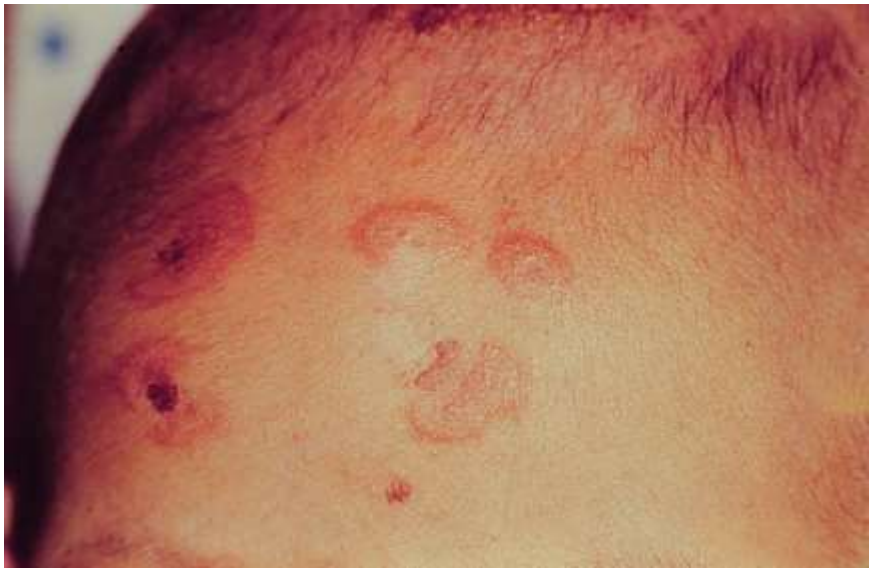
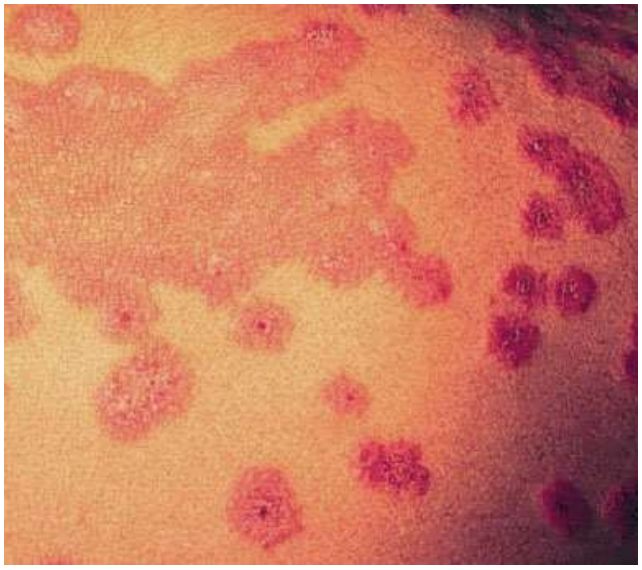
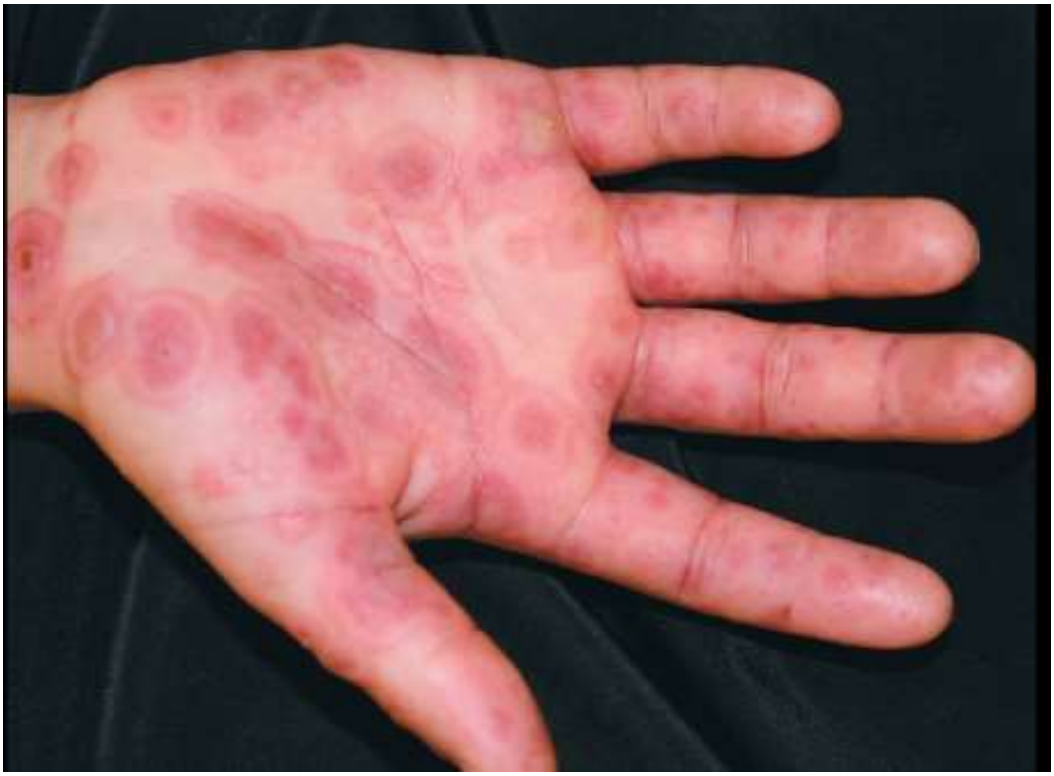
THE NORTHERN HOSPITAL

