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Erythema multiforme

P Farthing[1], J-V Bagan[2], C Scully[3]

[1]*Charles Clifford Dental School, University of Sheffield, Sheffield, UK;* [2]*University Hospital, University of Valencia, Spain;* [3]*Eastman Dental Institute, University College London, London, UK*

Erythema multiforme (EM) is an acute mucocutaneous hypersensitivity reaction characterised by a skin eruption, with or without oral or other mucous membrane lesions. Occasionally EM may involve the mouth alone. EM has been classified into a number of different variants based on the degree of mucosal involvement and the nature and distribution of the skin lesions. EM minor typically affects no more than one mucosa, is the most common form and may be associated with symmetrical target lesions on the extremities. EM major is more severe, typically involving two or more mucous membranes with more variable skin involvement – which is used to distinguish it from Stevens-Johnson syndrome (SJS), where there is extensive skin involvement and significant morbidity and a mortality rate of 5-15%. Both EM major and SJS can involve internal organs and typically are associated with systemic symptoms. Toxic epidermal necrolysis (TEN) may be a severe manifestation of EM, but some experts regard it as a discrete disease. EM can be triggered by a number of factors, but the best documented is preceding infection with herpes simplex virus (HSV), the lesions resulting from a cell mediated immune reaction triggered by HSV–DNA. SJS and TEN are usually initiated by drugs, and the tissue damage is mediated by soluble factors including Fas and FasL.
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Introduction

Erythema multiforme (EM) is an uncommon, acute inflammatory disorder, which affects the skin and/or mucous membranes. There is a spectrum of clinical presentations encompassed under the diagnosis, described below.

Correspondence: Prof. Crispian Scully, Eastman Dental Institute, University College London, 256 Grays Inn Road, London WC1X 8LD, UK. Tel: +44 (0) 20 7915 1038, Fax: +44 (0) 20 7915 1039, E-mail: cscully@eastman.ucl.ac.uk
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Erythema multiforme is a reactive mucocutaneous disorder that comprises variants ranging from a self-limited, mild, exanthematous, cutaneous variant with minimal oral involvement (EM minor) to a progressive, fulminating, severe variant with extensive mucocutaneous epithelial necrosis (Stevens-Johnson syndrome: SJS; and toxic epidermal necrolysis: TEN). All variants share two common features: typical or less typical cutaneous target lesions and satellite cell or more widespread necrosis of the epithelium. These features are considered to be sequelae of a cytotoxic immunologic attack on keratinocytes expressing non-self-antigens. These antigens are primarily microbial (viruses) or drugs. (Ayangco and Rogers, 2003). However, there are significant differences in severity and clinical expression between EM minor, EM major, SJS and TEN.

Erythema multiforme usually affects apparently healthy young adults and several reports suggest that males are affected more than females. The peak age at presentation is between 20 and 40 years although 20% of cases occur in children. The disease is often recurrent and is precipitated by preceding herpes infection in up to 70% of cases (Carrozzo *et al*, 1999).

Aetiology

A range of usually exogenous factors trigger what appears to be an immunologically related reaction with sub- and intra-epithelial vesiculation.

There may be a genetic predisposition to EM, with associations of recurrent EM with HLA-B15 (B62), HLA-B35, HLA-A33, HLA-DR53 and HLA-DQB1*0301. HLA DQ3 has been proven to be especially related to recurrent EM and may be a helpful marker for distinguishing HAEM (herpes-associated EM) from other diseases with EM-like lesions.

Patients with extensive mucosal involvement may have the rare HLA allele DQB1*0402.

Erythema multiforme has been reported to be triggered by numerous agents, particularly viruses, especially herpes simplex virus (HSV) but other herpesviruses (varicella-zoster virus, cytomegalovirus, Epstein-Barr

virus), adenoviruses, enteroviruses (Coxsackie virus B5, echoviruses), hepatitis viruses (A, B and C), influenza, paravaccinia, parvovirus B19, poliomyelitis, vaccinia and variola have all been implicated.

