Dermatological Emergencies

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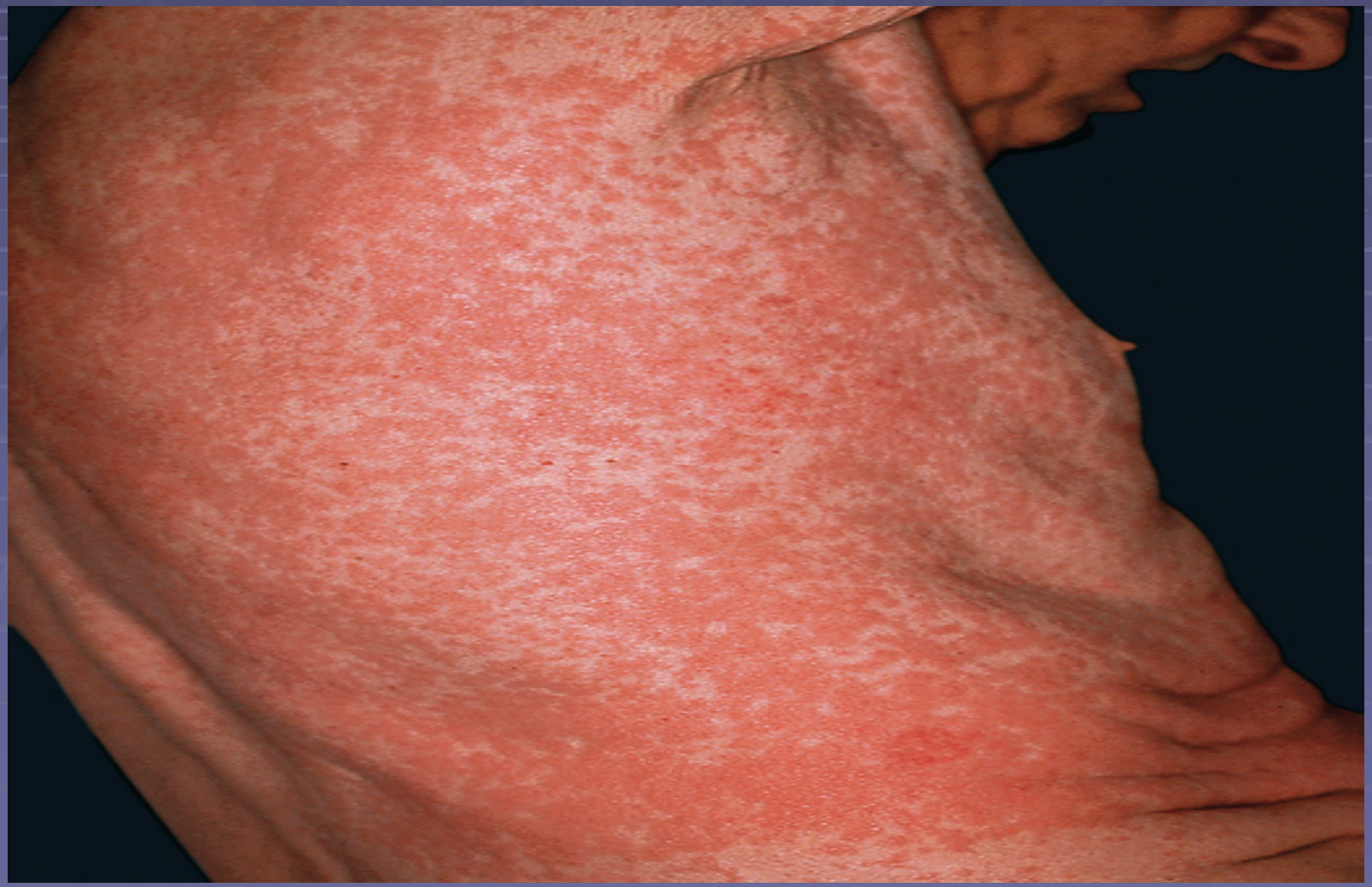
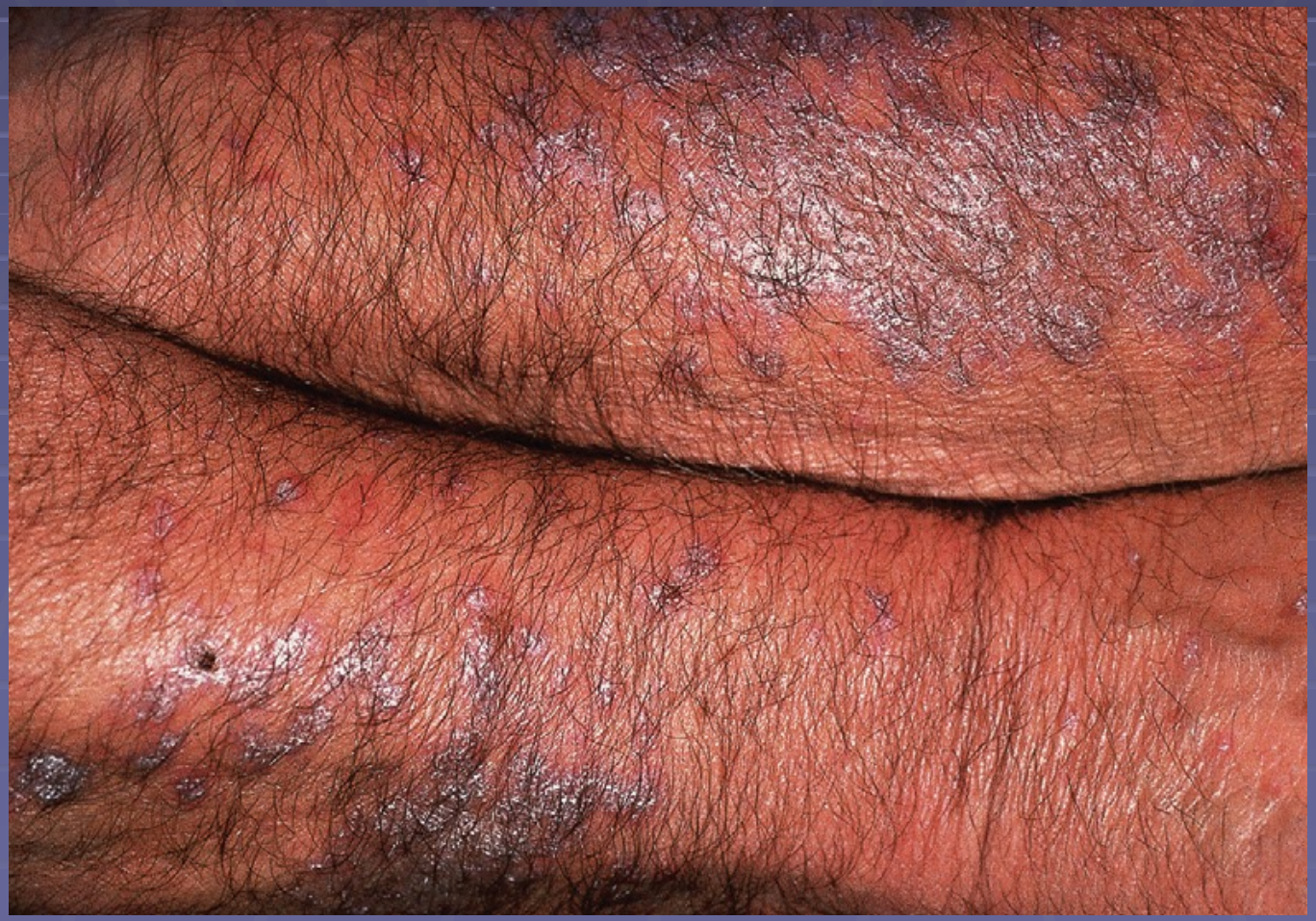
- Brainstorm
- Clinical case approach
- Pretest
- Review of topic
- Post test

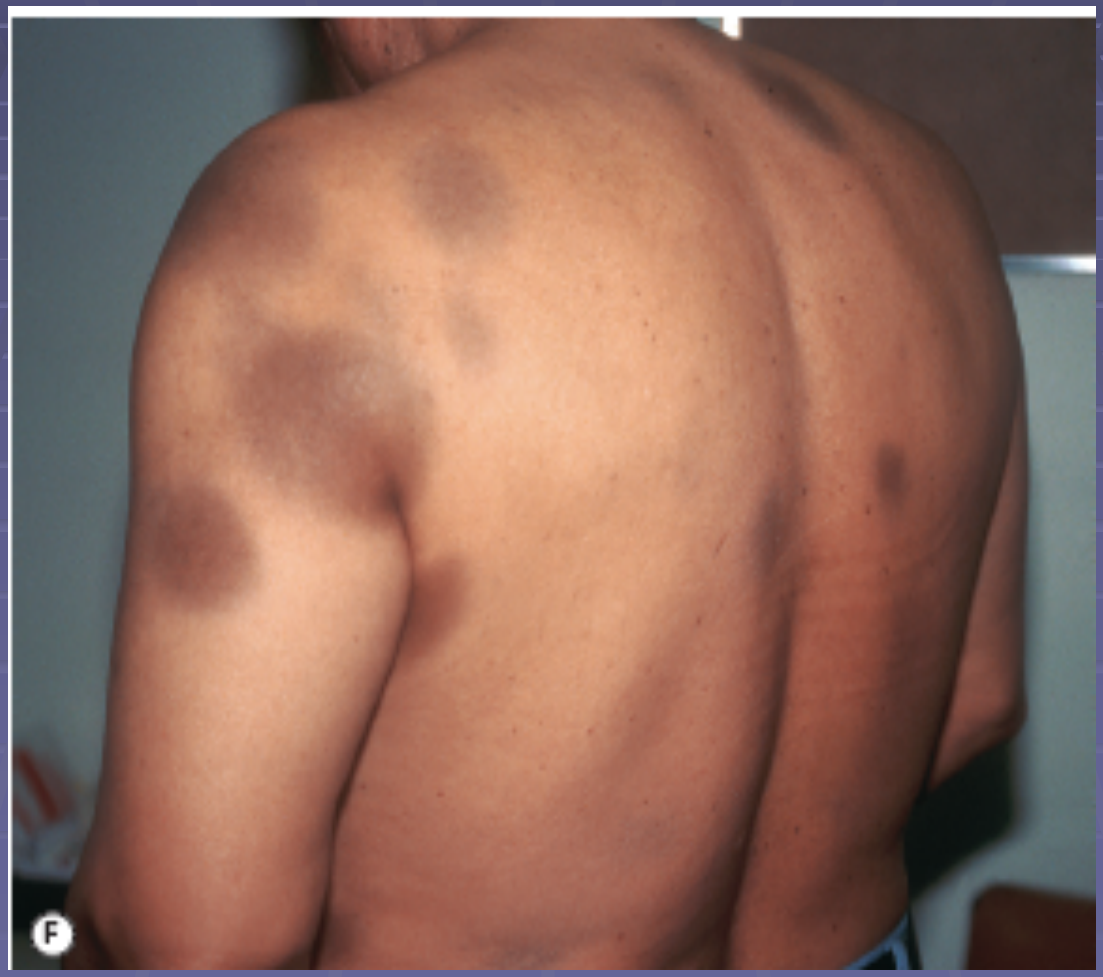
Exanthematous drug eruptions due to a cephalosporin



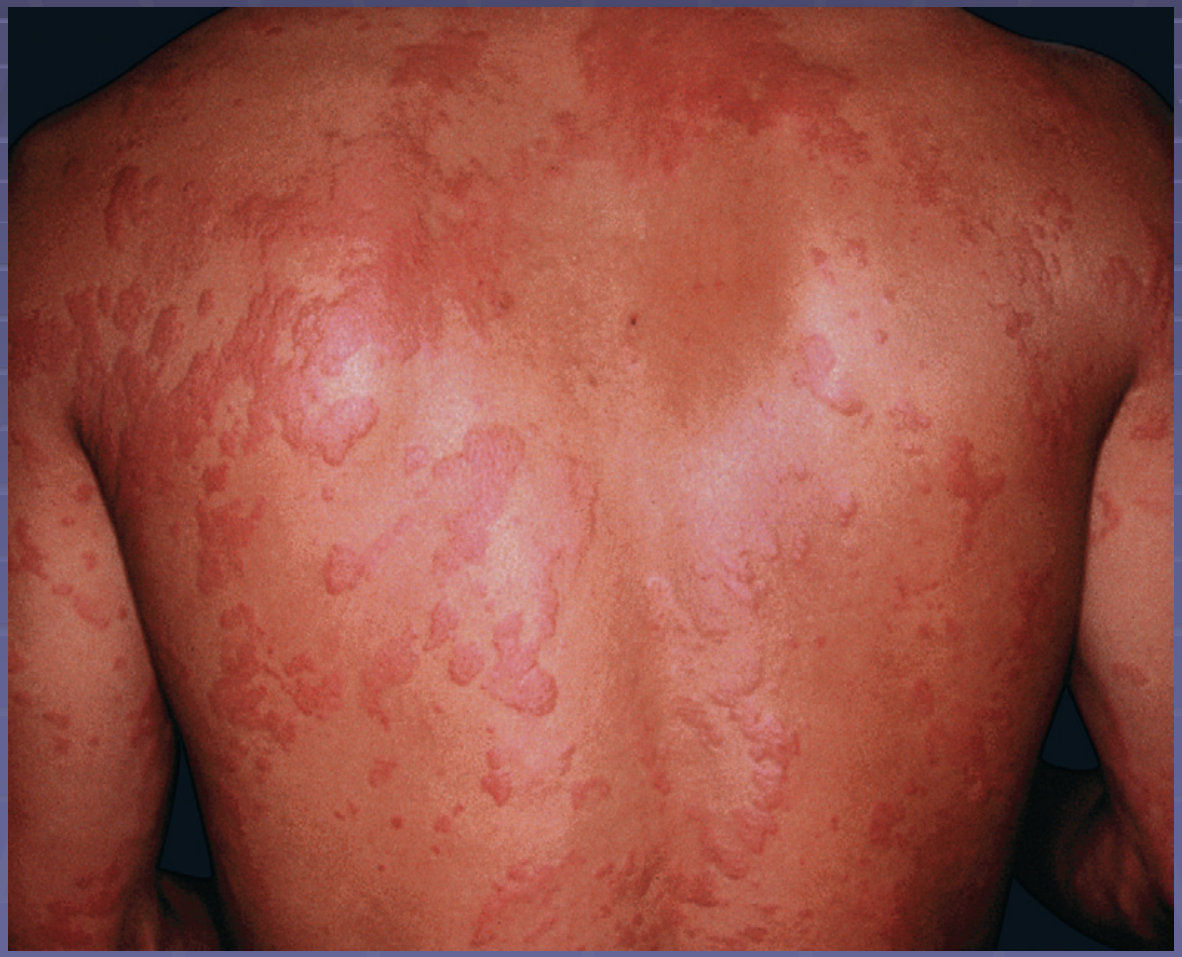
Photolichenoid drug eruption due to hydrochlorothiazide