ERYTHEMA MULTIFORME





Left: Typical target lesion of erythema multiforme. Right: Raised atypical targets and arcuate lesions, (eMedicine).



Classic "target lesions" help establish the diagnosis of erythema multiforme.

Introduction

The relationship between **Erythema multiforme (EM)**, **Stevens-Johnson Syndrome (SJS)** and **Toxic Epidermal Necrolysis (TEN)** has long been confused in the literature.

Traditionally all three were considered as merely varying degrees of severity in a continual spectrum of the same disease (in order if increasing severity: EM → SJS → TEN.

However, although some diversity of opinion still remains, common consensus now considers EM to be a *distinct entity* to SJS and that *severe* SJS is represented by TEN

EM is usually due to **infection**, and less commonly due to drugs and is a benign condition.

SJS - TEN is usually due to a **drug reaction**, and is a more severe condition which can be **potentially fatal.**

EM is usually caused by an infection and runs a benign course.

The main clinical challenge is to ensure differentiation from the much more serious condition SJS-TEN.

See separate document for SJS - TEN

Definitions:

Current formal definitions are as follows:

1. **Erythema multiforme**:

   - Erythema multiforme minor:
     - ♥ Skin involvement only.
   - Erythema multiforme major:
     - ♥ Skin involvement and **one** mucosal surface involvement.

2. **SJS - TEN:**

   Here there is skin involvement with **two or more** mucosal surfaces involved.

   Three **degrees** of severity are recognized:

   - Stevens Johnson Syndrome:
     - ♥ Involves **< 10 %** of the body surface area.

- SJS / TEN:
  - ♥ Involves **10 - 30 %** of the body surface area.
- TEN:
  - ♥ Involves > **30 %** of the body surface area.

Pathophysiology

Erythema multiforme (EM) is an acute, *immune-mediated condition.*

The development of EM secondary to **HSV infection** is thought to involve a cell-mediated immune process directed against viral antigens deposited in lesional skin.

The detection of HSV DNA in skin biopsy specimens from patients with EM supports this theory

Causes

Many causes have been attributed to EM, including

1. **Infections:**

   Infections (viral, bacterial, or fungal) account for approximately **90 %** of cases.