A variety of other infectious agents, which are less commonly implicated, may include bacteria such as *Mycoplasma pneumoniae*, borreliosis, cat scratch disease, diphtheria, haemolytic streptococci, legionellosis, leprosy, *Neisseria meningitidis*, *Mycobacterium avium complex*, pneumococcus, Proteus, Pseudomonas, Rickettsia, Salmonella, Staphylococcus, syphilis, tuberculosis, tularemia, typhoid, *Vibrio parahaemolyticus*, Yersinia, Chlamydia, lymphogranuloma venereum and psittacosis, fungal infections such as coccidiodomycosis, dermatophytes or histoplasmosis and parasites such as Trichomonas and *Toxoplasma gondii*.

Immune conditions such as BCG or hepatitis B immunisation, sarcoidosis, Graft versus Host Disease, inflammatory bowel disease, polyarteritis nodosa or systemic lupus erythematosus may be implicated (Ayangco and Rogers, 2003).

Food additives or chemicals such as benzoates, nitrobenzene, perfumes or terpenes have also been reported as aetiological agents.

Drugs such as sulphonamides (e.g. co-trimoxazole), cephalosporins, aminopenicillins, quinolones, chlormezanone, barbiturates, oxicam non-steroidal anti-inflammatory drugs, anticonvulsants, protease inhibitors, allopurinol or even corticosteroids may be implicated (Porter and Scully, 2000; Diz Dios and Scully, 2002; Abdollahi and Radfar, 2003; Scully and Bagan, 2004). In one series, antecedent medication use was identified in 59% of EM patients and 68% of SJS patients, and a striking increase in the number of cases in one series caused by cephalosporins (Stewart *et al*, 1994). In general there appears to be an association between the type of aetiological agent and the severity of the disease. Thus viral infections appear to trigger EM minor or major but drug ingestion tends to trigger more severe SJS or TEN. However this is not absolute and a small but significant proportion of EM minor and major cases are precipitated by drugs, while likewise some cases of SJS are virally associated (Auquier-Dunant *et al*, 2002).

The aetiology of EM is unclear in most patients, but appears to be an immunological hypersensitivity reaction with the appearance of cytotoxic effector cells, CD8+ T lymphocytes, in epithelium, inducing apoptosis of scattered keratinocytes and leading to satellite cell necrosis (Ayangco and Rogers, 2003) (see below).

Herpes associated erythema multiforme (HAEM)

The best-documented association is between HSV infection and EM minor/major and has been designated 'HAEM'. Evidence that EM may be triggered by HSV has come from a number of sources. In single episode and recurrent EM many patients give a history of a preceding herpes infection 2 weeks or less before onset of the disease (Leigh *et al*, 1985; Nesbit and Gobetti, 1986; Huff and Weston, 1989; Farthing *et al*, 1995) and the antiviral agent aciclovir is successful in treating a high proportion of patients with recurrent EM (Molin, 1987; Huff, 1988; Tatnall *et al*, 1995) even when there is no clear clinical association with HSV infection (Lozada and Silverman, 1978). A number of studies have sought HSV or HSV–DNA in lesions of EM. Infectious HSV has not been recovered from the lesions (Kokuba *et al*, 1998) but HSV–DNA has been detected in 36–81% (Brice *et al*, 1989; Darragh *et al*, 1991; Aslanzadeh *et al*, 1992; Miura *et al*, 1992; Imafuku *et al*, 1997; Kokuba *et al*, 1999). The large variation in detection rates may be due in part to differences in the selection criteria for cases included for analysis but it seems clear that detection of lesional HSV–DNA is not restricted to those cases showing a clinical association with HSV. One study looked at HSV–DNA expression in single episode and recurrent HAEM (documented to be related to HSV infection) as well as idiopathic EM not associated with either preceding HSV infection or drug ingestion (Ng *et al*, 2003) and found that similar proportions of lesions (up to 60%) were positive for HSV–DNA in both groups. This together with the observation that antiviral drugs are successful in treating some patients with recurrent lesions without a clinical association of HSV suggests that some cases of idiopathic EM may actually be related to a sub-clinical HSV infection or reactivation.

Little is known about the HSV genotype in relation to HAEM. One study found that the lip was the most common site of preceding HSV infection in recurrent EM implicating HSV-1 (Farthing *et al*, 1995). A more recent study using nested PCR found HSV-1 in 66%, HSV-2 in 28% and both HSV-1 and HSV-2 in 6% of the patients (Sun *et al*, 2003).