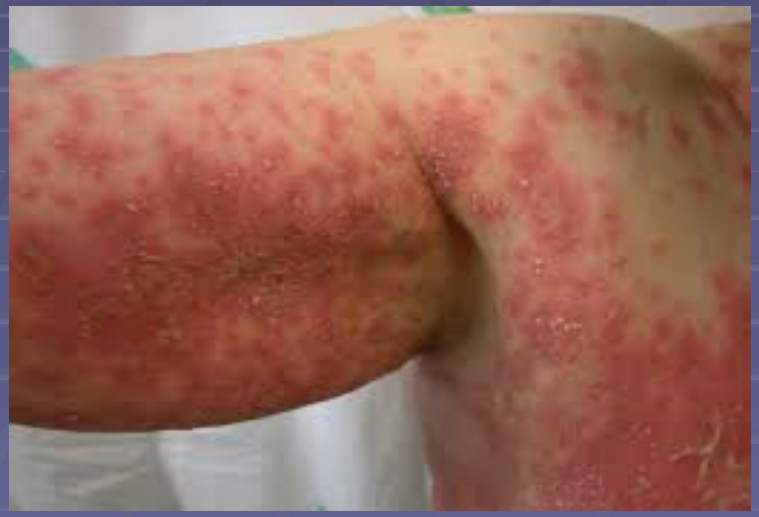
Fixed Drug reaction

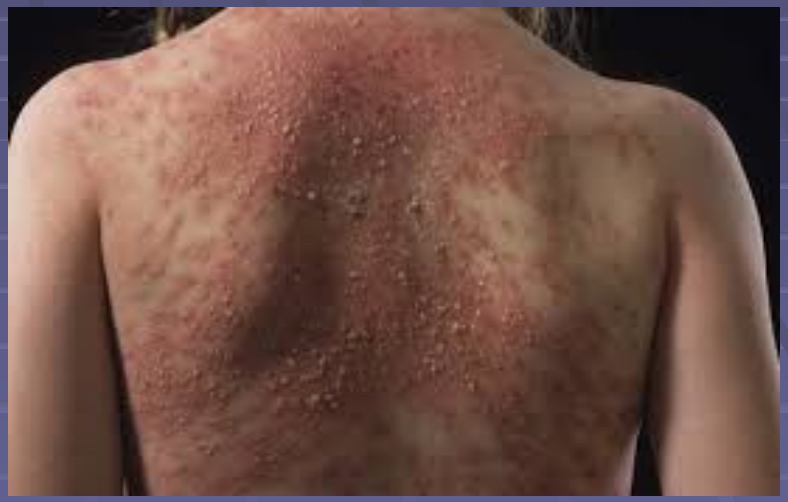


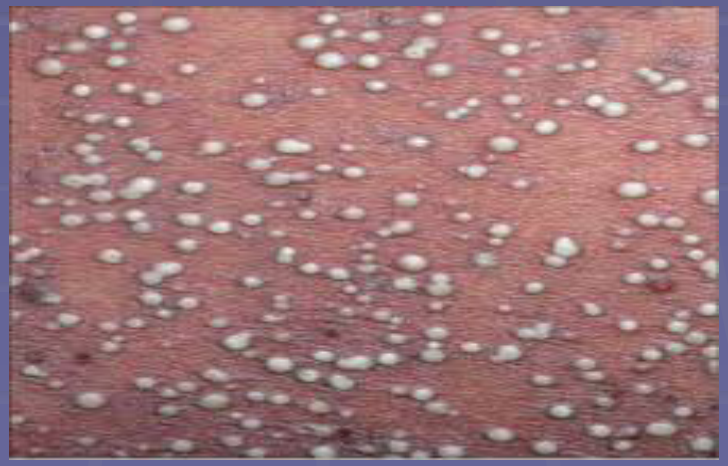
Urticaria secondary to penicillin



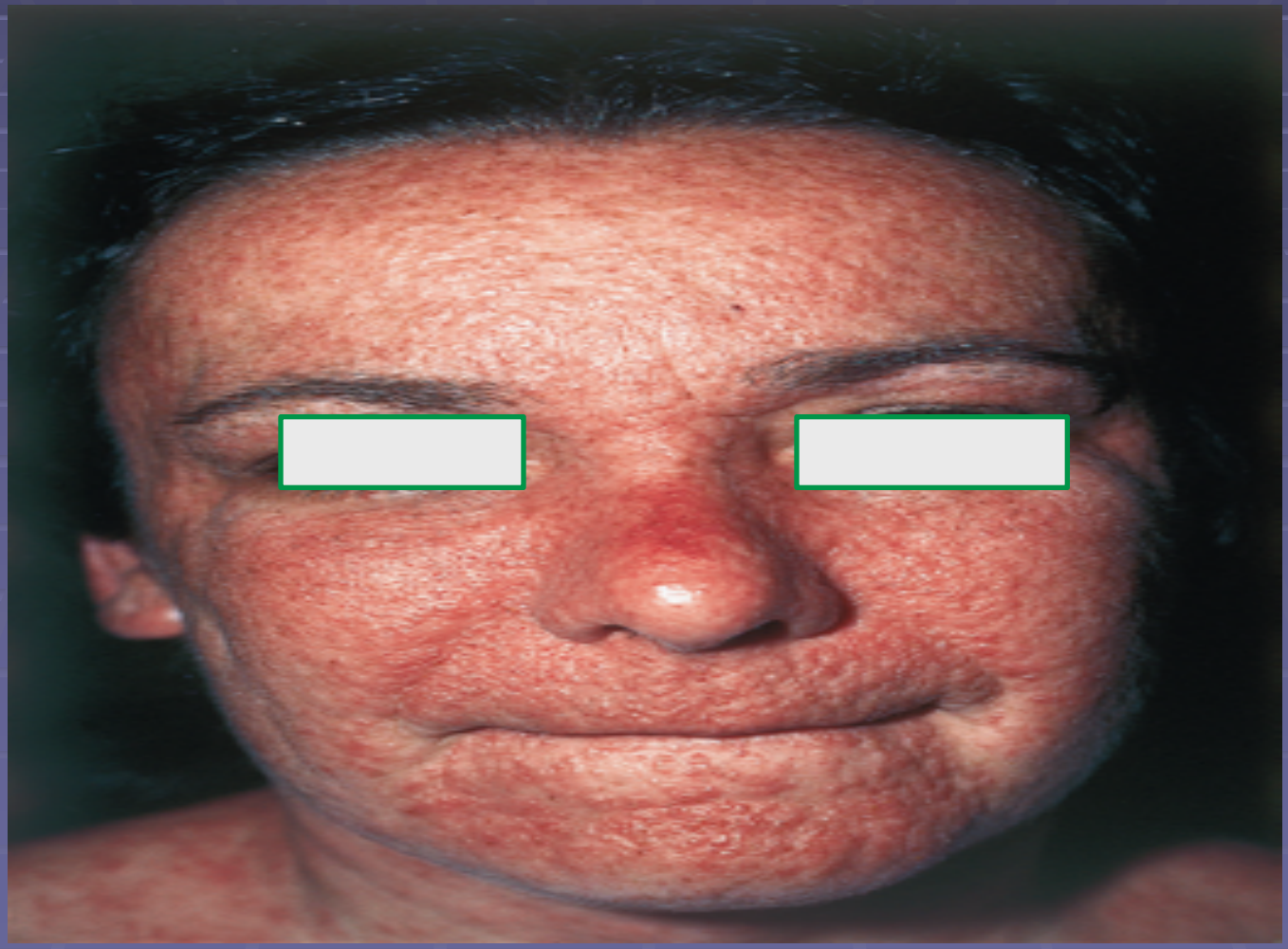
Acute generalized exanthematous pustulosis (AGEP)



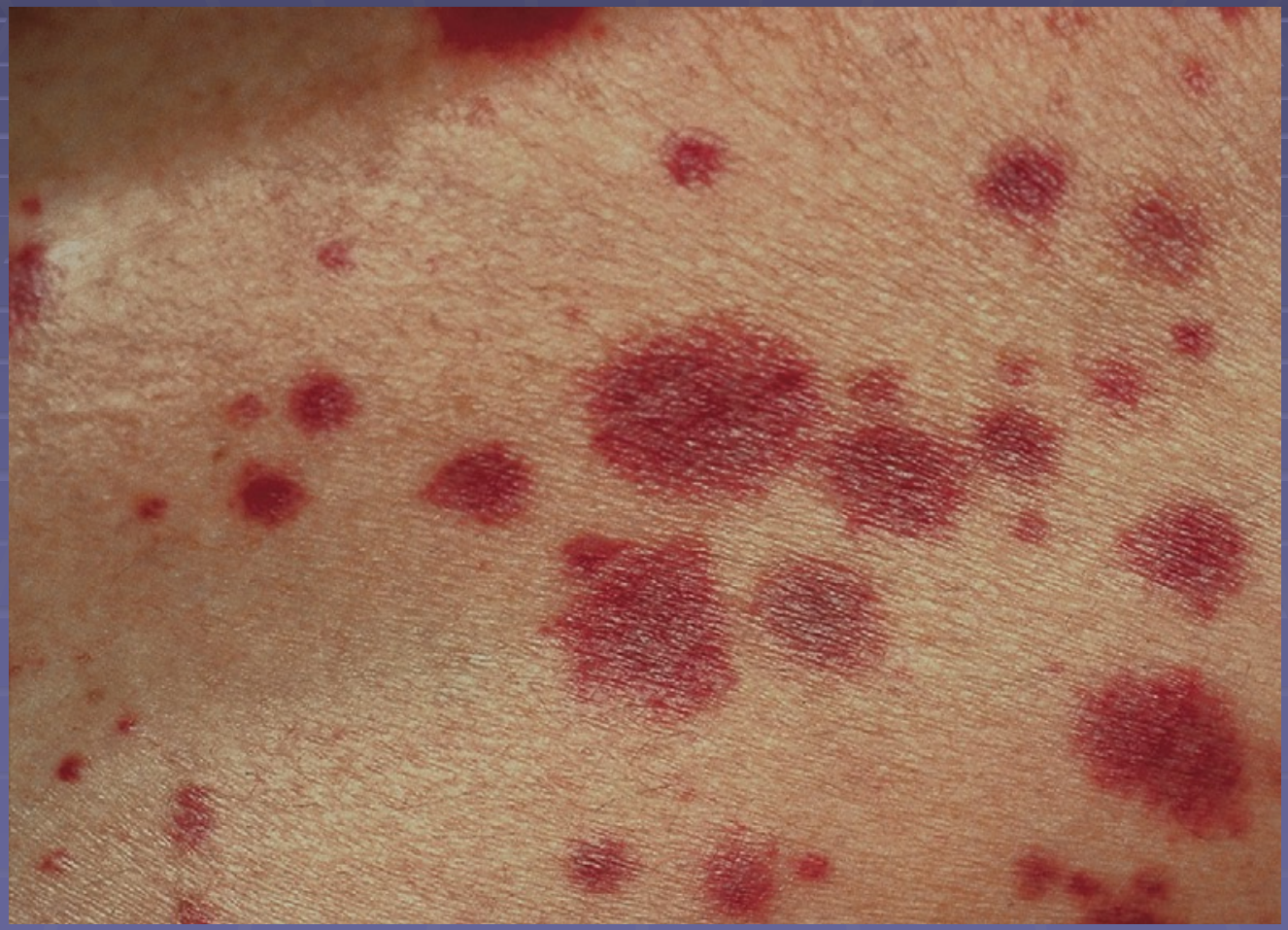




Drug reaction with eosinophilia and systemic symptoms (DRESS)/drug-induced hypersensitivity syndrome (DIHS) due to phenytoin



Cutaneous small vessel vasculitis due to Allopurinol



DRUGS RECEIVED BY MORE THAN 1000 PATIENTS WITH NO SKIN REACTIONS (RATES ESTIMATED TO BE ≤3 PER 1000)

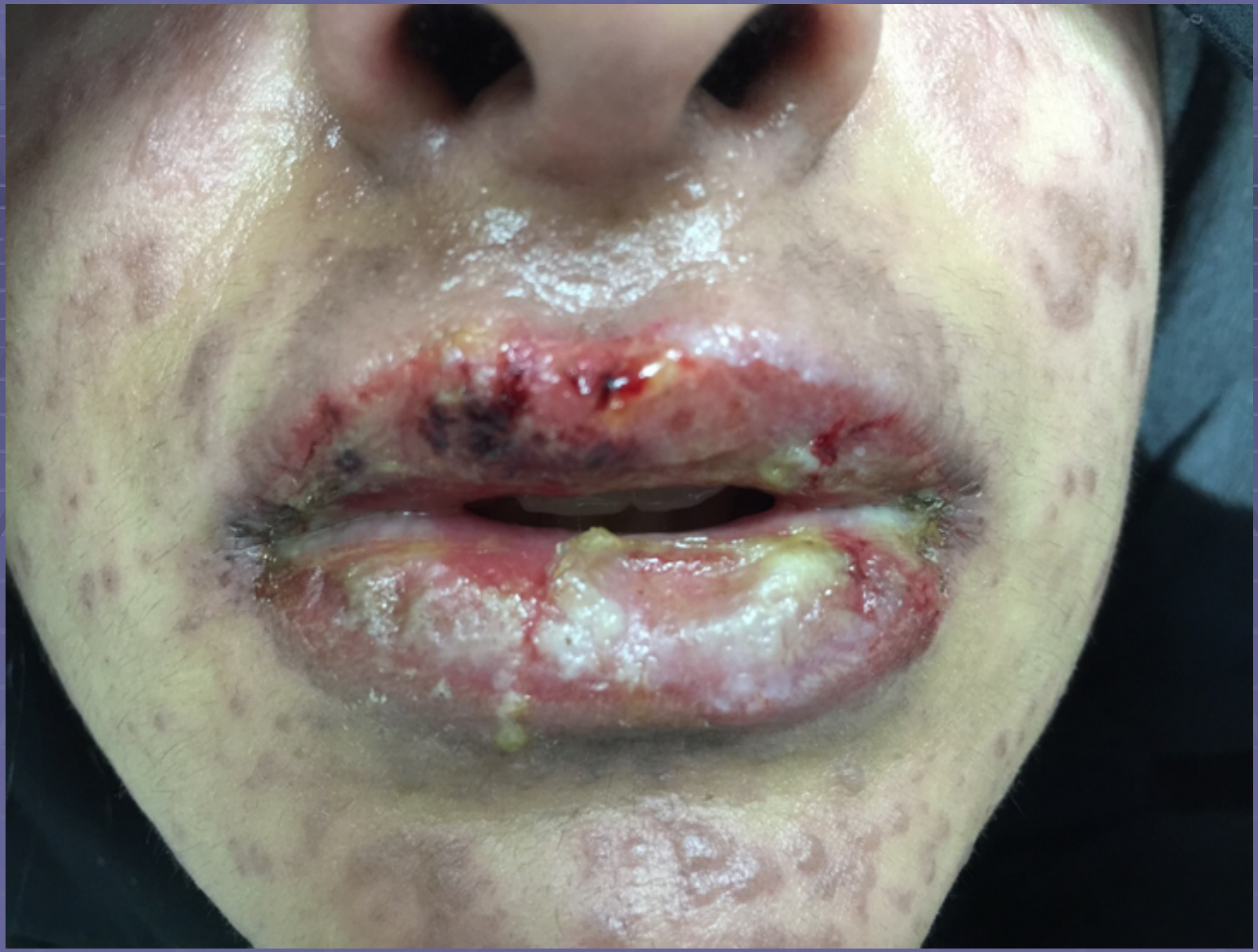
- Potassium chloride
- Milk of magnesia
- Digoxin
- Meperidine hydrochloride
- Dioctyl sodium sulfosuccinate
- Magnesium hydroxide
- Aluminum hydroxide
- Acetaminophen
- Multivitamins
- Bisacodyl
- Diphenhydramine hydrochloride
- Aspirin
- Aminophylline
- Prochlorperazine
- Ferrous sulfate
- Thiamine
- Prednisone
- Atropine
- Codeine
- Vitamin B complex and ascorbic acid
- Pentazocine
- Hydrochlorothiazide*
- Phosphate enema
- Castor oil
- Tetracycline*
- Morphine
- Regular insulin
- Warfarin
- Spironolactone

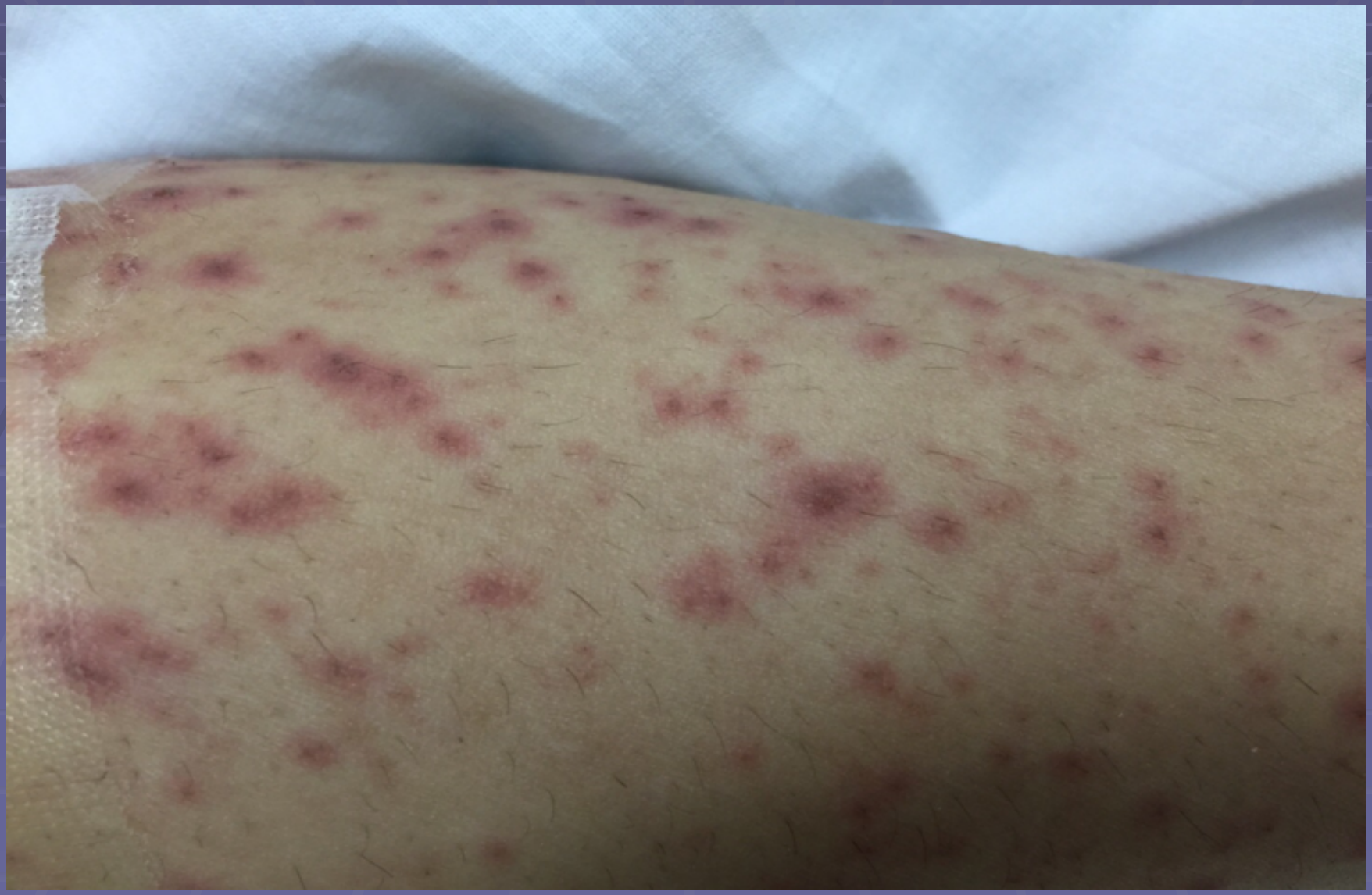
*Notably phototoxic reactions were not included.

