Epidermal necrolysis

Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (Lyell syndrome)

Form for Emergency Department Use

Definition:

- **Epidermal necrolysis (EN)** presents with purpuric macules progressing to vesicles and/or bullae and superficial skin detachment in flaps and painful mucosal erosions. EN is a spectrum which includes the Stevens-Johnson syndrome (SJS, detached-detachable surface of <10% of body surface area), the overlap syndrome (surface area of 10 to 29% affected) and Toxic Epidermal Necrolysis, TEN, or Lyell syndrome (surface area involved ≥ 30%). These are very serious acute dermatological diseases involving sudden destruction of the superficial layer of the skin and mucosal membranes and usually (in 85% of cases) are triggered by a medicinal product (first time in the person's life).

The main medicinal products which carry a risk of epidermal necrolysis are:

- Allopurinol
- Anti-infectious sulphonamides (sulfasalazine, sulfamethoxazole-trimethoprim, dapsone etc.)
- Nevirapine
- Anti-epileptics belonging to the aromatic amine family (carbamazepine, oxcarbazepine, phenobarbital and phenytoin) and lamotrigine
- Non-steroidal anti-inflammatory drugs (NSAID) particularly the oxicams
- Proton pump inhibitors (particularly pantoprazole)

The risk is particularly high in some populations (particularly Asian people from Han) for some of these medicinal products (allopurinol and the aromatic amines) because of genetic susceptibility.

The classical time for the disease to be triggered is 4 to 28 days.

When it is not drug-induced in origin, the disease may be secondary to infection (*Mycoplasma pneumoniae)* or a connective tissue disorder (lupus erythematosus or dermatomyositis). Some cases however remain idiopathic.

The incidence varies depending on country from 1-2 to 6 new cases/million people/year and increases with age.

The disease is characterised initially by several signs which are typically non-specific such as fever, reduced general health and ocular, oral or genital burning.

- The skin lesions often develop secondarily. The skin vesicles become confluent and detach with the least rubbing, exposing the bright red, weeping, painful dermis.
- Mucosal lesions affect the oropharynx, eyes, genital organs and anus. These painful erosions cause increased salivation, eating difficulties, photophobia and burning on micturition.
- Visceral effects are common, particularly with respiratory and gastrointestinal involvement.

At admission, the diagnosis is clinical and is confirmed secondarily by histopathological examination (skin biopsy):

- Diffuse rash, generally starting on the trunk, with purpuric macules progressing to vesicles and/or bullae;
- Superficial skin detachment in flaps ("wet dressing" appearance) with a positive Nikolsky sign (detachment of the epidermis on finger pressure);
- Mucosal erosions (at least two sites);
- Histologically necrotic epidermis throughout its entire depth with negative direct immunofluorescence.

Particular attention must be paid to their respiratory state, as respiratory involvement due to necrosis of the tracheobronchial epithelium may require prompt intensive care management or may even be life-threatening. The respiratory disease is especially common when significant ENT disease (pharyngo-laryngeal) is present.

The immediate complications of EN are a result of acute skin failure caused by the skin detachment with severe liquid and fluid/electrolyte losses (severe hypovolaemia), which carries a risk of acute renal failure due to reduced renal blood flow, serious systemic infections entering from the skin (particularly Staphylococcus aureus and Pseudomonas), heat regulation disorders, increased energy consumption and immune abnormalities.

In widespread forms of the disease, the prognosis is serious with a mortality rate of 20 to 25%. The mortality risk can be estimated in the first 5 days after admission using the SCORTEN, which is a score combining 7 clinical and laboratory criteria.
Age >40 years old and percentage skin surface area involved of >10% are two of the most important of these criteria.

To date, no immunomodulating therapy has truly been proven to be effective. Supportive care in a centre experienced in the management of EN is essential regardless of patient age [4–6].

Re-epithelization of the skin and mucous membranes begins around the 8^{th}-10^{th} day and lasts for a varying period of time depending on the patient, generally 2 to 3 weeks. Healing of the mucosal membranes may be slower.

Complications are common following the acute phase. More than 60% of patients are affected by ocular complications which are the most worrying because of their severity and progression. They may require use of scleral lenses. The other most common complications are cutaneous (pigmentation abnormalities and dystrophic scars) and psychological (generalised anxiety, fear of medicinal products and post-traumatic stress disorder). The other, skin, genital or oro-dental complications need to be better identified and treated. Long-lasting generalised asthenia is common.