Histology

Lesions of EM are similar histopathologically both in the oral mucosa and the skin. They are characterised by a lichenoid infiltrate in the basement membrane zone of the epidermis or epithelium. T lymphocytes and mononuclear cells are present in the dermis and lamina propria and extend into the epithelium or epidermis obscuring the basement membrane zone. The degree of mononuclear cell infiltration is variable and tends to be less in those lesions resembling TEN. The epithelium or epidermis may appear oedematous and spongiotic and there is necrosis both of basal and supra-basal epithelial cells, resulting in both intra and sub-epithelial bullae formation. Not infrequently the bullae contain mononuclear cells (Figure 1). Immunofluorescence shows granular staining for C3 at the basement membrane zone and occasionally within vessels or apoptotic keratinocytes (Ayangco and Rogers, 2003).

In cases resembling TEN there is prominent epidermal damage but with little inflammatory infiltration either within the epidermis or in the dermis.

Pathogenesis

Erythema multiforme appears to be the result of a cell mediated immune reaction to the precipitating agent. In

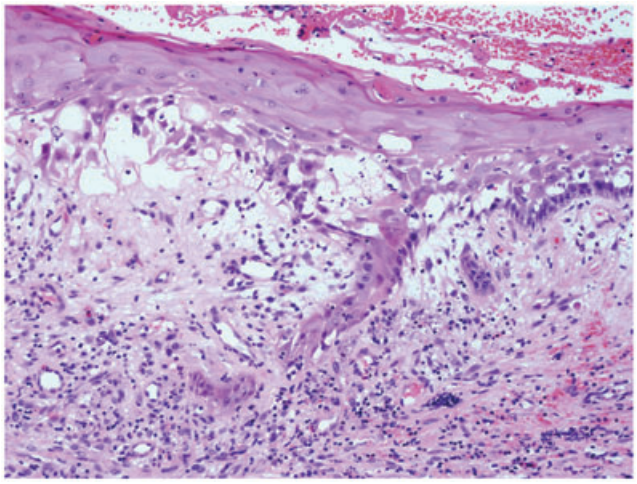

Figure 1 Histopathology of EM minor. The epithelium is oedematous and intra- and sub-epithelial vesicles are present. An infiltration of lymphocytes and macrophages is seen in the lamina propria and within the epithelium

HAEM it is most likely that HSV–DNA fragments in the skin or mucosa precipitate the disease. HSV–DNA fragments and in particular DNA polymerase (PoL) have been detected in the basal and suprabasal cell layers of the epidermis in lesions as well as healed lesions for up to 3 months (Imafuku *et al*, 1997) and the T cells accumulating in active lesions are CD4+ (Vβ2+) cells which respond to HSV antigens *in vitro* (Malmstrom *et al*, 1990; Kokuba *et al*, 1998). In addition there is a good correlation between PoL expression in lesions, CD4+ (Vβ2+) T cell accumulation and the duration of clinical symptoms (Kokuba *et al*, 1998). *In situ* RT-PCR and immunocytochemical staining have shown that mononuclear cells in both HAEM and HSV lesional skin tissues stain positively for IFN-γ, a cytokine, which is associated with tissue damage, and this expression correlates with HSV-protein expression (Kokuba *et al*, 1999). IFN-γ is produced by CD4+ T helper 1 (Th1) lymphocytes, cells characteristic of a delayed type hypersensitivity reaction (DTH) (Billiau *et al*, 1998) (Figure 2). IFN-γ is pro-inflammatory and induces