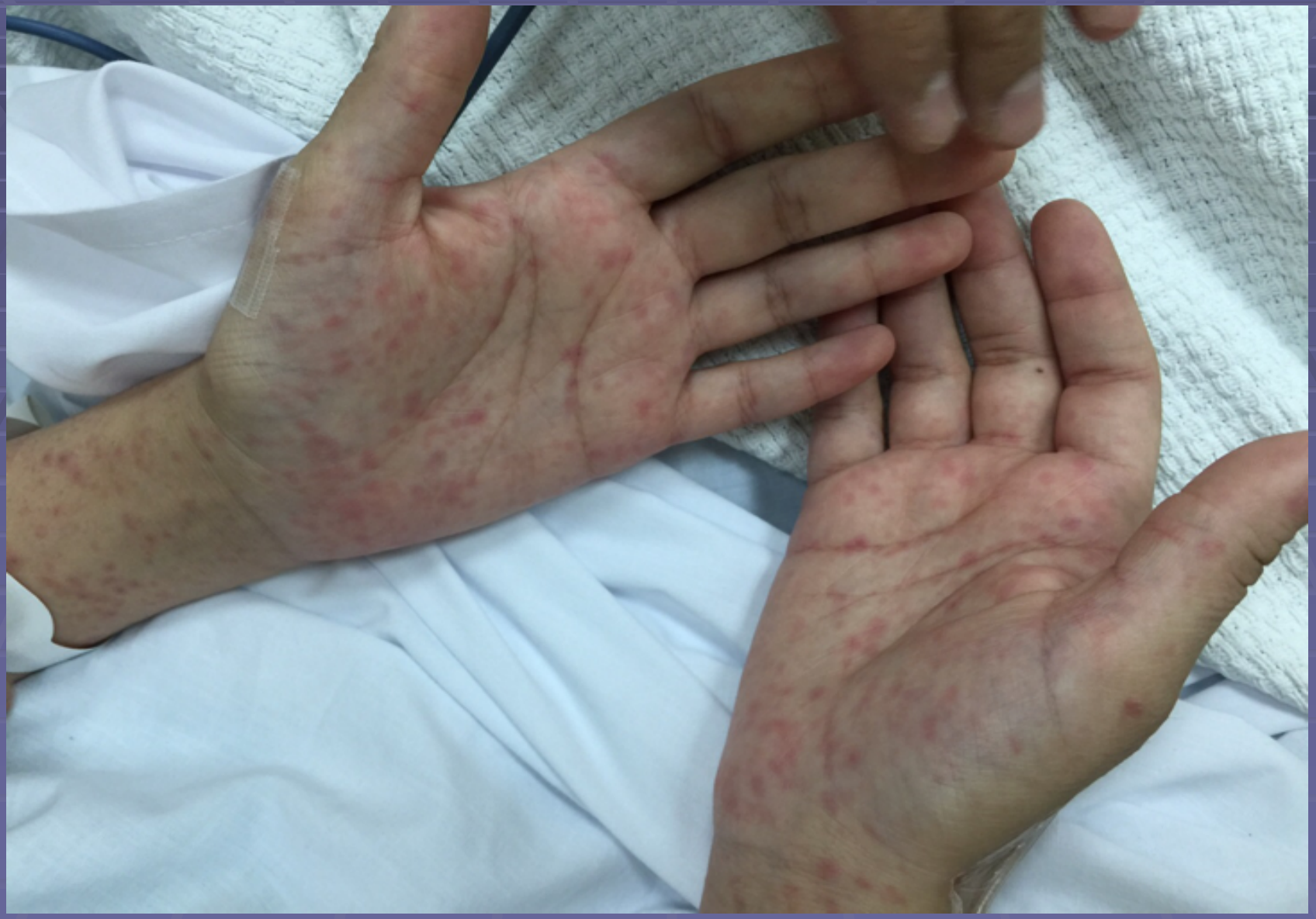
SKIN REACTIONS TO "DRUGS" RECEIVED BY AT LEAST 1000 PATIENTS	
Drugs	Reaction rate (per 1000 recipients)
Ampicillin	52
Penicillin G	16
Cephalosporins	13
Packed red blood cells	8.1
Heparin	7.7
Nitrazepam	6.3
Barbiturates	4.7
Chlordiazepoxide	4.2
Diazepam	3.8
Propoxyphene	3.4
Guaifenesin	2.9
Furosemide	2.6
Phytonadione	0.9
Flurazepam	0.5
Chloral hydrate	0.2

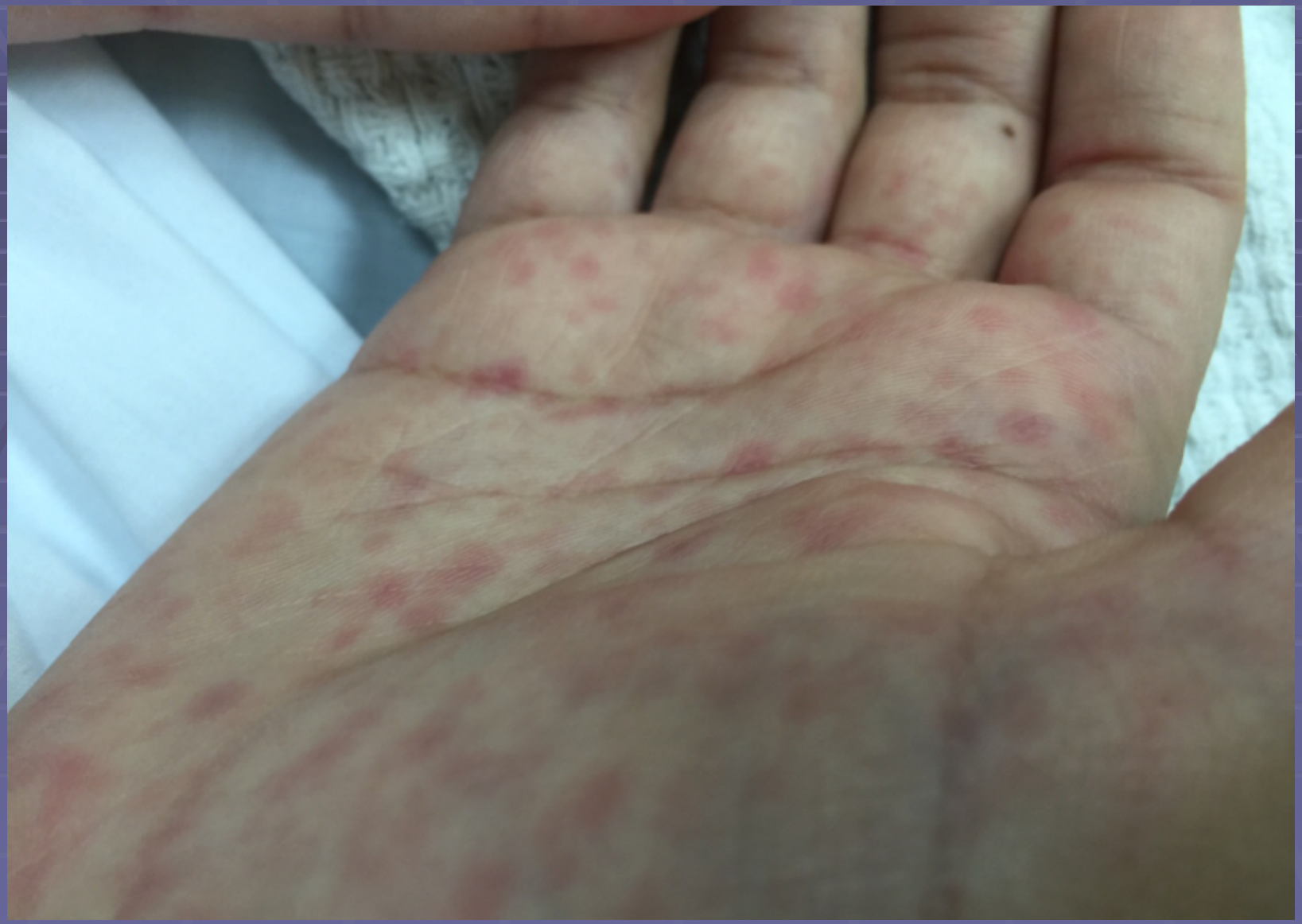
MECHANISMS OF CUTANEOUS DRUG-INDUCED REACTIONS	
Immunologic mechanism (unpredictable)	• IgE-dependent drug reactions • Cytotoxic drug-induced reactions • Immune complex-dependent drug reactions • Cell-mediated reactions
Non-immunologic mechanisms (sometimes predictable)	• Overdose • Pharmacologic side effects • Cumulative toxicity • Delayed toxicity • Drug–drug interactions • Alterations in metabolism • Exacerbation of disease
Idiosyncratic with a possible immunologic mechanism (unpredictable)	• DRESS (DIHS) • TEN/SJS • Drug reactions in the setting of HIV infection • Drug-induced lupus erythematosus

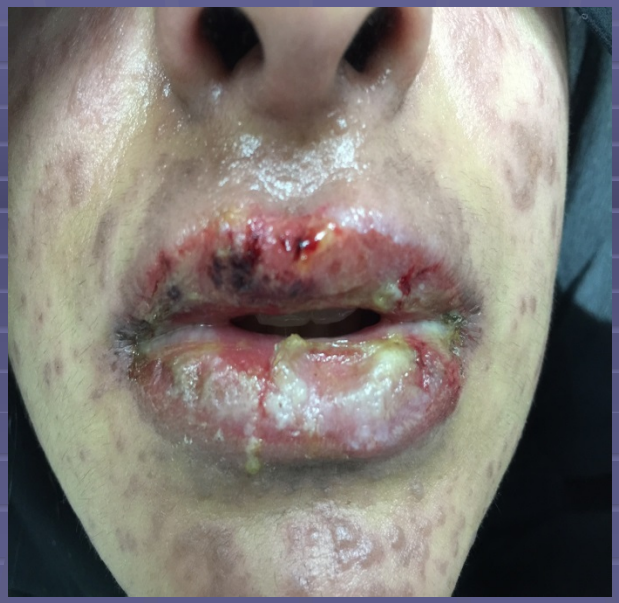
Clinical Real ER case

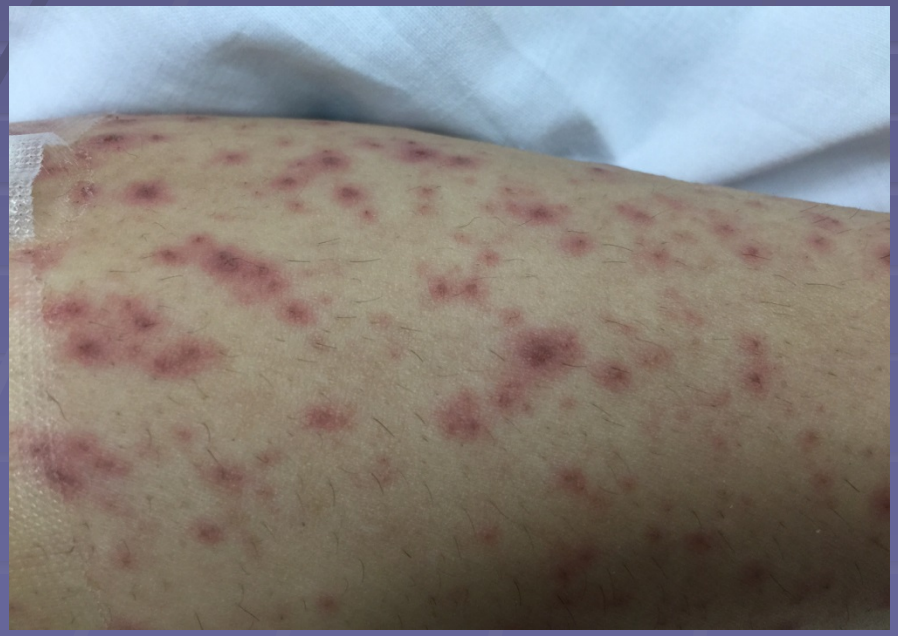


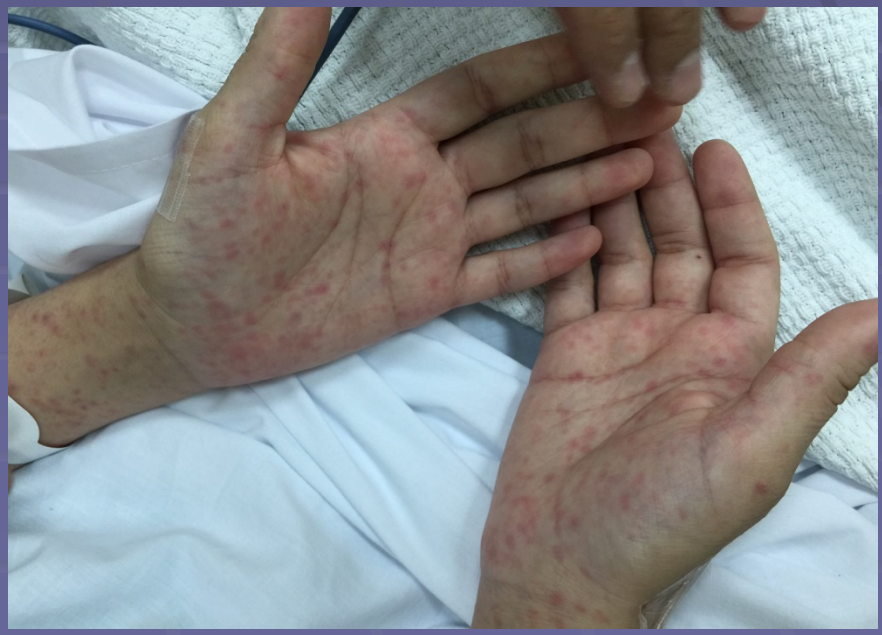












Approach

Hx

O/E

LAB

DDx

Mx

LOGICAL APPROACH TO DETERMINE THE CAUSE OF A DRUG ERUPTION

DRUG RESPONSIBILITY ASSESSMENT	
Clinical characteristics	• Type of primary lesion (e.g. urticaria, erythematous papule, pustule, purpuric papule, vesicle or bulla) • Distribution and number of lesions • Mucous membrane involvement, facial edema • Associated signs and symptoms: fever, pruritus, lymph node enlargement, visceral involvement
Chronological factors	• Document all drugs to which the patient has been exposed (including OTC and complementary) and the dates of administration • Date of eruption • Time interval between drug introduction (or reintroduction) and skin eruption • Response to removal of the suspected agent • Consider excipients (e.g. soybean oil) • Response to rechallenge*
Literature search	• Bibliographic research (e.g. Medline) • Drug Alert Registry or Medwatch • Data collected by pharmaceutical companies • In the case of more recently released medications, extrapolation based on the class of drug and in particular the first drug released in the class

*Often inadvertent.

CHARACTERISTICS OF MAJOR DRUG-INDUCED ERUPTIONS

Clinical presentation	Percentage that are drug-induced (%)	Time interval	Mortality (%)	Selected responsible drugs
Exanthematous eruption	Child: 10–20 Adult: 50–70	4–14 days	0	Aminopenicillins Sulfonamides Cephalosporins Anticonvulsants Allopurinol
Urticaria	<10	Minutes to hours	0	Penicillins Cephalosporins NSAIDs Monoclonal antibodies Contrast media†
Anaphylaxis	30	Minutes to hours	5	
Fixed drug eruption	100	First exposure: 1–2 weeks Re-exposure: <48 hours, usually within 24 hours	0	TMP-SMX NSAIDs Tetracydines Pseudoephedrine*
Acute generalized exanthematous pustulosis (AGEP)	70–90	< 4 days	1–2	β-Lactam antibiotics Macrolides Calcium channel blockers
Drug reaction with eosinophilia and systemic symptoms (DRESS)/ Drug-induced hypersensitivity syndrome (DIHS)	70–90	15–40 days	5–10	Anticonvulsants (aromatic) Sulfonamides Allopurinol Lamotrigine (especially in combination with valproate) Minocycline
Stevens-Johnson syndrome (SJS)	70–90	7–21 days	5	Sulfonamides Anticonvulsants (aromatic) Allopurinol NSAIDs Lamotrigine
Toxic epidermal necrolysis			30	

*Non-pigmenting.
†Often anaphylactoid reaction.

Review

- It has now become clear that Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are variants within a continuous spectrum of adverse drug reactions.

