary of any chest or abdominal pain
- be wary of any invasive vascular investigation
- unfamiliarity, hence delay in diagnosing complications

Specific pre-hospitalisation medical care

- avoid hypertension in cases of vascular lesions: target P_{sys} < 120 mmHg
- avoid arterial approaches and the subclavian venous approach
- intramuscular injections contraindicated
- tracheal intubation needs to be atraumatic
- rectal temperature measurement is contraindicated
- wherever it is suspected that a complication is linked to Ehlers-Danlos syndrome, vascular type, direct the patient to a technical facility where CT or MR angiography can be performed

Further information

- EDS - Ehlers-Danlos Support Group UK: www.ehlers-danlos.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.

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Recommendations for hospital emergency departments

- **Ask for any patient-held information on current treatment or precautions required**.
- Whenever an acute complication is suspected, it is recommended that doctors **contact the Reference Centre or one of the Specialist Treatment Centres by telephone before offering any surgical investigation or treatment**. It is best that these be carried out at a specialist centre where staff are thoroughly familiar with the very difficult management of these patients.

Emergency issues and recommendations

Emergency situations:

- Arterial accidents
- Gastrointestinal accidents
- Obstetric accidents
- Respiratory accidents
- Spontaneous carotid-cavernous fistula

1. Arterial accidents

Possibility of **arterial rupture and dissection**, most commonly **without any trigger factor. Spontaneous arterial rupture is the primary cause of mortality** amongst patients suffering from EDSv (78.5%). Such arterial accidents are rare during childhood, but 25% of patients will experience an initial event before they reach 20 years of age, 80% by 40 years of age.

- Any unusual pain syndrome is suspicious, particularly chest and abdominal pain, and must be regarded as a life-threatening emergency.

- **Emergency diagnostics**
  - **CT or MR angiography: investigations by primary intention** must be carried out, even if the clinical picture improves or if the symptoms appear to be minor. **Injections of contrast product** must be carried out at **low pressure** (cf. below).
- **Immediate treatment**
  - **If** an **arterial accident** is suspected or confirmed**, always give medical treatment** by primary intention: rest, analgesia, external compression of a haematoma and blood transfusion.
  - **Optimum blood pressure control (P_{sys}<120 mmHg)**, with the help of calcium-channel blockers that do not slow the heart-rate and of beta-blockers (unless the patient is in shock).
  - **Invasive vascular investigations**, a source of arterial complications: **for life-threatening emergencies only** (selective embolisation), ideally carried out in a **specialist setting.**
  - In view of vascular friability, **surgery is the last resort** (mortality: 19 to 44%). In such an event, a straightforward procedure (arterial clip ligation) must be carried out in preference to reconstruction surgery.

2. Gastrointestinal accidents

Common gastrointestinal complications: **spontaneous rupture** of the sigmoid colon (80%), less commonly of the small bowel and stomach. Spontaneous rupture of the spleen or of the liver have been described.

- **Emergency diagnostics**
  - **Abdominal CT scan**: whenever faced with an acute abdomen that may be consistent with gastrointestinal perforation or a ruptured blood vessel.
  - **Colonoscopy is contraindicated** on account of the risk of rupture of the gastrointestinal tract.
- **Immediate treatment**
  - In the event of peritonitis due to perforation, surgery is the treatment of primary intention:

- tissue fragility must always be borne in mind in anaesthesia (see below).
- Hartmann's colectomy, allowing post-operative complications to be limited (suture slack, anastomotic leaks, fistulae, arterial accidents).

3. Obstetric accidents

Pregnancy is a risk situation: high maternal mortality, estimated at 11.5%, related to uterine or arterial rupture during labour, delivery and the post-partum period; onset may be delayed.

- **Immediate treatment**
  - **Caesarean section** is preferable to vaginal delivery. Extended post-partum observation in hospital is required.
  - **Peridural anaesthesia is contraindicated.**
  - **In the event of vaginal delivery**, steps must be taken to **strengthen the perineum**.
  - Use of **forceps** is **not permitted**.

4. Respiratory accidents

Possible onset of spontaneous **pneumothorax** and **pneumomediastinum**, but such events are also encouraged by positive pressure mechanical ventilation and by setting up subclavian central venous lines.