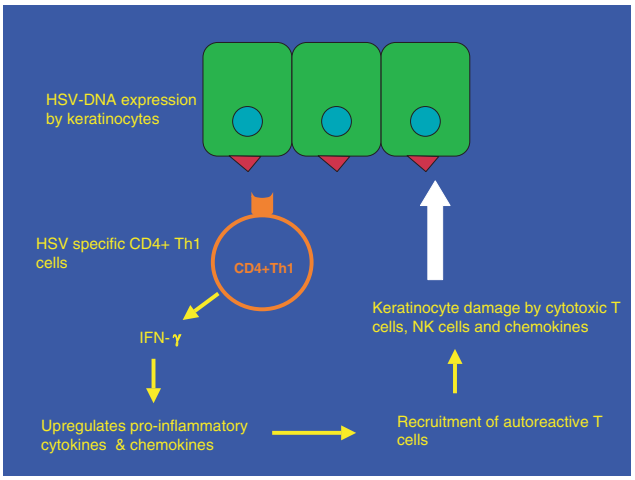

Figure 2 Pathogenesis of EM

adhesion molecule expression on keratinocytes and endothelial cells as well as stimulating production of chemokines and cytokines from a number of cell types. Thus it seems likely that the HSV–DNA fragments in skin or mucosa initiate a specific T-cell mediated DTH response resulting in the presence of HSV-specific T cells, which generate IFN-γ. This cytokine then amplifies the immune response and stimulates the production of additional cytokines and chemokines, which aids the recruitment of further reactive T cells to the area. These cytotoxic T cells, NK cells or chemokines can all induce epithelial damage.

The mechanisms of tissue damage in EM appear to differ between virally-induced and drug-induced EM and also differ from those in SJS and TEN, particularly those that are characterised by widespread epithelial damage but with a sparse inflammatory infiltrate. For example, in drug-induced EM it is thought that reactive metabolites of the initiating drug induce the disease (Knowles *et al*, 2000) but the mechanisms of damage are variable and unlike HAEM do not appear to be the result of a DTH response. Immunocytochemicial staining and *in situ* hybridisation has shown that T cells do not produce IFN-γ in drug-induced lesions but rather the lesions are characterised by tumour necrosis factor alpha (TNF-α) present in keratinocytes and also produced by macrophages and monocytes. In contrast, TNF-α has not been detected in HAEM and it has even been proposed that its presence may be used as a laboratory test to distinguish drug-induced lesions from HAEM (Aurelian *et al*, 2003). Much of the tissue damage in drug-induced lesions appears to be due to apoptosis and, because of the paucity of the inflammatory reaction; attention has recently been focused on soluble factors and cytokines. Locally produced TNF-α may be important since it has been shown to mediate keratinocyte apoptosis (Paul *et al*, 1996) and it is possible this mechanism plays a role in milder forms of drug-induced EM.

However, particularly in TEN and SJS, there is some evidence for a Fas–FasL interaction. FasL mediates apoptotic cell death by binding to Fas on cells and inducing the formation of caspases. Fas is present on keratinocytes (Sayama *et al*, 1994) and FasL is found on activated T cells and NK cells (Iwai *et al*, 1994) and thus binding of keratinocytes to T cells or NK cells can induce apoptosis. One report suggests that keratinocytes in TEN may express FasL, which could potentially induce cell death in a neighbouring keratinocyte (Viard *et al*, 1998) but it is not clear whether such a mechanism is generally operative. There is also evidence that soluble FasL (sFasL) produced by peripheral blood mononuclear cells may be important, since high levels of sFasL are present in the peripheral blood of patients with SJS and TEN, and sera from these patients are able to induce marked keratinocyte apoptosis *in vitro* (Abe *et al*, 2003). It has thus been proposed that sFasL levels may be an early marker for these two diseases.

In addition to soluble factors, there is some evidence that keratinocyte cell death may be mediated directly by cytotoxic T cells since lymphocytes isolated from the blister fluid of a patient with TEN were cytotoxic towards

autologous cells only in the presence of the precipitating drug (Nassif *et al*, 2002). The apoptotic mechanism appeared to be mediated by perforin/granzyme.

Clinical features

Erythema multiforme may present a wide spectrum of severity, from mild limited disease to a severe, widespread and life-threatening illness (Ayangco and Rogers, 2003). Skin lesions are usually symmetrical and consist of macules or erythematous papules, which develop into classical target or iris lesions. Occasionally bullae may be seen.

Skin lesions are often accompanied by ulceration of mucous membranes–particularly the oral cavity. Head and neck manifestations were present in 4 of 79 patients (5%) with EM and 26 of 28 patients (93%) with SJS in one series (Stewart *et al*, 1994). In SJS, mucosal involvement of the lip (93%), conjunctiva (82%), oral cavity (79%) and nose (36%) were most common.