History

- EM was first described by the Austrian dermatologist Ferdinand von Hebra in 1860.
- In 1922, two US physicians, Stevens and Johnson, described an acute mucocutaneous syndrome in two young boys.
- Characterized by severe purulent conjunctivitis, severe stomatitis with extensive mucosal necrosis, and “EM-like” cutaneous lesions. It became known as Stevens–Johnson syndrome (SJS) and was recognized as a severe mucocutaneous disease with a prolonged course and occasional fatalities.
- SJS was later designated as EM major by Bernard Thomas in 1950. However, recent clinical investigations have made it clear that the term “EM major” should not be used to describe SJS as they are distinct disorders.

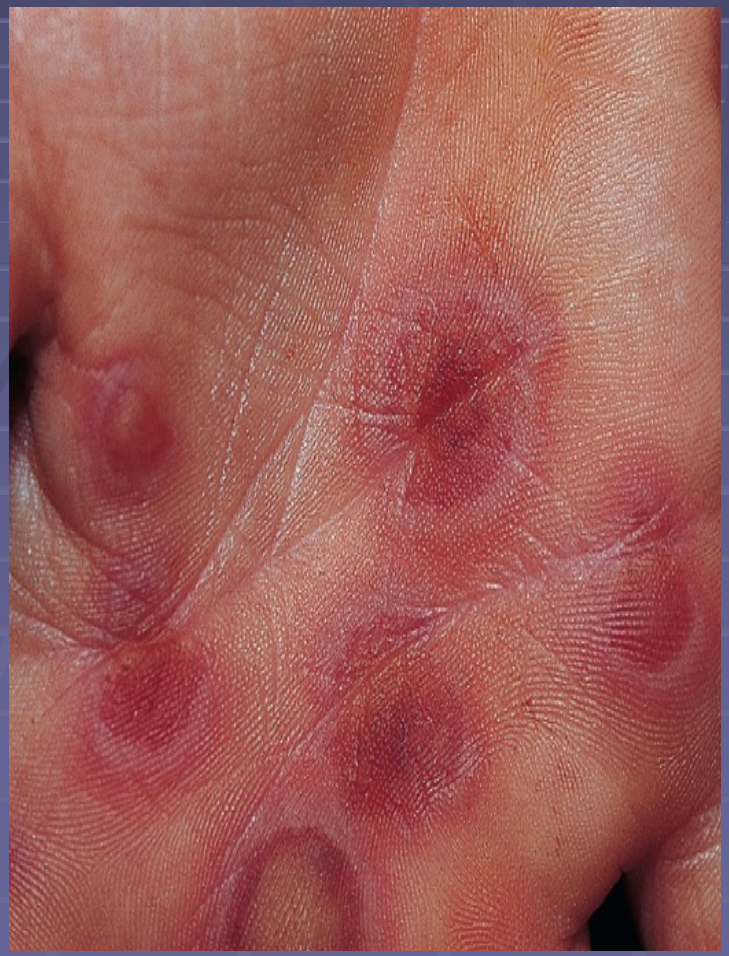
- In 1956, Alan Lyell described four pts with an eruption 'resembling scalding of the skin objectively and subjectively', which he called toxic epidermal necrolysis or TEN. 'Toxic' referred to toxemia – circulation of a toxin – which was though to be responsible for the constitutional symptoms and epidermal necrosis.
- Lyell coined the term 'necrolysis' by combining the key CF 'epidermolysis' with the characteristic histopathological feature 'necrosis'.
- He also described an attack on the mucous membranes as part of the syndrome, with very little inflammation in the dermis, a feature that was later referred to as 'dermal silence.

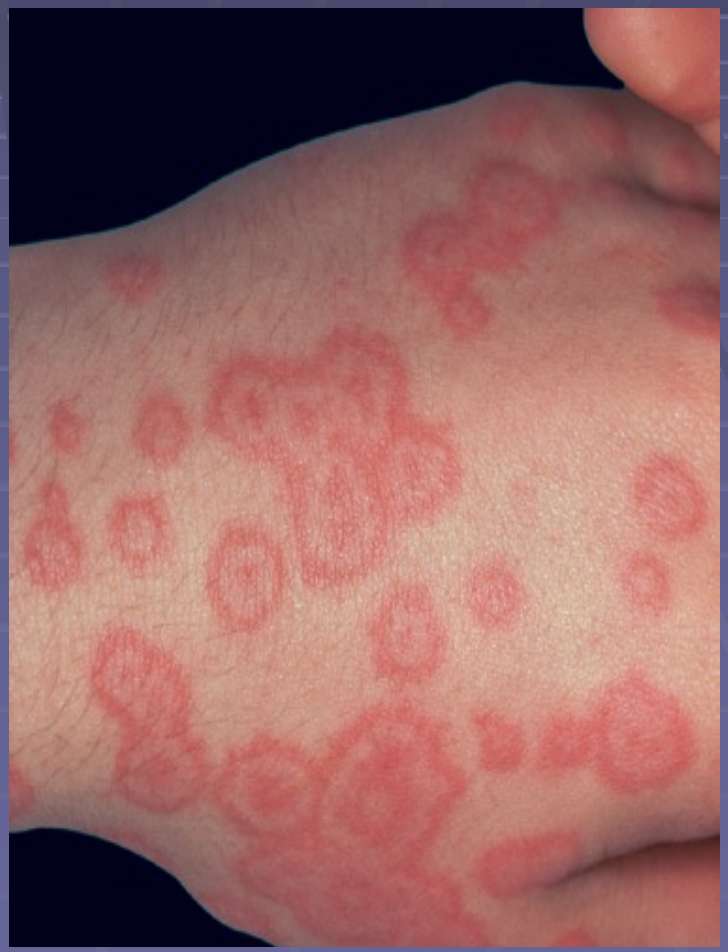
- Erythema multiform, SJS, and TEN were, at the time, considered to be part of a continuous spectrum of cutaneous reactions. It was clear, that HSV was the major cause of EM, and that this virus was not related to TEN.
- Recently, Assier et al. clarified this issue by providing clinical evidence that EM and SJS are clinically distinct disorders with different causes and prognosis.
- Increasingly, SJS, and TEN are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by the extent of skin detachment.

COMPARISON OF ERYTHEMA MULTIFORME (EM) MINOR, EM MAJOR AND STEVENS–JOHNSON SYNDROME (SJS)

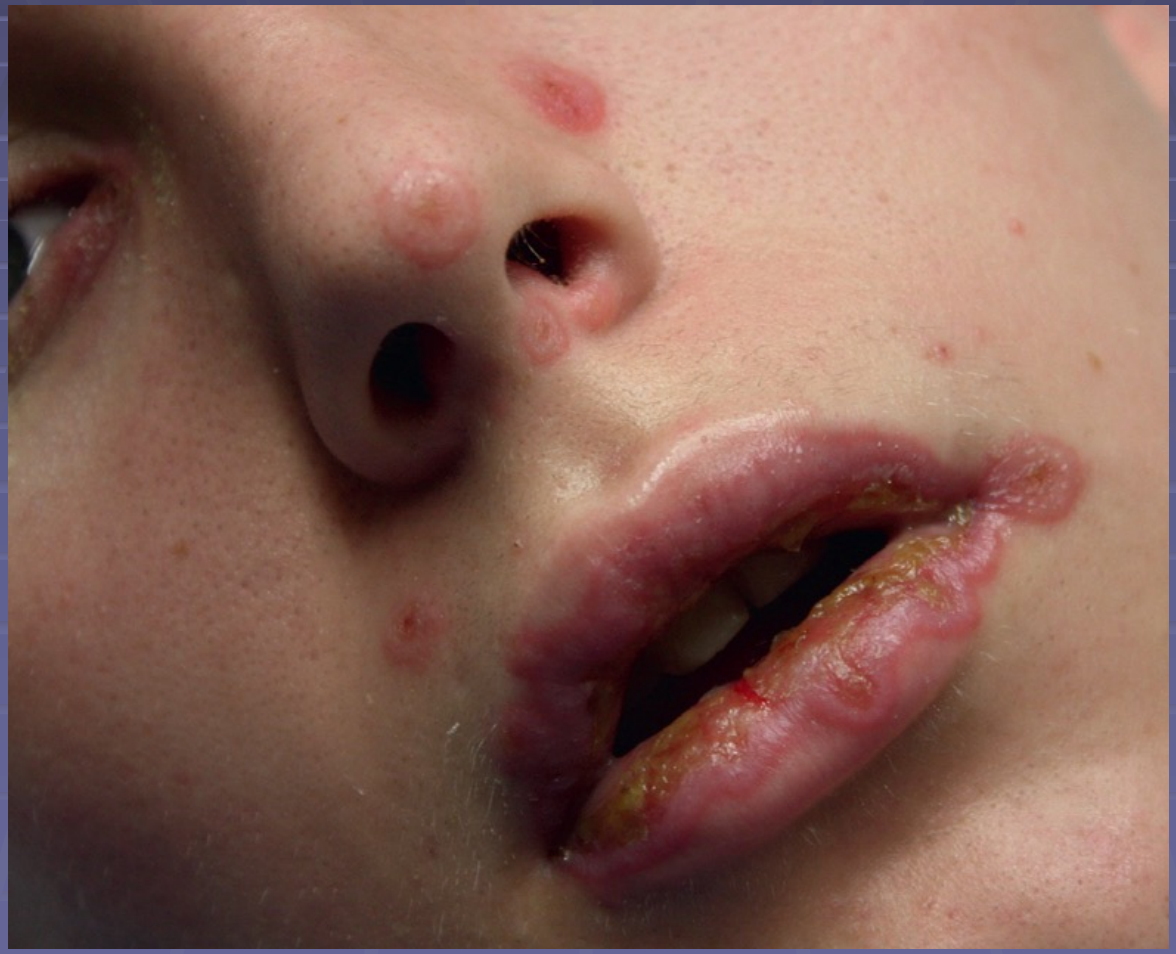
	Type of skin lesions	Distribution	Mucosal involvement	Systemic symptoms	Progression to TEN	Precipitating factors
EM minor	• Typical targets • ± *Papular* atypical targets	Extremities (especially elbows, knees, wrists, hands), face	Absent or mild	Absent	No	• Herpes simplex virus • Other infectious agents
EM major	• Typical targets • ± *Papular* atypical targets • Occasionally bullous lesions	Extremities, face	Severe	Present	No	• Herpes simplex virus • *Mycoplasma pneumoniae* • Other infectious agents • Rarely, drugs
SJS	• Dusky macules with or without epidermal detachment • *Macular* atypical targets • Bullous lesions (<10% BSA detachment)	Trunk, face	Severe	Present	Possible	• Drugs • Occasionally, *Mycoplasma pneumoniae* • Rarely, immunizations

EM



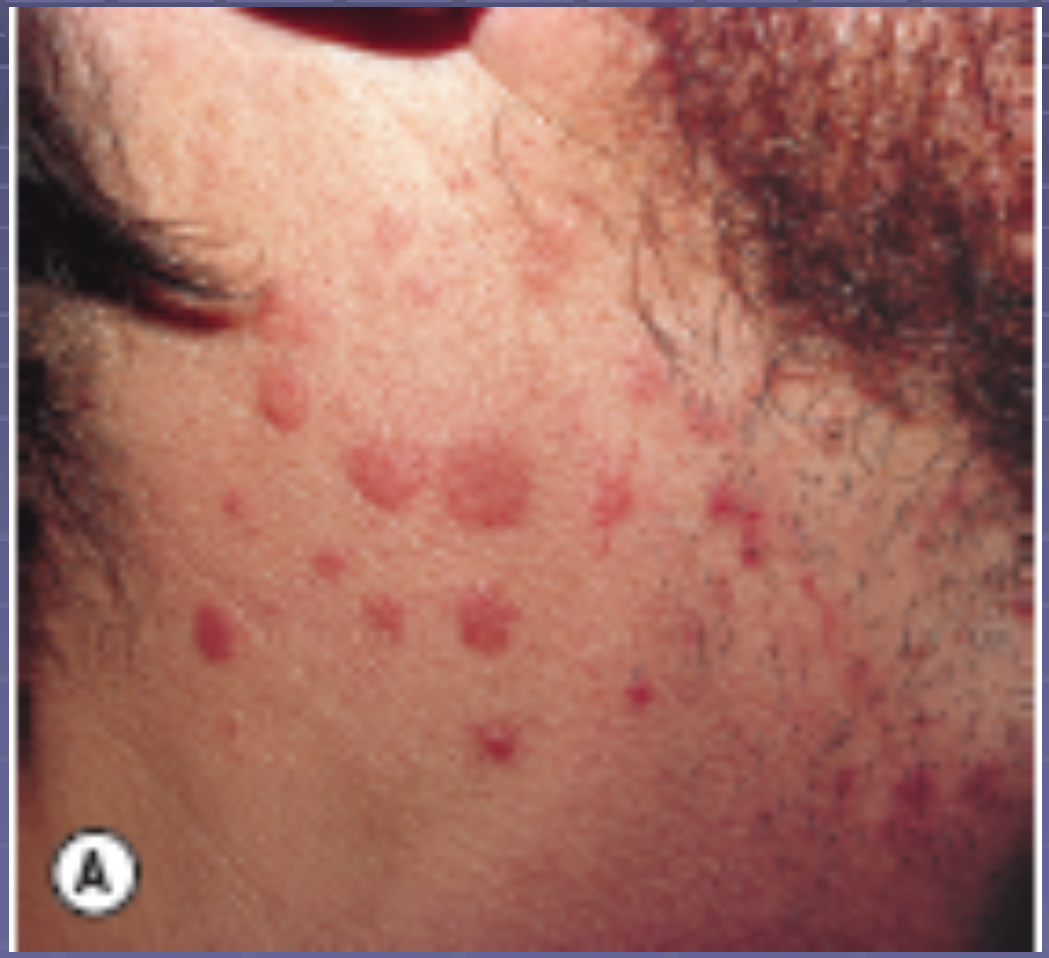


EM



PRECIPITATING FACTORS IN ERYTHEMA MULTIFORME		
Infections (approx. 90% of cases)	**Viral**	- **Herpes simplex virus (HSV-1, HSV-2)** - **Parapoxvirus (orf)** - **Vaccinia (smallpox vaccine)** - **Varicella zoster virus (chickenpox)** - **Adenovirus** - **Epstein-Barr virus** - **Cytomegalovirus** - **Hepatitis virus** - **Coxsackievirus** - **Parvovirus B19** - **Human immunodeficiency virus**
	Bacterial	- ***Mycoplasma pneumoniae**** - *Chlamydophila* (formerly *Chlamydia*) *psittaci* (ornithosis) - *Salmonella* - *Mycobacterium tuberculosis*
	Fungal	- *Histoplasma capsulatum* - Dermatophytes
Drugs (unusual)		Primarily: - **Nonsteroidal anti-inflammatory drugs** - **Sulfonamides** - **Anticonvulsants** - **Other antibiotics, e.g. aminopenicillins** - **Allopurinol**
Exposures (unusual)		- **Poison ivy**
Systemic disease (rare)		- **Inflammatory bowel disease** - **Lupus erythematosus†** (Rowell's syndrome) - **Behçet's disease†**