   The principal infectious agents include:

   - Herpes simplex virus
   - Mycoplasma pneumoniae (particularly in children).

Less common causes are thought to include:

2. Drugs:

   The most common associations are with:

   - Antibiotics (sulfonamides)
   - Antiepileptic drugs
   - NSAIDs

3. Malignancy

4. Autoimmune connective tissue diseases

Clinical features

The clinical course of EM is usually self-limited, resolving within weeks without significant sequelae. However, in a minority of cases, the disease recurs frequently over the course of years.

Erythema multiforme is characterized by the appearance of distinctive target-like lesions on the skin which may be accompanied by erosions or bullae involving a single mucosal surface

Erythema multiforme minor refers to EM without mucosal involvement.

Erythema multiforme major is the term used to describe EM with mucosal involvement.

Skin lesions:

The term "multiforme" describes the *myriad* clinical morphologies that may be observed. Target lesions are most characteristic but they make take other atypical forms as well

Characteristics include:

1. Discrete round to oval lesions

2. These are triphasic target (or iris-like) lesions with:

    - A central purple or dusky area
    - Surrounded by a whitish oedematous concentric rim
    - Surrounded again by a red halo.

3. As the lesions evolve, a central blister or erosion may occur.

4. Distribution:

    Cutaneous lesions frequently begin on the extensor acral (i.e distal) extremities, and may then spread centripetally to other areas.

    Lesions are predominantly seen on:

    - Distal limbs
    - The face
    - Less often, the proximal limbs and the trunk.

5. Pruritus may occur, but is uncommon.

Mucosal lesions:

These, when they occur are confined to a single mucosal surface and do not usually cause significant complications.

Natural history:

EM not associated with any mortality.

Most cases are self-limited and resolve without sequelae within 2 - 4 weeks.

EM lesions usually appear over the course of 3-5 days and resolve within approximately 2-4 weeks.

Although the skin lesions do not scar, post inflammatory hyperpigmentation may remain for months after resolution, particularly in patients with darker skin.

A small number of patients with erythema multiforme experience frequent episodes over many years leading to substantial morbidity, a condition termed **recurrent EM**.

Persistent erythema multiforme is a **rare** variant of EM characterized by the ongoing appearance of typical and atypical EM lesions

Differential diagnosis

EM must be differentiated from the far more serious condition **SJS-TEN**

SJS-TEN is suspected when there is:

1. Significant systemic upset/ organ compromise.

2. Greater than one mucosal surface involved.

3. A well recognized drug for the causation of SJS-TEN is being taken by the patient.

Investigations

In clear cut cases, where the patient remains well, no particular investigations may be necessary at all.

In selected patients the following may be considered:

1. Blood tests:

    - FBE

- CRP
- U&Es/ glucose
- LFTs

2. Swabs for PCR studies:
    - Herpes simplex virus
    - Mycoplasma pneumoniae
3. Skin biopsy:

    This may be considered;

    - Where the diagnosis is uncertain, and the patient is unwell
    - When other more serious diseases need to be excluded.
    - Where lesions are persistent

Management

Avoid any suspected triggers, such as drugs, and advise the patient accordingly.

The following may be considered:

1. Topical steroids.
2. Antihistamines.
3. Antiseptic mouth washes.
4. Prednisolone:
    - More significant symptoms may respond to oral steroids, but these should be discussed with the Dermatology Unit.
5. Treat infection
    - Antiviral agents are for useful those patients with definite herpes simplex associated EM
    - Antibiotics can be used for mycoplasma infections.

Disposition:

Urgent dermatological review is only required when there is a need to distinguish the presentation from SJS - TEN.

References

1. eTG - November 2015

    - Dermatology Therapeutic Guidelines 4th ed 2015.

2. Dunn R. et al. Dermatology Emergencies in Cameron et al. Textbook of Adult Emergency Medicine, Cameron 4th ed 2015.

3. David A Wetter et al. Erythema Multiforme in Up to Date Website, Apr 13, 2016.

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Reviewed June 2016.