Most patients with EM (70%) of either minor or major forms have oral lesions (Figure 3). Oral involvement may precede lesions on other stratified squamous epithelia, or may arise in isolation. It typically presents with;

- lesions that progress through diffuse and widespread macules to blisters and ulceration;
- lips that become swollen and cracked, bleeding and crusted;
- intraoral lesions typically on the non-keratinised mucosae and most pronounced in the anterior parts of the mouth.

Recurrences are seen in about 25%; the periodicity can vary from weeks to years; usually attacks last for 10–20 days once or twice a year and usually resolve after about six episodes (range: 2–24) within a mean period of 10 years (range: 2–36 years).

Skin lesions

Skin lesions have been classified as 'typical targets', 'raised atypical targets', 'flat atypical targets' and 'erythematous macules with or without blisters' (Bastuji-Garin *et al*, 1993) and these have been used to sub-classify EM (see below). 'Typical targets' are defined as 'individual lesions less than 3 cm diameter with a regular round shape, a well-defined border, and two concentric palpable, oedematous rings, paler than the centre disc'. These lesions are most common in EM minor and milder forms of EM major in a symmetrical distribution on the extensor surfaces of the extremities.

'Raised atypical targets' appear similar to target lesions and are palpable erythematous lesions with a rounded shape but poorly defined borders and a dark central area, which may erode and become necrotic. These lesions are most common in severe EM major or in SJS.

'Flat atypical targets' – as their name suggests are not palpable and they form ill-defined erythematous areas with a tendency to central blister formation. These lesions are most common in SJS.

'Erythematous or purpuric macules with or without blister formation' are of variable size and may become confluent. These lesions are most common in SJS and TEN.

Other mucosae

Eye involvement may cause lacrimation and photophobia.

Genital lesions are painful and may result in urinary retention.

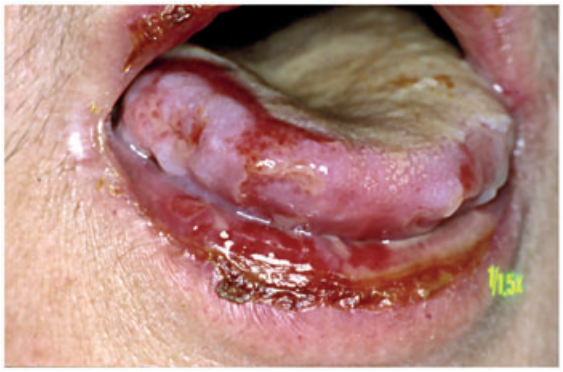

Figure 3 Clinical appearance of EM

Clinical variants

Erythema multiforme has been subdivided into different clinical types based on the severity of the presentation. Originally the disease was classified as either EM minor or major (Huff *et al*, 1983) and distinction between the two depended principally on the extent of mucosal involvement. SJS was considered to be a severe variant of EM major. Then TEN was added to the disease spectrum (Lyell, 1993) and confusion arose over the diagnostic criteria for the different subtypes.

A consensus paper (Bastuji-Garin *et al*, 1993) has defined the more severe clinical variants based on morphology of the skin lesions, their extent and distribution and the extent of epidermal detachment, as bullous EM, SJS, SJS/TEN overlap, TEN with spots with or without blisters and TEN without spots – but it remains to be determined whether each represents distinct aetiopathological entities.

Erythema multiforme minor

Erythema multiforme minor is considered the mildest form of EM and is characterised by skin lesions, which are usually symmetrically distributed on the extensor surfaces of the arms and legs. Rashes are various but typically are 'iris' or 'target' lesions or bullae on extremities. The lesions may be itchy and accompanied by systemic symptoms such as fever and malaise (Ayangco and Rogers, 2003).

By definition, mucous membrane involvement is limited to only one site and usually it is the oral mucosa alone that is affected (Huff *et al*, 1983). Occasionally lesions may occur orally prior to their appearance on the skin or sometimes only the oral cavity is affected. Intraoral lesions occur predominantly on the non-keratinised mucosae and are most pronounced in the

anterior parts of the mouth. The lips are also commonly affected and are swollen and cracked, bleeding and crusted. Typically oral lesions progress through diffuse widespread macules to blisters and ulceration although only ulceration may be seen at presentation. In these cases, diagnosis may be difficult.

Although considered by some to be a benign self-limiting disease, some cases of recurrent EM minor may be very severe, particularly if accompanied by widespread oral ulceration (Farthing *et al*, 1995). In these cases the lips tend to be spared.