*Also precipitating factor for Stevens–Johnson syndrome and isolated oral mucositis.
†May be a pattern of cutaneous lesions in the disease rather than a precipitating factor.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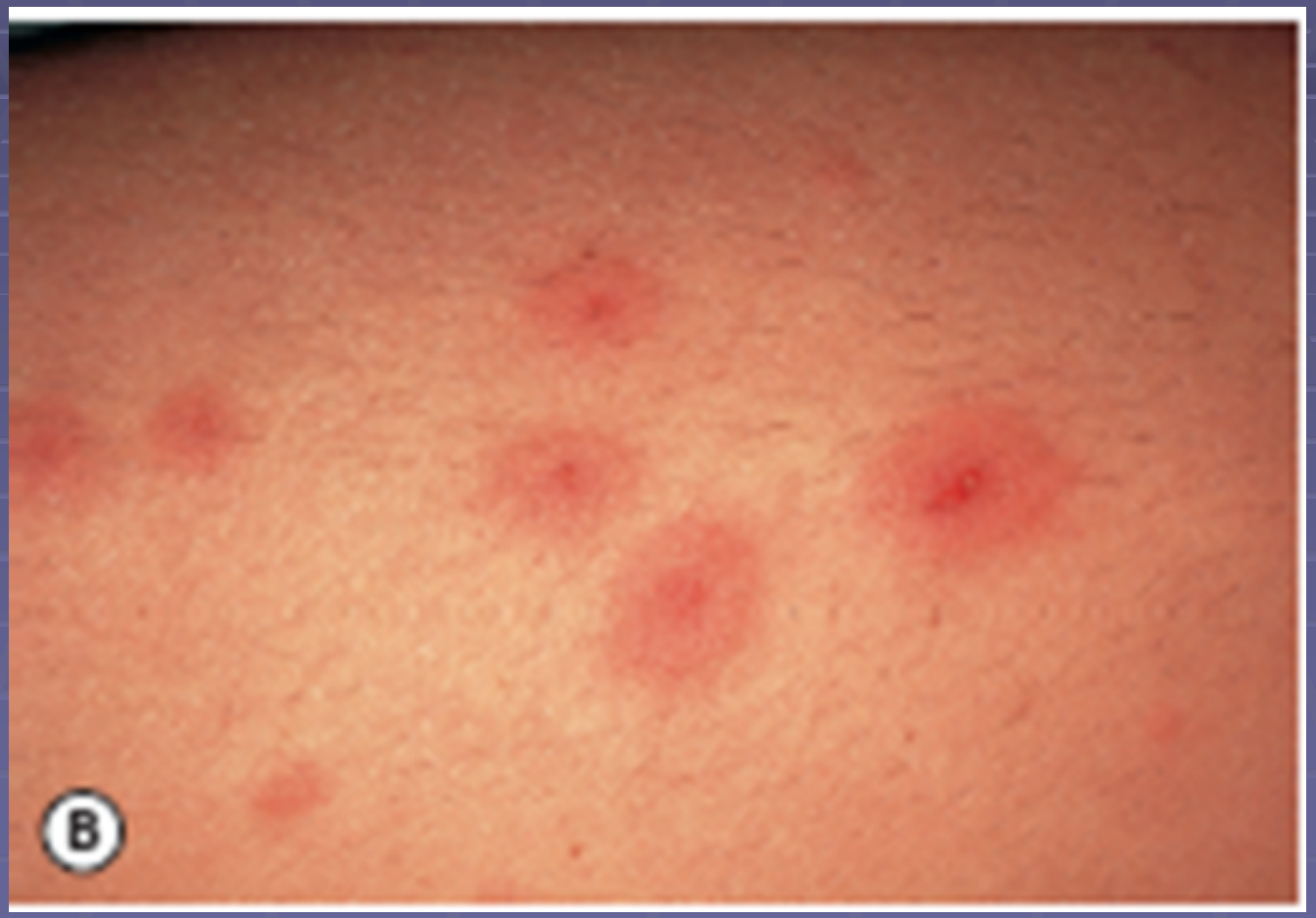
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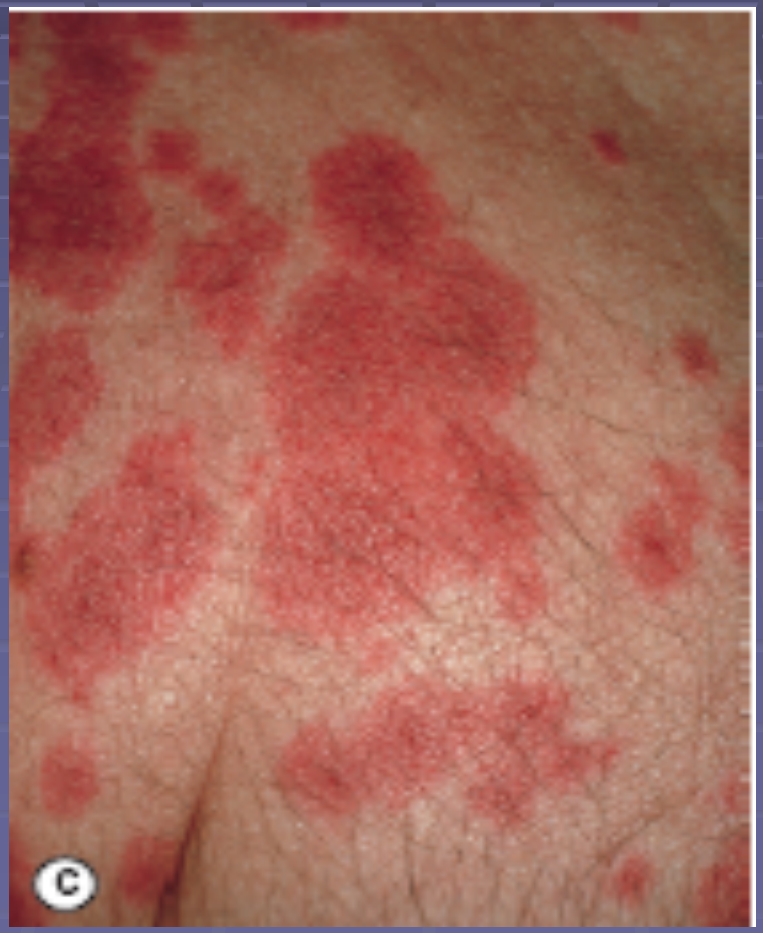
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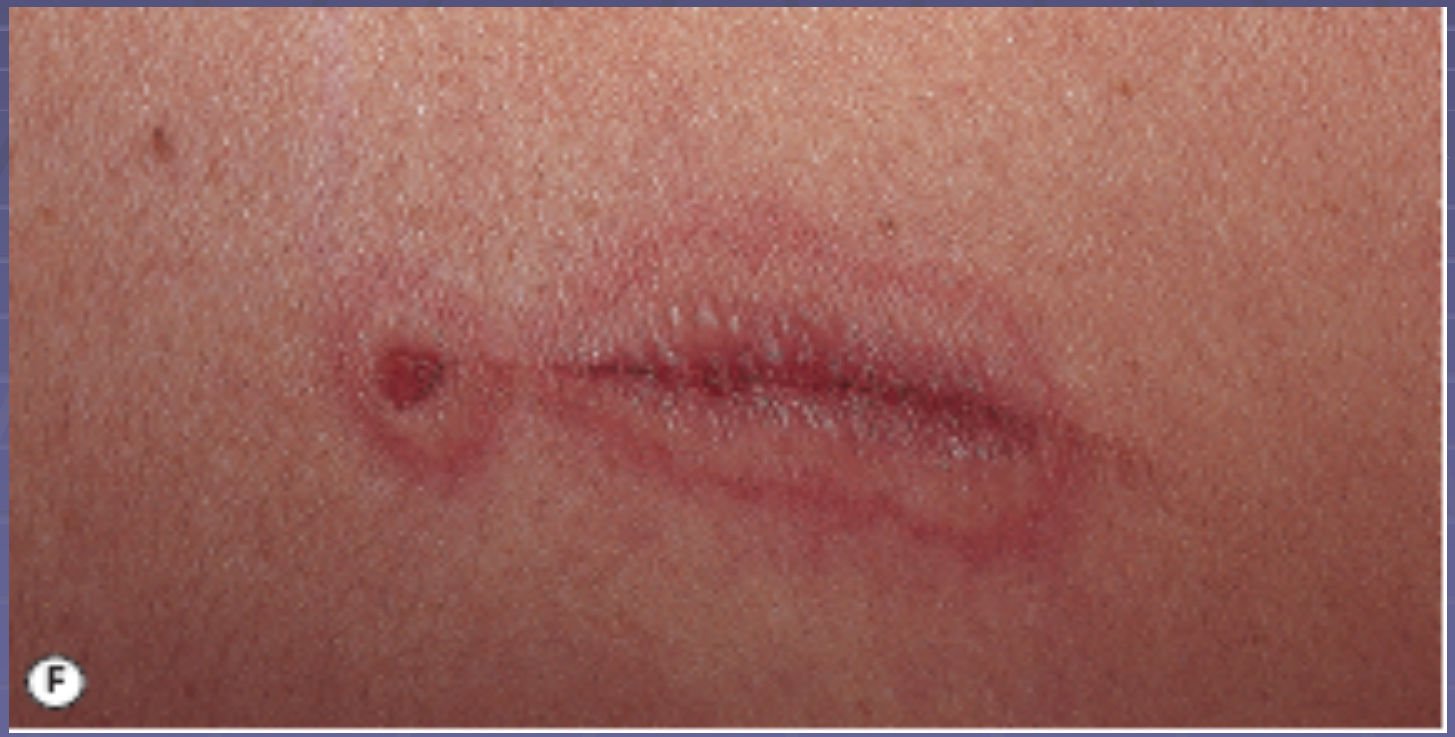
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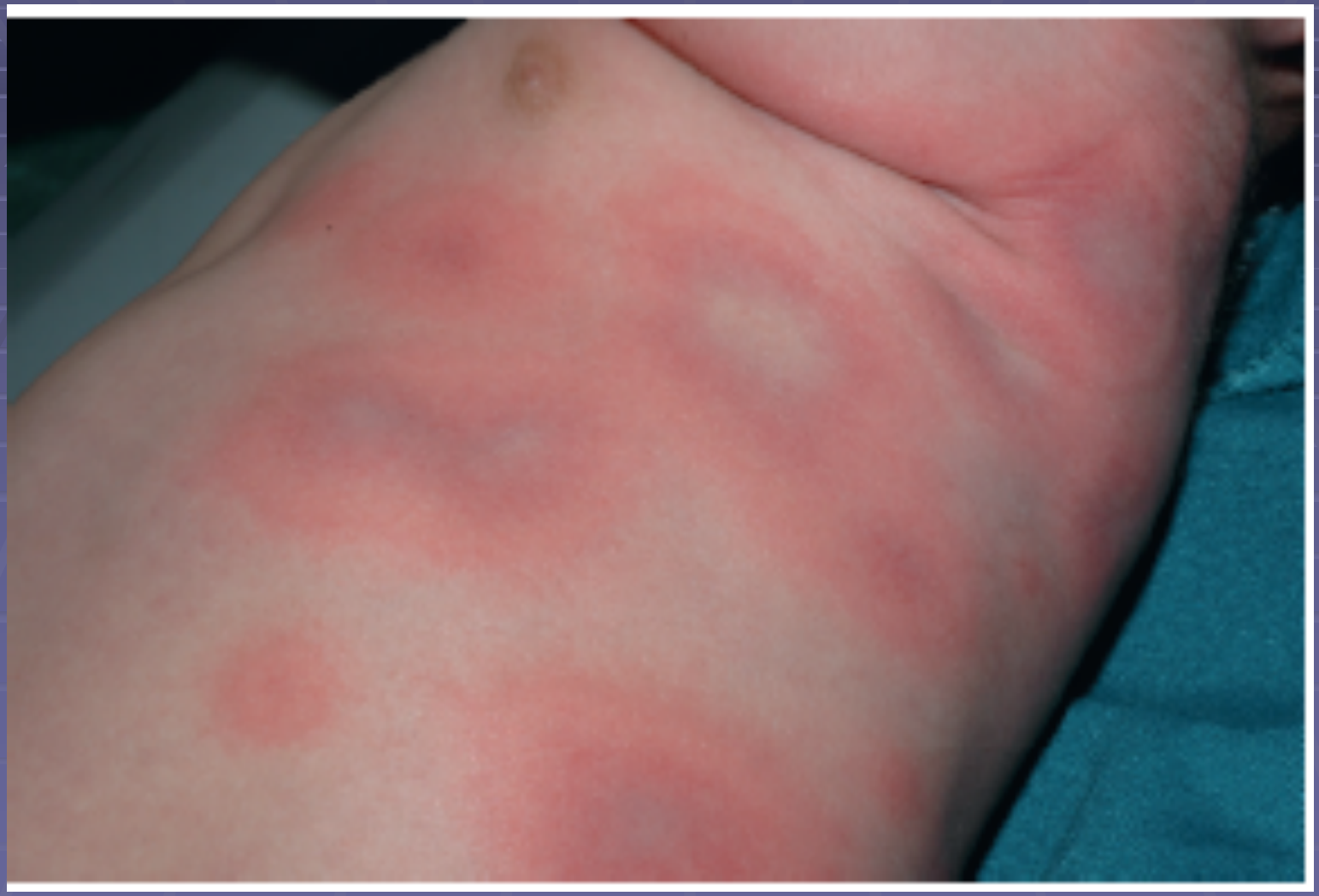
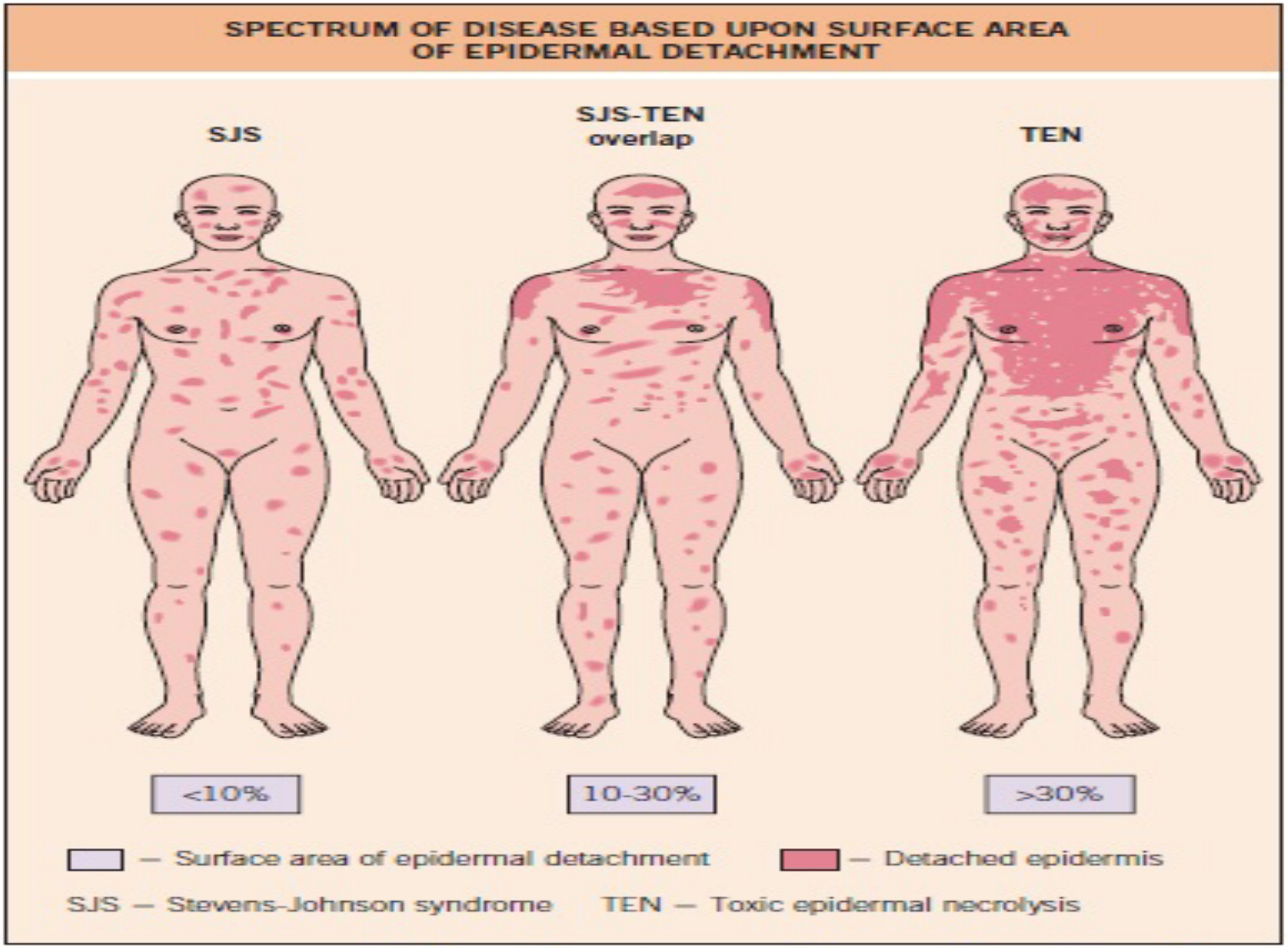
DIFFERENCES BETWEEN URTICARIA AND ERYTHEMA MULTIFORME	
Urticaria	Erythema multiforme
Central zone is normal skin	Central zone is damaged skin (dusky, bullous or crusted)
Lesions are transient, lasting less than 24 hours	Lesions "fixed" for at least 7 days
New lesions appear daily	All lesions appear within first 72 hours
Associated with swelling of face, hands or feet (angioedema)	No edema




SPECTRUM OF DISEASE BASED UPON SURFACE AREA OF EPIDERMAL DETACHMENT
SJS
SJS-TEN overlap
TEN
<10%
10-30%
>30%
— Surface area of epidermal detachment
— Detached epidermis
SJS — Stevens-Johnson syndrome
TEN — Toxic epidermal necrolysis

Epidemiology:

STEVENS–JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN): EPIDEMIOLOGY AND RISK FACTORS	
Annual incidence	1.2–6 per million (SJS) 0.4–1.2 per million (TEN)
Ratio women : men	1.5 : 1
Risk factors	Slow acetylator genotypes
	Immunosuppression (e.g. HIV infection, lymphoma)
	Concomitant administration of radiotherapy and anticonvulsants (most commonly, those with brain tumors)
	HLA-B*1502: Asians and East Indians exposed to carbamazepine
	HLA-B*5801: Han Chinese exposed to allopurinol
	HLA-A*3101: Europeans exposed to carbamazepine

- Mortality rates range from 25 to 50% (average: 30-35%) for patients with TEN .
- On average, death occurs in every third patient with TEN, and it is mainly due to infections (S. aureus and Pseudomonas aeruginosa)
- Drug use is reported in over 95% of patients with TEN.
- Other rare causes include infections and immunization.
- More than 100 drugs have been identified to date as being associated with SJS/TEN

MEDICATIONS MOST FREQUENTLY ASSOCIATED WITH STEVENS–JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS

Allopurinol
Aminopenicillins
Amithiozone (thioacetazone)*,†
Antiretroviral drugs, especially NNRTIs
Barbiturates
Carbamazepine
Chlormezanone*,‡
Phenytoin anticonvulsants
Lamotrigine
Phenylbutazone*,§
Piroxicam
Sulfadiazine*,†
Sulfadoxine†
Sulfasalazine
Trimethoprim–sulfamethoxazole