- **Emergency diagnostics**
  - Chest pain, even atypical, must prompt the diagnosis, warranting additional **radiological investigations**.
- **Immediate treatment**
  - **Incomplete pneumothorax: straightforward observation** in a specialist setting.
  - **Complete pneumothorax: careful pleural drainage**. Prevent sudden pressure changes during drainage.
  - **Analgesia**

5. Carotid-cavernous fistula

Relatively common complication, with the specific feature of being **spontaneous in the majority of cases. Emergency treatment** required since this is potentially life-threatening and could compromise vision.

- **Emergency diagnostics**
  - **Possible symptoms**: pulsating exophthalmos, a thrill that is noticeable to the patient, dilatation of the episcleral veins plus chemosis**.**
- **Immediate treatment**
  - Such cases need to **be managed at a specialist centre**, bearing in mind the **morbidity and mortality associated with an embolisation** procedure, even listed.

Drug interactions

- The patient's usual treatment needs to be borne in mind. Increasingly, this involves long-term use of beta-blockers.

Precautions for anaesthesia

- **Avoid orotracheal intubation** in view of the **risk of wounds to the orotracheal lining** and, wherever possible, **give preference to mask ventilation or** to the use of a **laryngeal mask airway**. If intubation is needed, this must be carried out with care by a senior member of staff.
- In view of the **high risk of pneumothorax, avoid positive pressure ventilation** wherever possible.
- **Prevent and treat hypertensive episodes** at induction, intubation and during recovery.
- **In principle, the use of subclavian central venous catheters is contraindicated.** Central access is possible in the event of a life-threatening emergency, using the femoral and internal jugular routes, but this must be done with ultrasound scanning for guidance. One sensible alternative might be to set up central venous access via a peripheral vein in an arm or via the external jugular vein.
- **Peridural anaesthesia is not advisable**.

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- **As a matter of principle**, the use of **beta-blocker treatment during surgery must be discussed** in the context of planned surgical procedures.

Preventive measures

- **Efforts to counter delays in diagnosing** potentially life-threatening **lesions** must take centre-stage when dealing with patients suffering from EDSv, in particular **where there is no validated preventive treatment**.
- It is essential that iatrogenic risks be limited by **avoiding arterial puncture and injection of contrast products under high pressure** (CT scan).
- Where an arterial lesion has been confirmed, it is essential that the **blood pressure be kept under optimum control, (P_{sys}<120 mmHg)**.
- **Discuss** pre-term **Caesarean section**.

Additional therapeutic measures and hospitalisation

- **Blood gases** and **arterial specimen collection** are **contraindicated**.
- **Intramuscular injections** are **contraindicated.**
- **Rectal temperature measurement** and **wash-outs** are **not permitted**.
- **Prevent constipation** (mild polyethylene-glycol-type laxatives).

Organ donation

- On the basis of current knowledge, there are no data relating to the collection of organs for transplantation. Nonetheless, bearing in mind tissue fragility secondary to the type III collagen abnormality, along with the possibility of arterial and organ rupture, **the collection of organs for transplantation is contraindicated.**

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

- Perdu J, Boutouyrie P, Lahlou-Laforet K, Khau Van Kien P, Denarie N, Mousseaux E et al. [Vascular Ehlers-Danlos syndrome]. Presse Med 2006;35:1864-1875.
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- Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. N Engl J Med 2000;342:673-680.

These recommendations have been compiled in collaboration with Dr Michael Frank, Reference Centre for Rare Vascular Diseases, Georges Pompidou European Hospital, Paris and with Dr Gilles Bagou SAMU-69 Lyon, and have been validated by a Reading Committee made up of: Prof. Jeunemaître (Genetics, Reference Centre for Rare Vascular Diseases), Prof. Fiessinger (Vascular Medicine/Hypertension), Prof. Emmerich (Vascular Medicine /Hypertension), Dr Messas (Reference Centre for Rare Vascular Diseases) - GPEH, Paris, and Dr Boucand, representing the Association Française des Syndromes d’Ehlers-Danlos [French Ehlers-Danlos Syndrome Association] (AFSED).

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