Erythema multiforme major

Erythema multiforme major is characterised by involvement of multiple mucous membranes (Huff *et al*, 1983). Generally EM major is a more severe form of the disease than EM minor and, in addition to the oral cavity, the genital, ocular, laryngeal and oesophageal mucosae may be affected. The skin lesions however, may resemble those of EM minor with a characteristic symmetrical distribution on the extremities. Nevertheless, the skin lesions may be atypical and characterised by bullae and affect a greater area. If 10% or less of the body surface is affected then the disease fulfils the criteria for bullous EM (Bastuji-Garin *et al*, 1993). HSV-induced EM major is characterised by mucosal erosions plus typical or raised atypical targets and epidermal detachment involving less than 10% of the body surface and usually located on the extremities and/or the face.

Although EM minor and EM major have been described, the value of distinguishing clinically between them has been called into question. One large study of patients with recurrent EM showed that, in 90% of patients only one mucosal surface was affected in the primary attack but in subsequent episodes this proportion dropped to 61%, and in the other patients there were multiple mucosal sites affected (Farthing *et al*, 1995). This indicates that patients who initially presented with apparent EM minor may present with EM major in subsequent attacks and that the minor and major forms of the disease are closely linked.

Stevens-Johnson syndrome

Stevens-Johnson syndrome causes widespread lesions affecting the mouth, eyes, pharynx, larynx, oesophagus, skin and genitals. It almost invariably involves the oral mucosa. A prodrome occurs in about 30% of cases, may begin within 1–3 weeks of starting a new drug and it lasts 1–2 weeks before the onset of the mucocutaneous manifestations, and presents with flu-like symptoms, sore throat, headache, arthralgias, myalgias, fever, bullous and other rashes, pneumonia, nephritis or myocarditis. Ocular changes, which resemble those of mucous membrane pemphigoid – dry eyes and symblepharon – may result. Balanitis, urethritis and vulval ulcers may occur and it, may be followed by sicca syndrome, or even Sjogren's syndrome (de Roux Serratrice *et al*, 2001).

Drug-induced SJS is characterised by mucosal erosions plus widespread distribution of flat atypical targets or purpuric macules and epithelial detachment involving less than 10% of body surface on the trunk, face and extremities.

Diagnosis

A diagnosis of EM can be difficult to readily establish, and there can be a need to differentiate from viral stomatitides, pemphigus, TEN and the sub-epithelial immune blistering disorders (pemphigoid and others) (Ayangco and Rogers, 2003).

There are no specific diagnostic tests for EM and the diagnosis is mainly clinical supported if necessary by biopsy. Biopsy of perilesional tissue, with histological and immunostaining examination are essential if a specific diagnosis is required. Biopsy shows intraepithelial oedema and spongiosis early on, with satellite cell necrosis (individual eosinophilic necrotic keratinocytes surrounded by lymphocytes), vacuolar degeneration of the junctional zone and severe papillary oedema with sub- or intra-epithelial vesiculation, and intense lymphocytic infiltration and immune deposits of fibrin and C3 at the basement membrane zone. There may be a perivascular lymphocytic infiltrate (CD4+ more than CD8+ T lymphocytes) with a few neutrophils and occasional eosinophils, and perivascular IgM, C3 and fibrin deposits. However, pathology can be variable and immunostaining is not specific for EM.

In EM major a complete blood count, urea and electrolytes, erythrocyte sedimentation rate (ESR), liver function tests, and cultures from blood, sputum and erosive areas should be taken. To identify an aetiological agent it may be helpful to undertake serology for HSV or *M. pneumoniae*, or other micro-organisms.

Management

Spontaneous healing of EM can be slow – up to 2–3 weeks in minor and up to 6 weeks in major EM. Treatment is thus indicated but controversial (Katz *et al*, 1999).

No specific treatment is available but supportive care is important; a liquid diet and intravenous fluid therapy may be necessary. Early ophthalmological and dermatological consultation is needed for diagnosis and management. Precipitating factors, when identified, should be treated.