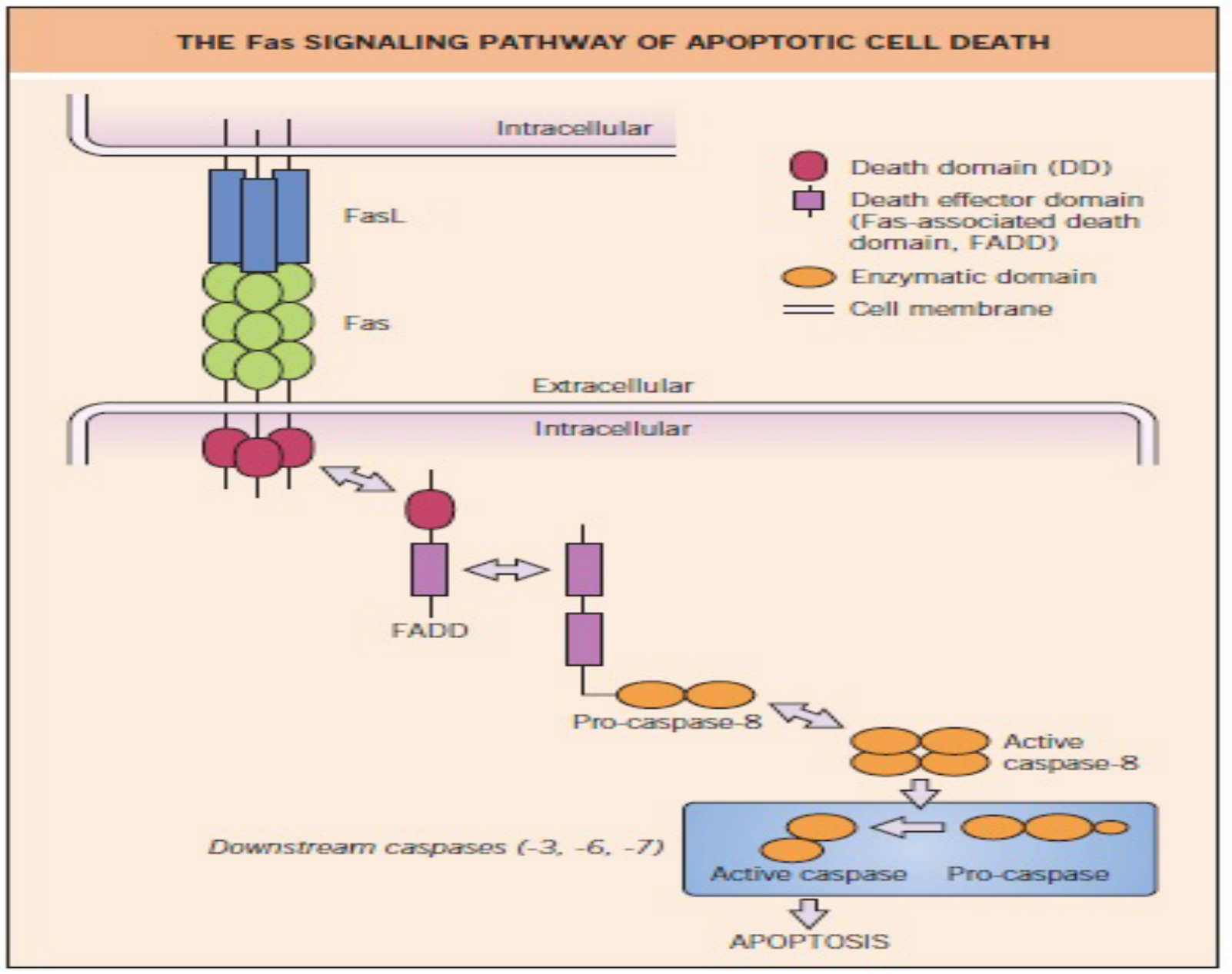
*Not available in the US.
†Antibacterial.
‡Sedative/hypnotic.
§Nonsteroidal anti-inflammatory drug.

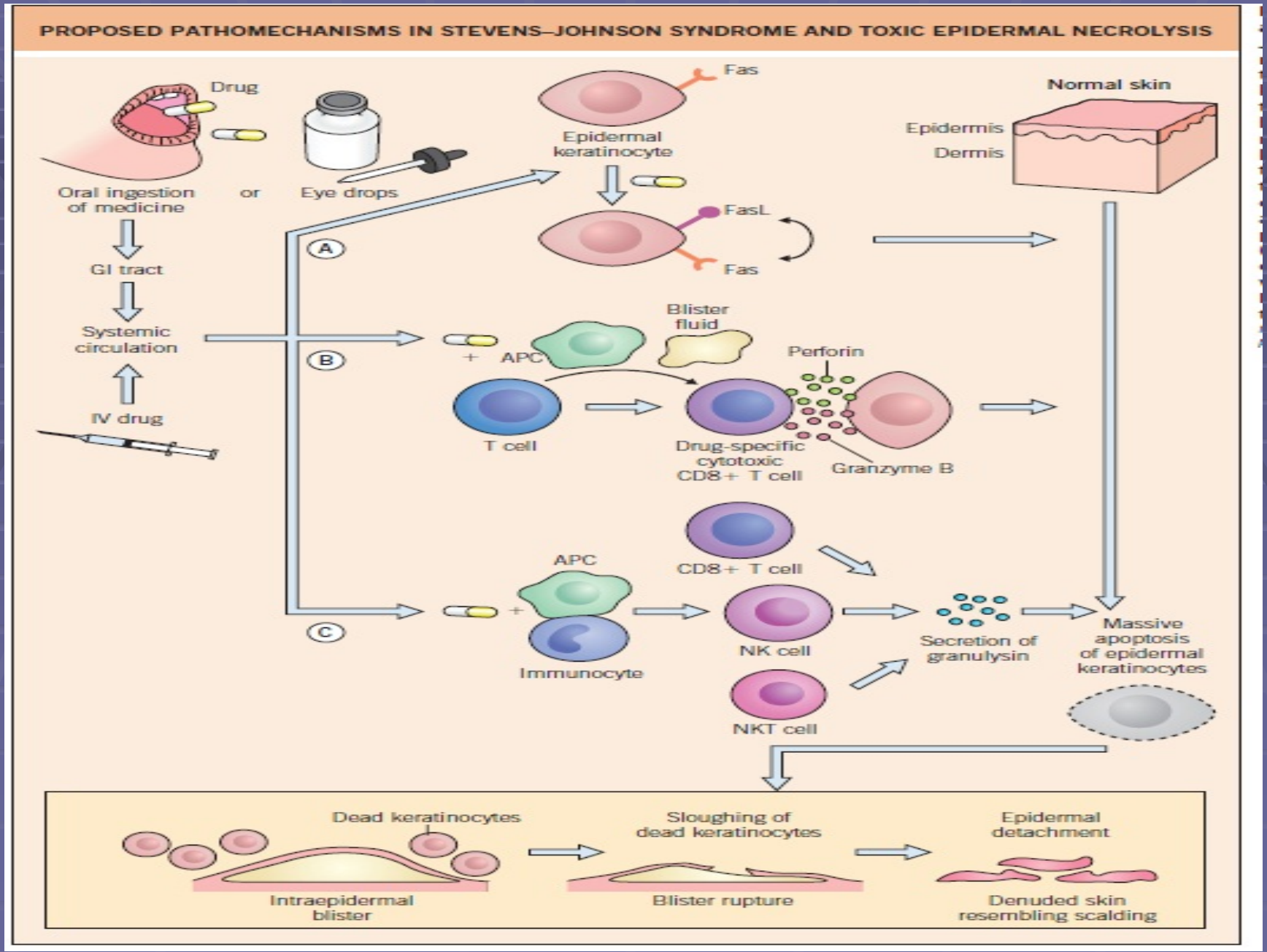
Drugs Associated with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Drugs Most Frequently Associated*	Drugs Also Associated
Sulfadoxine	Cephalosporins
Sulfadiazine	Fluoroquinolones
Sulfasalazine	Vancomycin
Co-trimoxazole	Rifampin
Hydantoins	Ethambutol
Carbamazepine	Fenbufen
Barbiturates	Tenoxicam
Benoxaprofen†	Tiaprofenic acid
Phenylbutazone	Diclofenac
Isoxicam†	Sulindac
Piroxicam	Ibuprofen
Chlormezanone	Ketoprofen
Allopurinol	Naproxen
Amithiozone	Thiabendazole
Aminopenicillins	

Pathogenesis of SJS/TEN :

- An idiosyncratic, delayed hypersensitivity reaction.
- TEN is associated with an impaired capacity to detoxify reactive intermediate drug metabolites.
- Slow acetylators.
- Immunocompromised pts.
- HIV,With AIDS, the risk of developing TEN is 1000-fold higher than in the general population[45]
- It is thought to be initiated by an immune response to an antigenic complex formed by the reaction of such metabolites with certain host tissues.
- There is evidence that systemic lupus is a risk factor
- Genetic susceptibility (increased incidence of HLA-B12 in affected individuals)


THE Fas SIGNALING PATHWAY OF APOPTOTIC CELL DEATH
Intracellular
FasL
Fas
Extracellular
Intracellular
FADD
Pro-caspase-8
Active caspase-8
Downstream caspases (-3, -6, -7)
Active caspase
Pro-caspase
APOPTOSIS
Death domain (DD)
Death effector domain (Fas-associated death domain, FADD)
Enzymatic domain
Cell membrane


PROPOSED PATHOMECHANISMS IN STEVENS–JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS
Drug
Oral ingestion of medicine
or
Eye drops
GI tract
Systemic circulation
IV drug
A
B
C
Fas
Epidermal keratinocyte
FasL
Fas
Normal skin
Epidermis
Dermis
Blister fluid
APC
Perforin
T cell
Drug-specific cytotoxic CD8+ T cell
Granzyme B
CD8+ T cell
APC
Immunocyte
NK cell
NKT cell
Secretion of granulysin
Massive apoptosis of epidermal keratinocytes
Dead keratinocytes
Intraepidermal blister
Sloughing of dead keratinocytes
Blister rupture
Epidermal detachment
Denuded skin resembling scalding

Clinical Features of SJS

- Fever
- Stinging eyes
- Cough productive of thick, purulent sputum
- Headache, Malaise ,Arthralgia
- Burning rash that begins symmetrically on the face and the upper part of the trunk.
- Erythema and erosions of the buccal, ocular and genital mucosae are present in more than 90% of patients.
- The epithelium of the respiratory tract is involved in 25% of patients with TEN, and gastrointestinal lesions (e.g. esophagitis, diarrhea) can also occur

The cutaneous lesions are characterized as follows:

- The rash can begin as macules that develop into papules, vesicles, bullae, urticarial plaques, or confluent erythema
- The typical lesion has the appearance of a target – like ; this is considered pathognomonic
- In contrast to the typical lesions of erythema multiforme, these lesions have only 2 zones of color
- The lesion's core may be vesicular, purpuric, or necrotic; that zone is surrounded by macular erythema.
- The lesions have a tendency to coalesce.

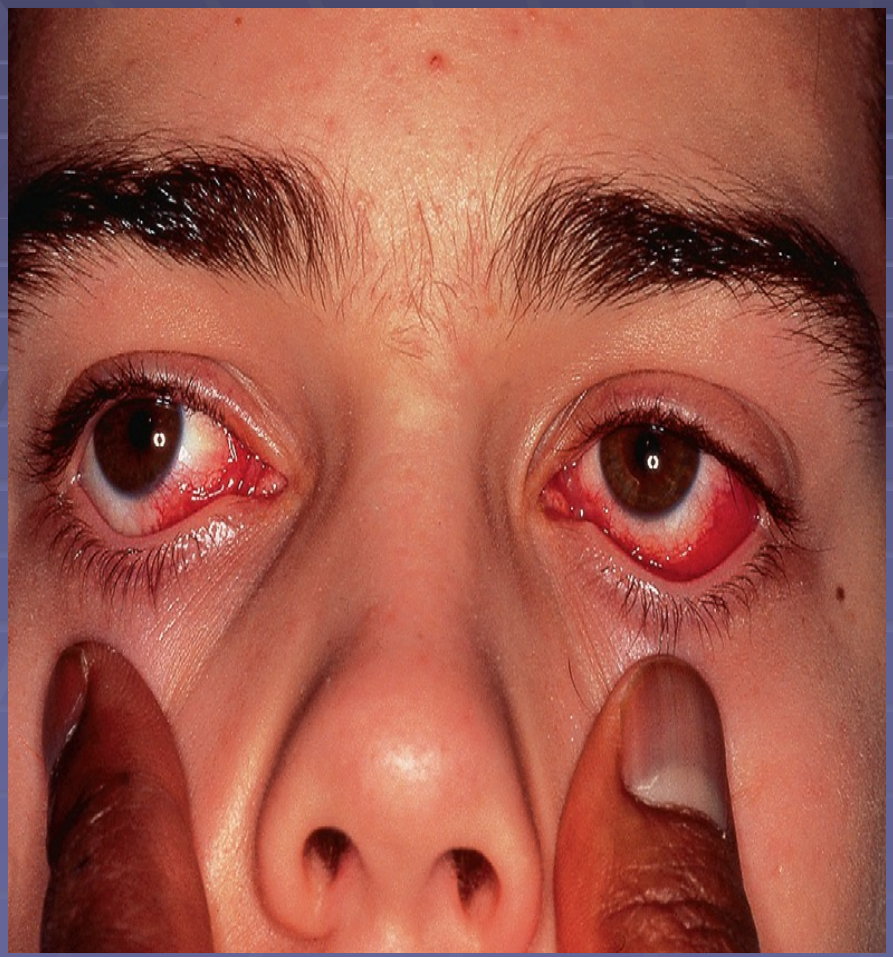
- Lesions may become bullous and later rupture, leaving denuded skin; the skin becomes susceptible to secondary infection
- Urticarial lesions typically are not pruritic
- Infection may be responsible for the scarring associated with morbidity.
- Although lesions may occur anywhere, the palms, soles, dorsum of the hands, and extensor surfaces are most commonly affected.
- Nikolsky sign

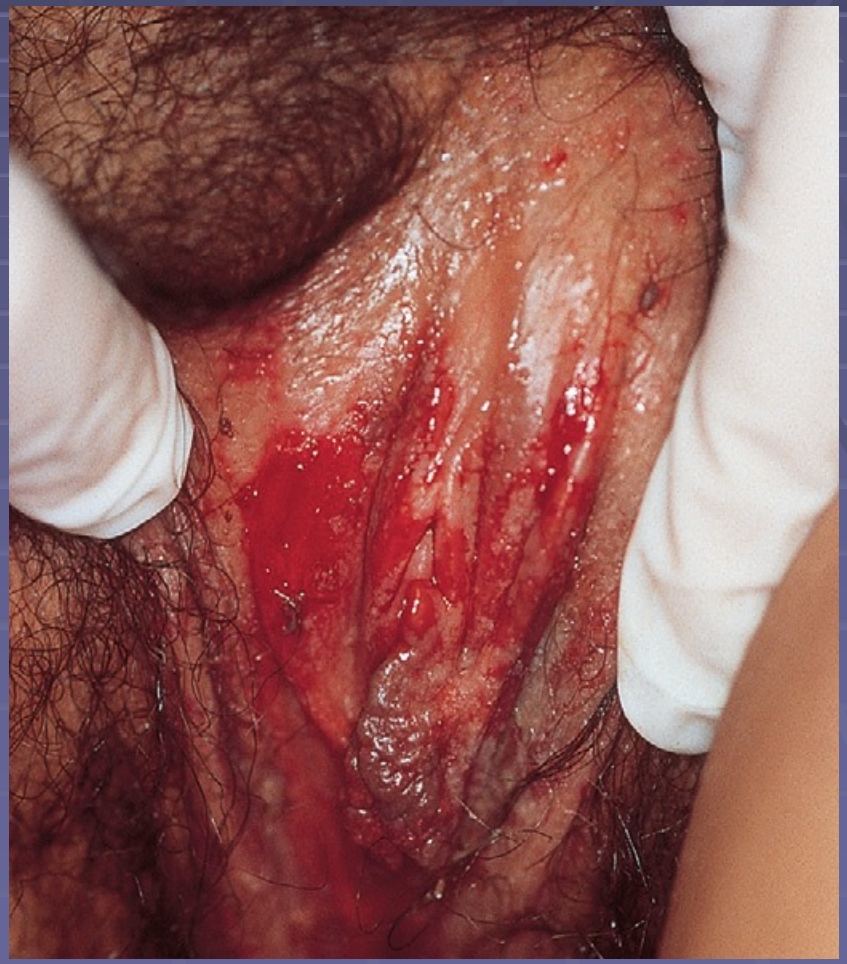
- Signs of mucosal involvement can include the following:

- • Erythema
- • Edema
- • Sloughing
- • Blistering
- • Ulceration
- • Necrosis

- The following ocular signs may be noted on slit-lamp examination:
- Eyelids: Trichiasis, distichiasis, meibomian gland dysfunction, blepharitis
- Conjunctiva: Papillae, follicles, keratinization, subepithelial fibrosis, conjunctival shrinkage, foreshortening of fornices, symblepharon, ankyloblepharon
- Cornea: Superficial punctate keratitis, epithelial defect, stromal ulcer, neovascularization, keratinization, limbitis, conjunctivalization, stromal opacity, perforation

SJS

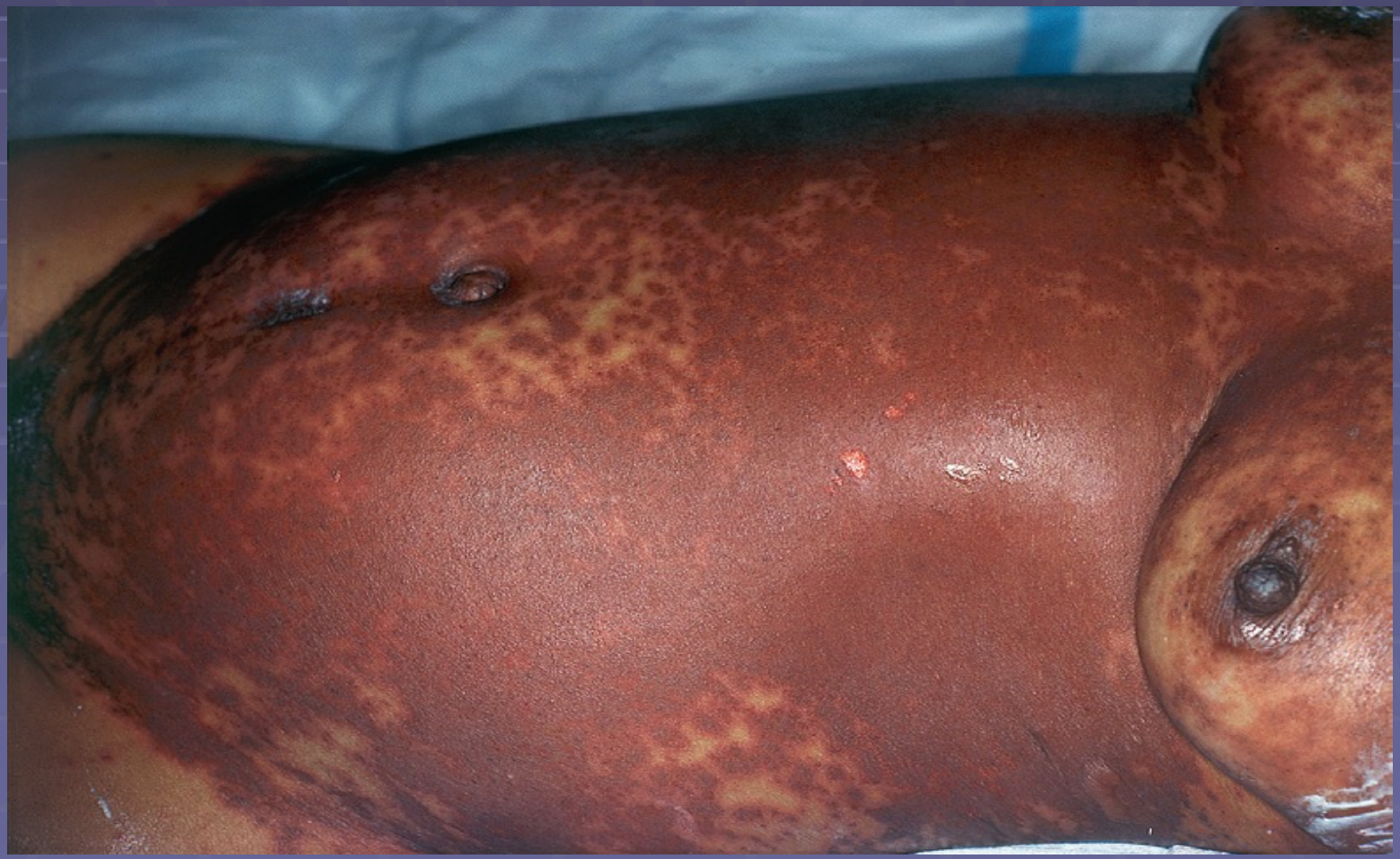




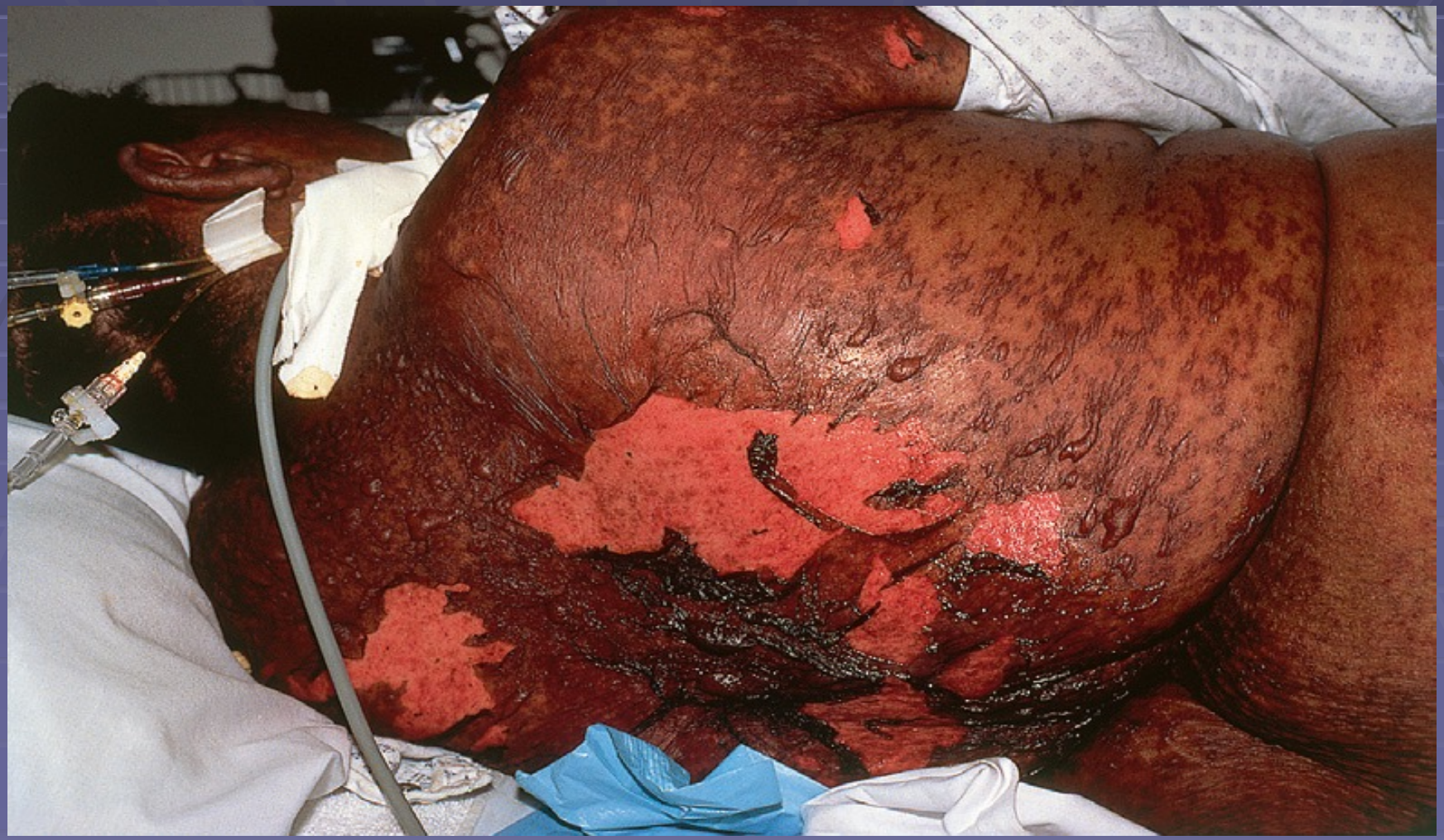
Clinical Features of TEN

- Fever, stinging eyes, and pain upon swallowing, any of which can precede cutaneous manifestations by 1 to 3 days.
- Skin lesions tend to appear first on the trunk, spreading to the neck, face, and proximal upper extremities.
- The scalp , distal portions of the arms as well the legs are relatively spared, but the palms and soles can be an early site of involvement.

- First, erythematous, dusky-red, or purpuric macules of irregular size and shape, and have a tendency to coalesce.
- At this stage, and in the presence of mucosal involvement and tenderness, the risk of rapid progression to SJS or TEN should be strongly suspected.
- In the absence of spontaneous epidermal detachment, a Nikolsky sign should be sought by exerting tangential mechanical pressure with a finger on several erythematous zones. This sign is considered positive if dermo-epidermal cleavage is induced.
-

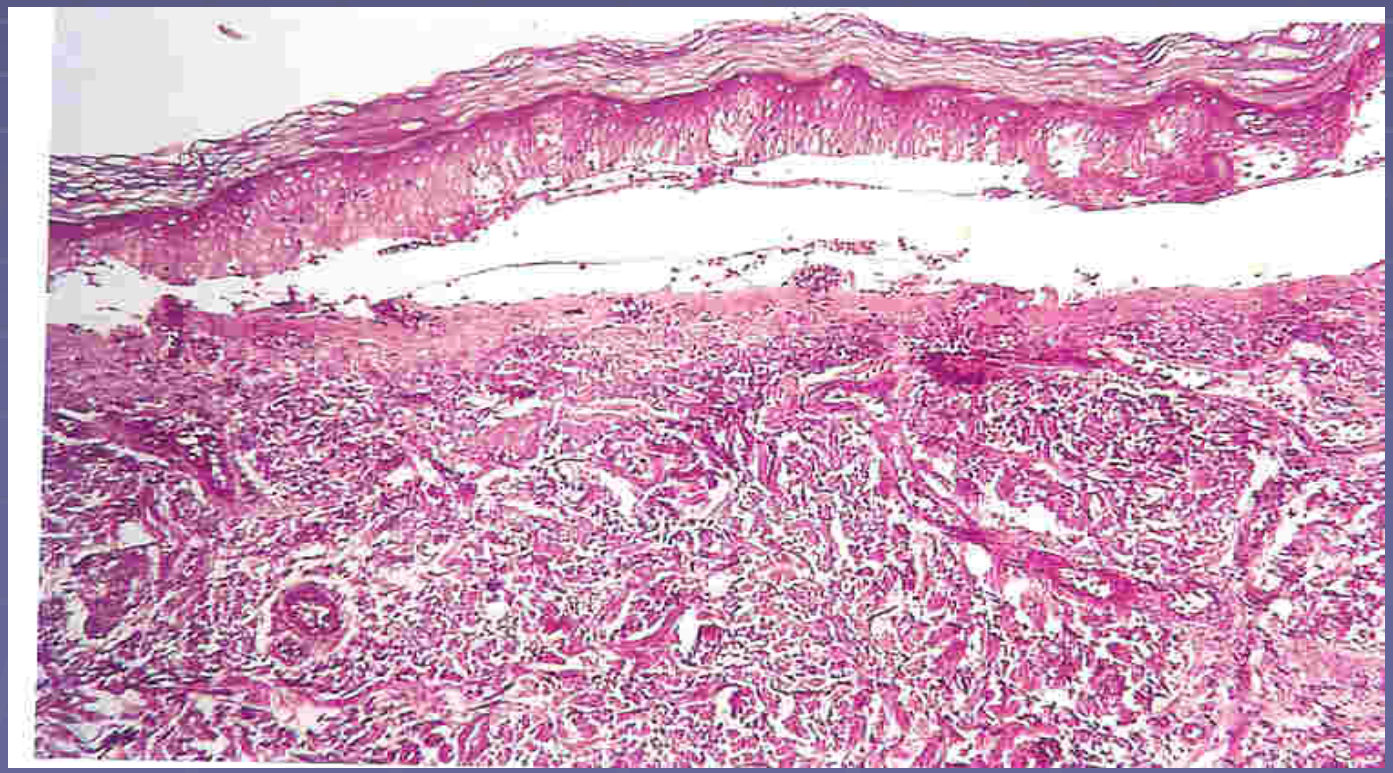


- a target-like appearance.
- With progression the dusky-red macular lesions take on a characteristic gray hue
- This process can be very rapid (hours), or several days.
- The necrotic epidermis then detaches from the underlying dermis, and fluid fills the space between the dermis and the epidermis, giving rise to blisters
- The blisters break easily (flaccid) and can be extended sideways by slight pressure of the thumb as more necrotic epidermis is displaced laterally (Asboe-Hansen sign).
- Tense blisters are usually seen only on the palmar & plantar surfaces when the epidermis is thicker more resistant to mild trauma.



Pathology of TEN

- A subepidermal blister with overlying confluent necrosis of the entire epidermis ad a sparse perivascular infiltrate composed primarily of lymphocytes.

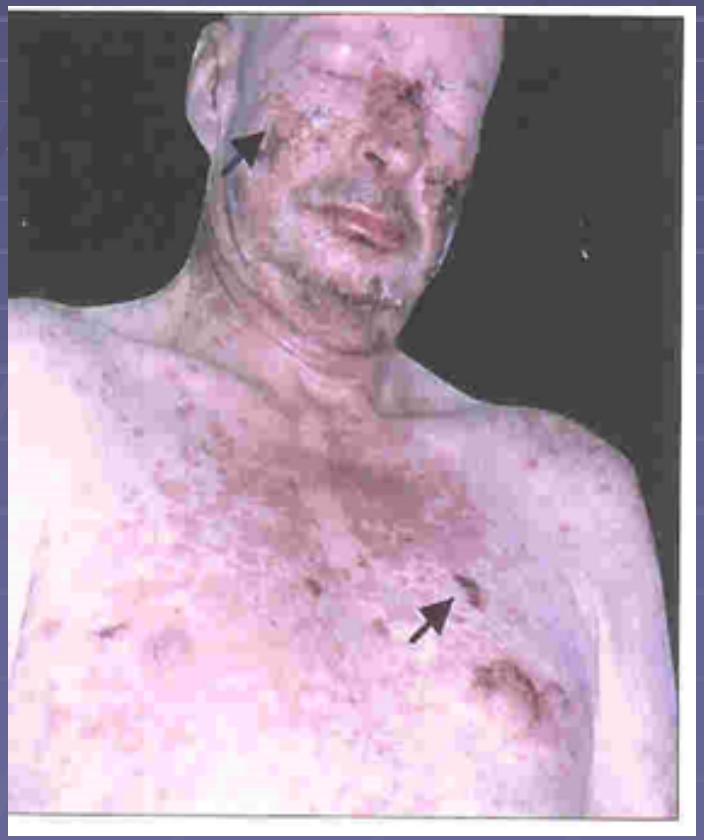


DDx of TEN

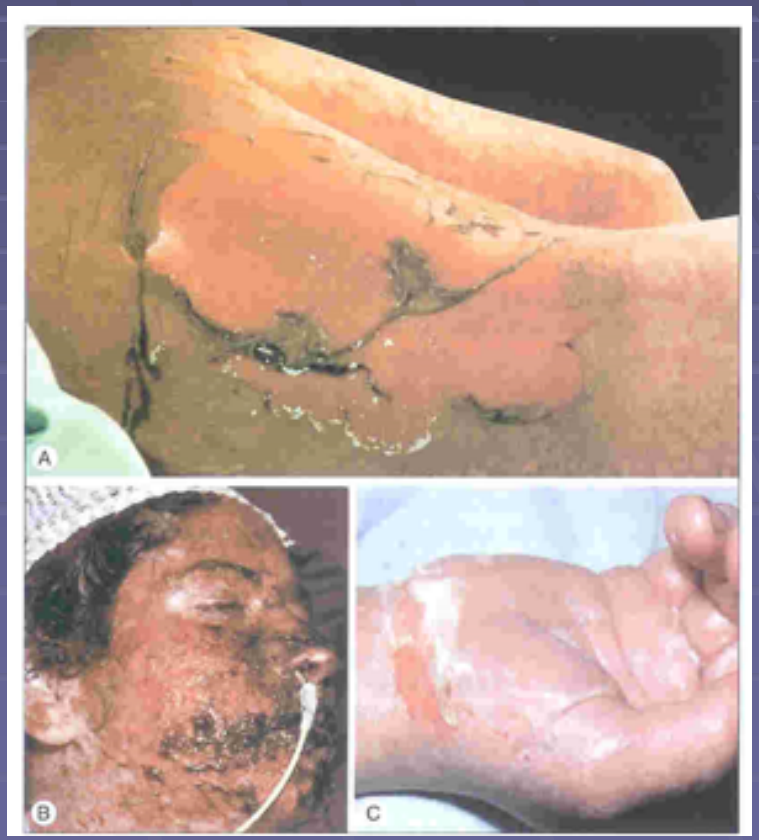
- Stevens-Johnson Syndrome
- Staphylococcal Scalded Skin Syndrome
- Toxic Shock Syndrome