Emergency Management

Epidermal necrolysis (EN) is an emergency

- **Early diagnosis and immediate discontinuation of the suspected medicinal product(s)**
- General symptomatic measures
- Protection of affected areas during procedures and transfers
- **Early transfer to an expert centre or burns centre**

In any case of suspected EN:

- Urgently request a **patient evaluation by the dermatologist to confirm the diagnosis and help for drug imputability and transfer to specialized unit**
- Consider a transfer to a specialist centre following the **decision-making algorithm** (Annex 1).

Particular attention must be paid to the patient's clinical background (age and immunosuppression), the extent of detached-detachable skin surface area (serious if ≥10%) and the possible presence of respiratory signs (congestion, abundant sputum, dyspnoea and a fall in saturation). ENT involvement is suspected from dysphonia, cough and congestion. In this case, practitioners should be prudent because of the risk of rapid onset respiratory disease. A chest radiogram may be normal initially. Orotracheal intubation and mechanical ventilation are occasionally required. Non-invasive ventilation is contraindicated because of the skin damage and risk of congestion.

Pending transfer to a specialist unit, symptomatic measures must be taken.

Emergency Guidelines

General guidelines in any case of suspected epidermal necrolysis, even if no severity indicators are present:

- **Ask urgently for a dermatological advice**
- **Contact the Specialist Centre (departments of dermatology, intensive care or burn units)**
- **Stop all suspected medicinal products, classically started 4 to 28 days before the onset of clinical features**
- **Organise transfer to the specialist centre following the algorithm (Annex 1)**
- **Inform the closest Intensive Care department**
- **Digitalized photographs are required (with the patient's agreement) to confirm the diagnosis and to organize the contact with the expert centre.**

- **Assess severity indicators:**

- Detached or detachable body skin surface area (BSA) ≥ 10 %
- Age (children and the elderly)
- **Haemodynamic and respiratory repercussions:**
    - heart and respiratory rate;
    - blood pressure;
    - O_2 saturation on ambient air;
    - temperature (repeated measures);

- urine output;

- **Skin pain;**

- **<u>Urgent investigations:</u>**
  - Full blood count - platelets;
  - Blood electrolytes;
  - Urea – creatinine;
  - Liver profile;
  - Blood glucose;
  - Arterial blood gases (PO_2) with arterial lactate (systemic repercussions);
  - Blood cultures

The clinical and laboratory criteria are used to calculate the **SCORTEN** (Annex 2).

Organise transfer by an appropriate means of transport as soon as the patient is stable. **It is essential to assess the patient's haemodynamic and respiratory state before transfer.**

1. Immediate therapeutic measures

- **Monitoring and hydration**

  Warm the room to between 28 and 32°C
  Monitor heart rate, blood pressure, temperature and respiratory rate every two hours
  Monitor skin and mucosal membrane detachment, **care should be taken with any patient manipulations**
  Monitor laboratory parameters
  Vascular access: a peripheral venous access should be used in preference with priority given to achieving access through healthy skin.

  <u>Hydration for the first 24 hours</u> adapted to the initial detached surface area and then according to urine output (note: initial renal blood flow is frequently reduced):
  Initial equation: 1.5 mL x % detached-detachable surface x kg/day
  Target urine output 0.5 to 1 ml/kg/h (monitor every 4 hours)
  Solutes:
    - until enteral feeding starts: glucose 10% 1 L + NaCl 8 g/L + the remainder as physiological saline
    - then physiological saline + KCl and phosphate depending on requirements

  If urine output is insufficient, pass 1 litre of physiological saline over 8 hours and increase the basal flow rate.
  Correct electrolyte disorders (e.g. hypophosphatemia)
  Renal blood flow is commonly reduced. Sufficient hydration is a major aim of emergency management pending transfer to a specialist centre.