Antimicrobials may be indicated, aciclovir in HAEM or tetracycline in EM related to *M. pneumoniae*. A 5-day course of aciclovir at the first sign of lesions, or 400 mg qds for 6 months is useful for prophylaxis in HAEM. Continuous therapy of valacyclovir, 500 mg twice a day, has also been reported to be effective.

The use of corticosteroids is controversial. Minor EM may respond to topical corticosteroids, though systemic corticosteroids may be required and patients with major EM or SJS may need to be admitted for hospital care and should be treated with systemic corticosteroids (prednisolone 0.5–1.0 mg kg^{-1} day^{-1} tapered over 7–10 days) and/or azathioprine or other immunomodulatory drugs. Fifty per cent of SJS patients in one series

required supplemental hydration or alimentation because of the severity of the oral cavity involvement (Stewart *et al*, 1994).

Other treatments used may include cyclophosphamide, dapsone, ciclosporin, azathioprine, levamisole and thalidomide (Schofield *et al*, 1993; Conejo-Mir *et al*, 2003). Plasmapheresis possibly has a place in the management of severe disease.

Oral antacids may be helpful for management of discrete oral ulcers. Electrolytes and nutritional support should be started as soon as possible. Oral hygiene should be improved with 0.2% aqueous chlorhexidine mouthbaths.

Toxic epidermal necrolysis (Lyell's disease)

Toxic epidermal necrolysis is a rare clinicopathologic entity, with a high mortality, characterised by extensive detachment of full thickness epithelium usually induced by drugs. The distinction of TEN from EM is unclear, but most cases are drug-induced and the lesions are extremely widespread.

Drugs appear to trigger what appears to be an immunologically related reaction with sub- and intra-epithelial vesiculation.

Recently an increased number of cases in HIV/AIDS patients have been recorded.

Clinical features

Toxic epidermal necrolysis presents with a cough, sore throat, burning eyes, malaise and low fever, followed after about 1–2 days by skin and mucous membrane lesions. The entire skin surface and oral mucosa may be involved, with up to 100% sloughing.

Oral mucosae are involved in almost all cases. Gingival lesions are common and clinically are inflamed, with blister formation leading to painful widespread erosions.

Table 1 Drug-related EM (SJS and TEN)

Drugs most commonly implicated	*Drugs occasionally implicated*
Allopurinol	Busulphan
Barbiturates	Cephalosporins
Carbamazepine	Chlorpropamide
NSAIDs	Clindamycin
Penicillin	Codeine
Phenytoin	Ethambutol
Sulphonamides	Furosemide
	Gold
	Minoxidil
	Oestrogens
	Phenothiazines
	Phenylbutazone
	Progestogens
	Protease inhibitors
	Rifampicin
	Tetracyclines
	Tolbutamide
	Vancomycin
	Verapamil

Diagnosis of toxic epidermal necrolysis

Sheet-like loss of the epithelium and a positive Nikolsky sign are characteristic. Biopsy of perilesional tissue, with histological and immunostaining examination are essential to the diagnosis. Histopathologic examination is characteristic showing necrosis of the whole epithelium detached from the lamina propria.

Management of toxic epidermal necrolysis

Patients must be admitted to hospital as soon as possible to an intensive care unit for management.

Drug-related erythema multiforme

A wide range of drugs may give rise to EM (Table 1), and it may be impossible to clinically distinguish drug-induced EM from disease due to other causes (Roujeau, 1997; Ayangco and Rogers, 2003). Lesions typically affect the oral mucosa, the lips and bulbar conjunctivae. Initial bullae rupture to give rise to haemorrhagic pseudomembrane of the lips and widespread superficial oral ulceration. Other mucocutaneous surfaces less commonly affected include the nasopharyngeal, respiratory and genital mucosae.

Drug-related toxic epidermal necrolysis

Toxic epidermal necrolysis (Lyell syndrome) is clinically characterised by extensive mucocutaneous epidermolysis preceded by a macular or maculopapular exanthema and enanthema (Lyell, 1979; Rasmussen *et al*, 1989). Intraorally there is widespread painful blistering and ulceration of all mucosal mucosal surfaces. Toxic epidermolysis may be associated with antimicrobials (sulphonamides and thiacetazone), analgesics (phenazones). antiepileptics, allopurinol, chlormezanone, rifampicin, fluconazole and vancomycin (Ayangco and Rogers, 2003).

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