

# Erythema Multiforme

Erythema multiforme is the name given to a short-lasting illness, which sometimes recurs. It causes a characteristic rash and often blisters in the mouth and elsewhere.

---



---

*The information contained within the Grand Rounds Archive is intended for use by doctors and other health care professionals. These documents were prepared by resident physicians for presentation and discussion at a conference held at The Baylor College of Medicine in Houston, Texas. No guarantees are made with respect to accuracy or timeliness of this material. **This material should not be used as a basis for treatment decisions, and is not a substitute for professional consultation and/or peer-reviewed medical literature.***

## **ERYTHEMA MULTIFORME AND TOXIC EPIDERMAL NECROLYSIS**

Michael G. Stewart, MD  
February 20, 1992

### **Clinical Features**

The diagnostic criteria for erythema multiforme (EM) is individual "target" skin lesions less than 3 cm in diameter, less than 20% of body surface area involved, with minimal mucous membrane involvement, and biopsy compatible with EM. The cutaneous lesions are typically symmetric, and involve the extremities, with the dorsal hands and exTENor aspects most commonly involved.

Many authors use the designation erythema multiforme minor and major, with EM minor meaning skin lesions only, and EM major being synonymous with Stevens-Johnson syndrome.

Stevens-Johnson syndrome has similar skin lesions with the additional involvement of at least two mucous membranes, and fever. The appearance of the mucosal lesion is erythema and edema, which progresses to erosions and pseudomembrane formation. In a review of the mucosal involvement of 34 patients with Stevens-Johnson, 100% had stomatitis, 86% had ocular involvement, 41% had genital mucosal or urethral involvement, but only 3% had involvement of the anal mucosa. Although not reported in this series, upper airway mucosal involvement and pneumonia may be seen in up to 30% of cases. In addition to the target lesions, virtually all patients will develop a characteristic maculopapular rash, usually early in the disease. Prodromal symptoms, such as fever, malaise, and cough are sometimes reported as a

feature, and they usually occur seven to ten days prior to full-blown presentation. The majority of cases of erythema multiforme and Stevens-Johnson syndrome are between ages 20 and 40, and 20% of cases occur in children and adolescents. The mortality of Stevens-Johnson syndrome is reported as 3 to 19%.

Toxic epidermal necrolysis (TEN) is distinguished by larger body surface area involvement, and the development of bullae. The epidermis of the skin peels off in sheets greater than 3 cm, and the skin becomes tender within 48 hours. TEN should be distinguished from staphylococcal scalded skin syndrome. In the largest retrospective series of TEN in the literature, the mean age was 45, although there were several cases in children. Body surface area involved was 47%, and 43% of survivors had some permanent sequelae, most of which were ocular (including three cases of blindness), or permanent skin pigmentary changes. The most common cause of death was sepsis, mostly from *Staph aureus* or *Pseudomonas aeruginosa* infections. The mortality rate is 30% to 70%.

The incidence of cases of EM, Stevens-Johnson syndrome, and TEN severe enough to require hospitalization is about 3 to 8 per million per year. Although the idea that erythema multiforme and TEN are related is not universally accepted, most authors currently consider these syndromes to exist along a continuum of disease, with localized fixed drug reaction being the most mild manifestation, with progression to erythema multiforme minor, Stevens-Johnson syndrome and TEN as the disease process worsens. There are overlapping manifestations between syndromes, and many patients do not fit easily into one named syndrome.

### **Etiology**

Medications are reported as the most common probable etiologic factor in erythema multiforme and TEN. Antibiotics are reported to cause at least 30 to 40% of cases, with sulfonamides, tetracyclines, amoxicillin, and ampicillin most commonly implicated. Nonsteroidal anti-inflammatory medications are also implicated, and anticonvulsants, especially Tegretol and phenobarbital, are also reported. There have also been single reports of erythema multiforme occurring after numerous other medications.

Patients are often given antibiotics for an infection, and it is difficult to determine whether the antibiotic or the infection was responsible for the disease. Viral upper respiratory infections, *Mycoplasma pneumoniae*, pharyngitis and Herpes simplex infection are also reported to cause erythema multiforme. The list of other possible etiologies is exTENive, and includes systemic lupus erythematosus, histoplasmosis, pregnancy, malignancy and external-beam radiation. In most series, some cases remain idiopathic. Several authors have postulated an immunologic etiology for erythema multiforme, although no one has been able to demonstrate conclusively the pathogenesis of erythema multiforme.

### **Differential Diagnosis**

Other mucocutaneous syndromes which need to be excluded include Kawasaki's disease, Behcet's syndrome, small-vessel vasculitis syndromes, lupus erythematosus, pemphigus, pemphigoid, epidermolysis bullosa, and dermatitis herpetiformis.

### **Ocular Complications**

The most common and serious long-term sequelae of Stevens-Johnson and TEN are the ocular complications. The conjunctivitis damages or completely destroys the goblet cells of the conjunctiva, which results in instability of the precorneal tear film, and corneal drying and opacification. The corneal damage can lead to decreased visual acuity and even blindness. The incidence of long-term ocular complications from Stevens-Johnson and TEN are reported at 10 to 27% of patients.

### **Treatment**

EM minor should be treated symptomatically, with analgesics, antipruritics, and if involved, local care to lips and gums.

EM major should receive similar supportive care. Mouthwashing with hydrogen peroxide helps to gently debride crusts. An ophthalmologist should be involved, because the ocular complications may be devastating. Crusted skin lesions should be kept moist.

TEN should be treated like a major burn, with aggressive fluid management, and careful assessment of fluid losses. Strict antisepsis is very important. Eroded skin should be cleaned regularly and covered with topical antimicrobial ointment. Spontaneously sloughing skin should be debrided. Again, an ophthalmologist should be involved.

The one long-standing controversy in erythema multiforme and TEN has been the use of corticosteroids.

Although steroids have been a mainstay of treatment in the past, several reviews have concluded that steroids do not shorten the disease course, and they produce more medical complications, namely secondary infections. Because of this data, most authors today do not recommend the routine use of systemic steroids in the treatment of erythema multiforme or toxic epidermal necrolysis. There have been no randomized prospective trials, however, and some authorities still believe that a short-term pulse of steroids early in the disease course may be of benefit in selected patients.