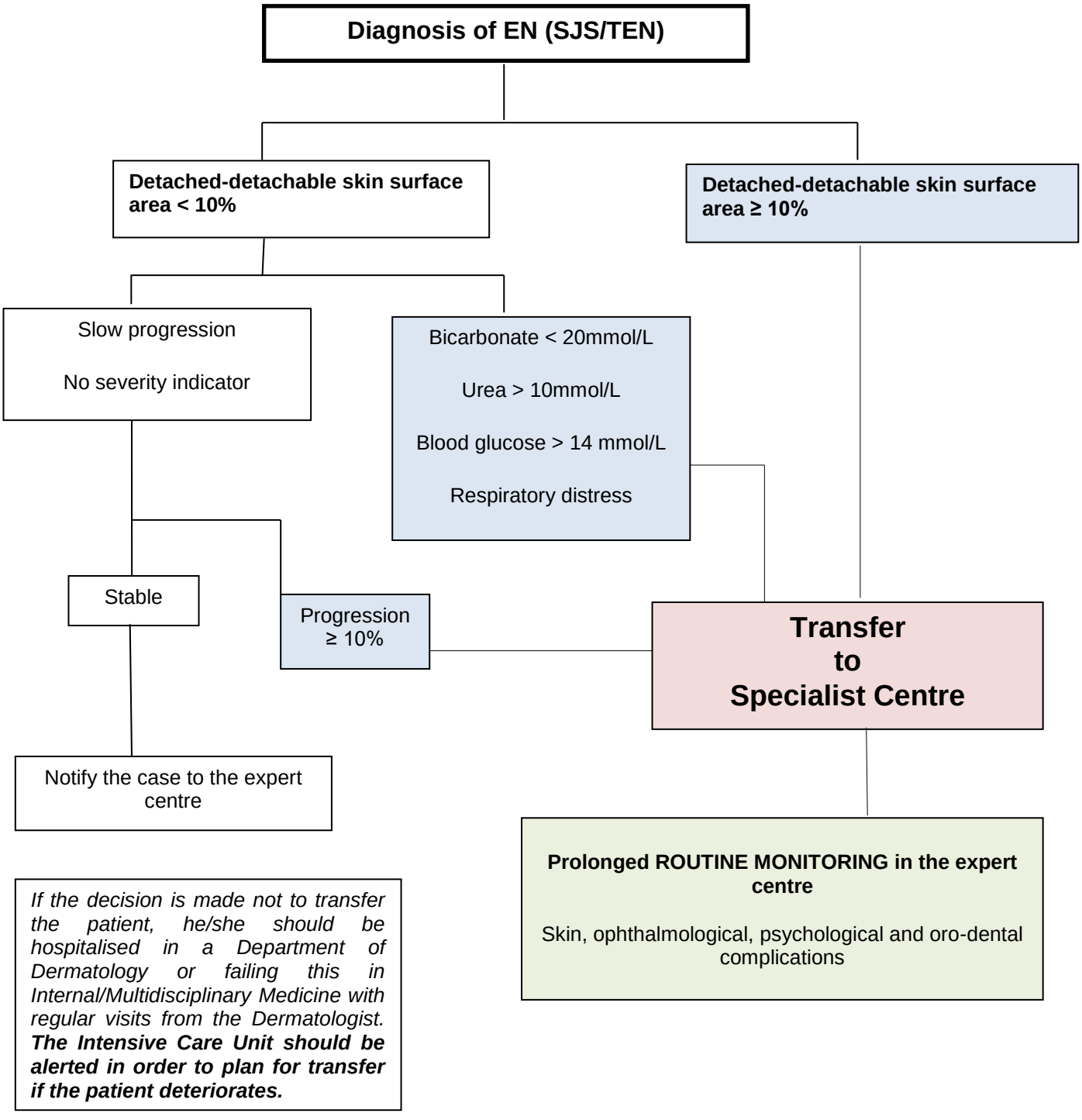
- **Other symptomatic measures:**

  - Strict asepsis: isolating the patient with usual contact measures: non-sterile gloves, gown, mask and hairnet

- Protection of the skin with non-adhesive bandages, Vaseline over the whole body, avoiding adhesive electrodes.
- The necrotic epidermis must not be debrided.
- Urgent ophthalmological examination within the first 24 hours and eye care every two hours with lubricating preservative-free eye lotions and/or ophthalmic vitamin A ointment.
- ENT examination.
- Antiseptic and analgesic mouth care every 2 to 4 hours.
- Genital care with Vaseline 2 to 3 times daily.
- Prophylactic antibiotic therapy is not recommended. Antibiotic therapy is only justified in cases of documented invasive infection or haemodynamic instability after discussion with the expert centre.
- Appropriate analgesic treatment particularly before care procedures (morphine derivatives are often required).
- Oxygen therapy if required.
- Anxiolytics if required.

Contact details of expert centre

Annex 1: Algorithm for transfer to a specialist unit



Annex 2: SCORTEN

Composite 7-item score (1 point per item)

Age > 40 years old
Cancer, blood disease
Skin detachment > 10 %
Heart rate > 120/min
Bicarbonate < 20 mmol/L
Urea > 10 mmol/L
Blood glucose > 14 mmol/L

Total score	Estimated risk of death in the acute phase
0 -1	3%
2	12%
3	35%
4	58%
≥5	90%