CLINICAL FEATURES THAT DISTINGUISH STEVENS–JOHNSON SYNDROME (SJS), TOXIC EPIDERMAL NECROLYSIS (TEN), AND SJS–TEN OVERLAP			
Clinical entity	**SJS**	**SJS–TEN**	**TEN**
Primary lesions	Dusky and/or dusky red lesions Flat atypical targets	Dusky and/or dusky red lesions Flat atypical targets	Poorly delineated erythematous plaques
			Epidermal detachment – spontaneous or by friction
			Dusky red lesions
			Flat atypical targets
Distribution	Isolated lesions	Isolated lesions	Isolated lesions (rare)
	Confluence (+) on face and trunk	Confluence (++) on face and trunk	Confluence (+++) on face, trunk and elsewhere
Mucosal involvement	Yes	Yes	Yes
Systemic symptoms	Usually	Always	Always
Detachment (% BSA)	**<10**	**10–30**	**>30**

SJS



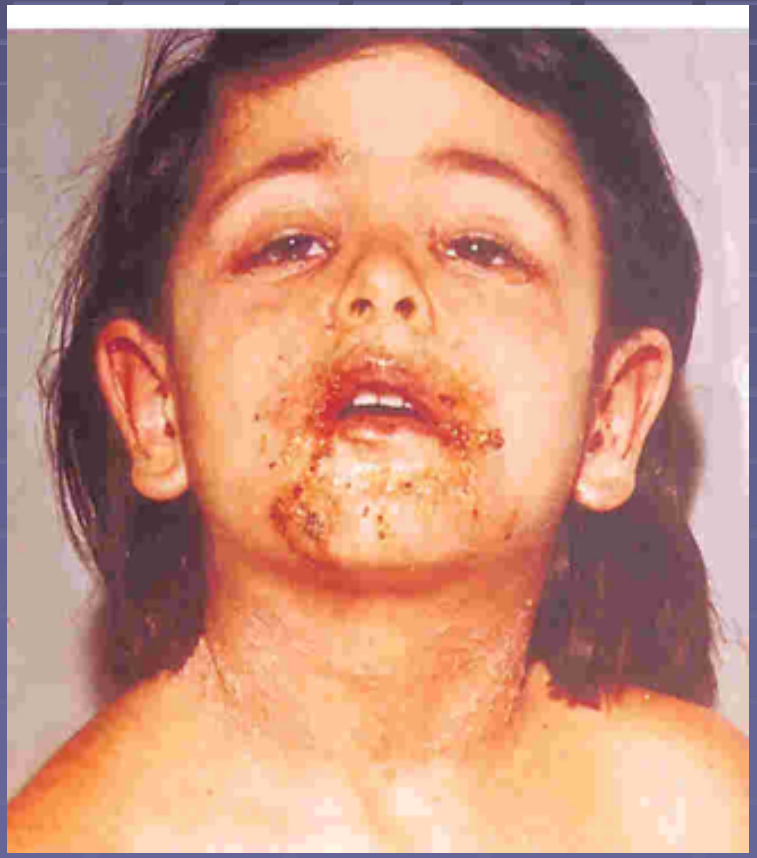
TEN

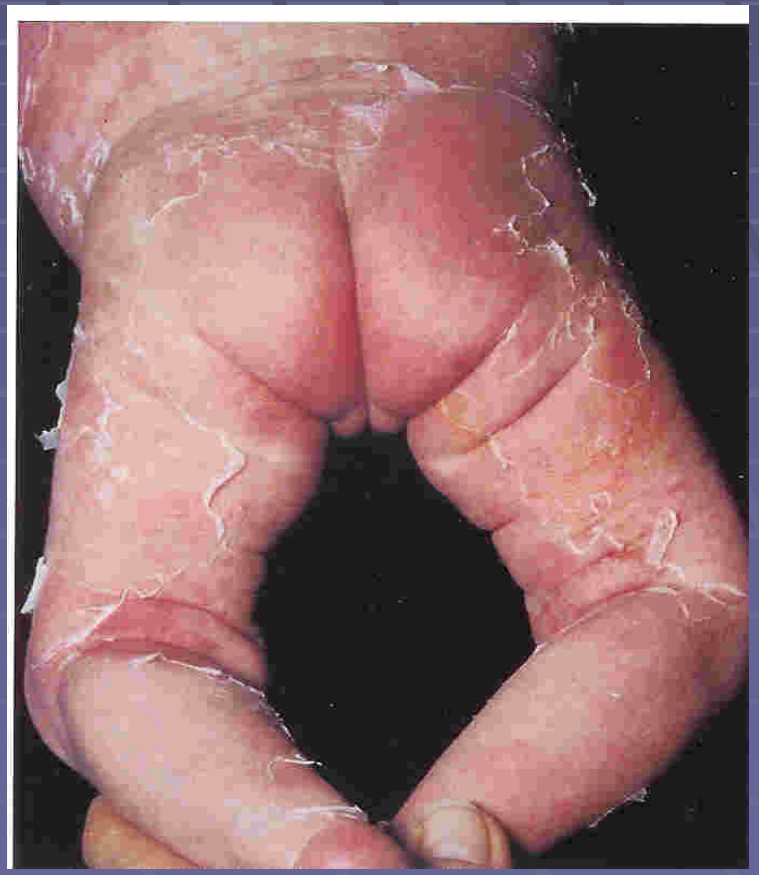


Staphylococcal scalded skin syndrome

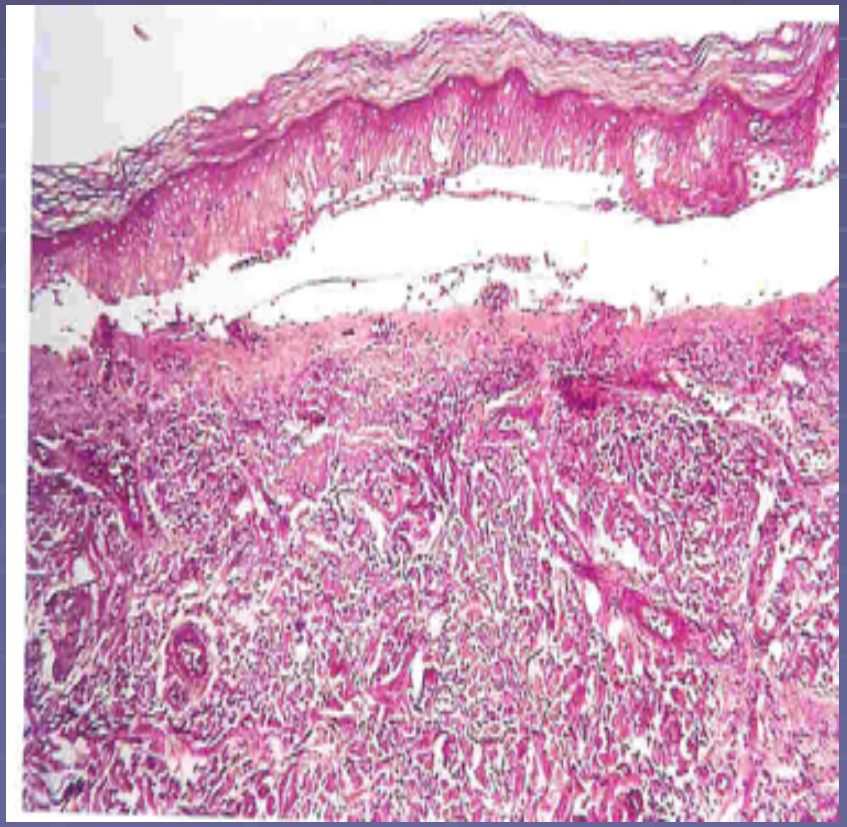
- usually occur in newborns and young children.
- it is induced by a staphylococcal exotoxin (epidermolysin) that targets desmoglein 1.
- The areas of erythema are tender and widespread, but spare the mucous membranes, palms, and soles.
- The Nikolsky sign may be positive as in TEN, but it results in a superficial subcorneal cleavage, not a dermo-epidermal separation. Fragile bullous lesions then develop, and they are rapidly followed by exfoliation of sheets of epidermis.
- Histologicallly shows a subcorneal split with normal underlying epidermis.

SSSS

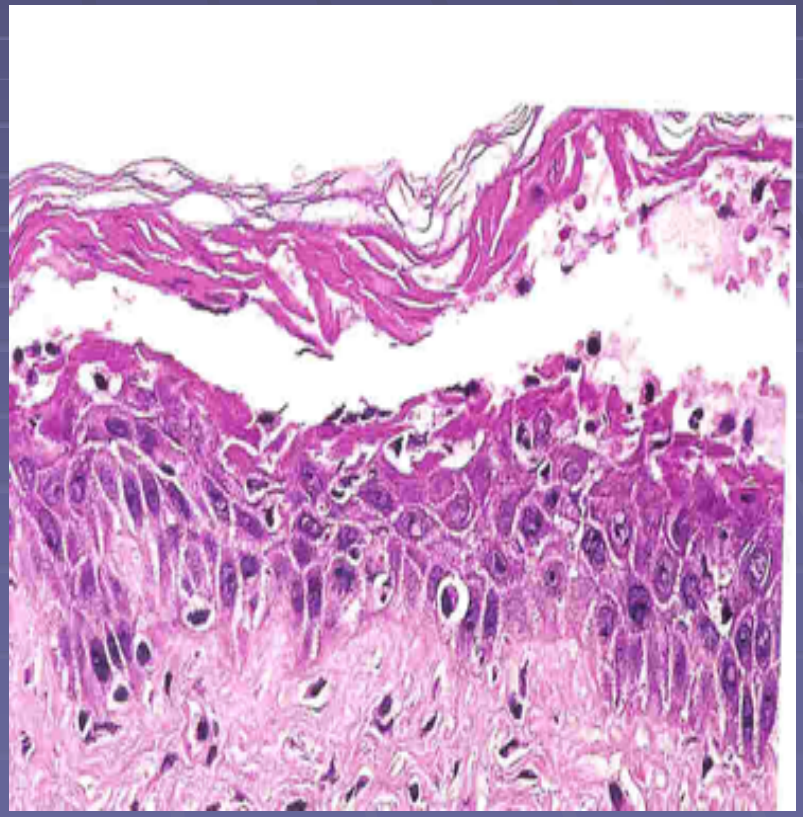




TEN



SSSS



COMPARISON BETWEEN TOXIC EPIDERMAL NECROLYSIS (TEN) AND STAPHYLOCOCCAL SCALDED SKIN SYNDROME

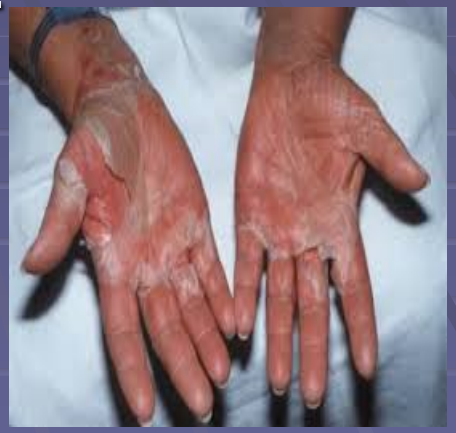
	TEN	SSSS
Cause	Usually drug-induced	Toxin-producing *S. aureus* infection
Age	Adults	Infants and young children
Histology	Dermo–epidermal separation; dermis has a dense inflammatory infiltrate	Granular layer split in epidermis; dermis lacks inflammatory infiltrate
Distribution of rash	Areas of sparing present	Generalized
Mucous membranes	Involved	Uninvolved
Nikolsky's sign	In some areas, difficult to elicit	Present in seemingly uninvolved skin
Face	Lip and mucous membrane redness, edema	Perioral crusting and fissuring with mild facial swelling and erosions
Treatment	Standard burn treatment, IVIG, corticosteroids (controversial)	Antibiotics (β-lactamase resistant) and supportive care

Toxic shock syndrome (TSS):

- Is an inflammatory response syndrome characterized by fever, rash, hypotension and multiorgan involvement.
- TSS has been typically associated with tampon use in healthy menstruating women.
- The disease is now known to also exist in men, neonates, and nonmenstruating women.
- It has been linked to many bacterial infections, including pneumonia, osteomyelitis, sinusitis, and skin and gynecologic infections.

- Staphylococcal TSS- (15-35 years).
- Streptococcal TSS— (20-50 years).
- Staphylococcal TSS- higher in women .
- Streptococcal TSS, both sex
- Staph TSS, mortality rate is less than 3%.
- Strept TSS, mortality rate is 30-70%.

- Prodromal period of 2-3 days:
- Fever ,nausea and/or vomiting
- Profuse watery diarrhea with abdominal pain.
- Pharyngitis and/or headache, confusion.
- Hypotension
- Skin findings:
- Diffuse rash, occasionally patchy and erythematous, with desquamation occurring approximately 1-2 weeks later
- Rash initially appearing on trunk, spreading to arms and legs, and involving palms and soles
- Signs of multiorgan involvement



Prognosis

SCORTEN	
Prognostic factors	**Points**
Age >40 years	1
Heart rate >120 bpm	1
Cancer or hematologic malignancy	1
BSA involved on day 1 above 10%	1
Serum urea level (>10 mmol/l)	1
Serum bicarbonate level (<20 mmol/l)	1
Serum glucose level (>14 mmol/l)	1
SCORTEN	**Mortality rate (%)**
0–1	3.2
2	12.1
3	35.8
4	58.3
≥5	90

Treatment

General measures:-

- Early diagnosis.
- Immediate discontinuation of the causative drug(s)
- Management on a specialist ICU or burn unit.
- Multidisciplinary teamwork.
- supportive care.
- specific therapy.

Supportive care.

- Pt should be manipulated as little as possible as every movement is a potential cause of epidermal detachment
- all patient manipulations should be performed sterilely.
- venous catheters should be placed, if possible, in a region of non-involved skin
- Non-detached areas are kept dry and not manipulated.
- Detached areas, should be covered with Vaseline® gauze until re-epithlialization has occurred.

- Careful monitoring of fluid & electrolyte status with therapy for any imbalance.
- Nutritional support.
- Warming of environment to reduce the increase in metabolic rate.
- Appropriate analgesia.
- Prevention, early detection & treatment of infection.
- There is NO evidence that prophylactic antibiotic provide benefit & most authors reserve antibiotics therapy for treatment of proven infection (care must be taken in screening for sepsis & surveillance of lines/catheters to allow prompt intervention).

- For the eyes regular examination by an ophthalmologist is recommended.
- Eyelids should gently cleansed daily with isotonic sterile sodium chloride solution, and an ophthalmic antibiotic ointment applied to the eyelids.

specific therapy

- To date, no specific therapies for TEN have reached evidence based medicine standards of acceptance

Intravenous Immunoglobulins (IVIG)

- contain antibodies against Fas that are able to block the binding of FasL to Fas.
- When used in high doses (0.75 g/ kg/day for 4 consecutive days) to treat patients with TEN, IVIG consistently and rapidly blocked the progression of epidermal detachment and disease in 10 of the 10 patients treated in a preliminary pilot study

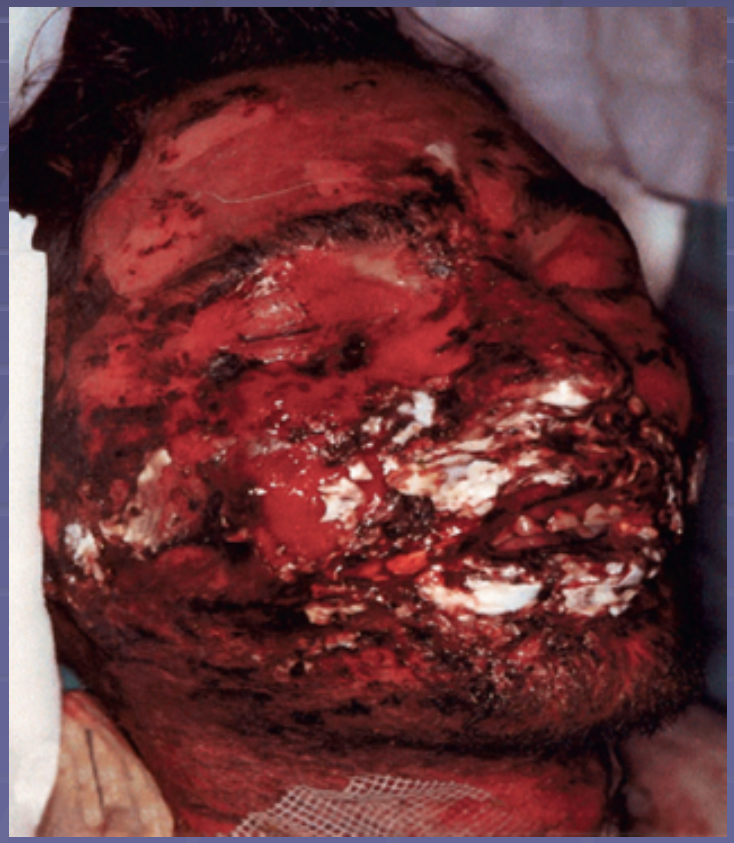
PUBLISHED STUDIES (WITH ≥10 PATIENTS) ON THE USE OF IVIG FOR THE TREATMENT OF TOXIC EPIDERMAL NECROLYSIS

	Viard 1998	Trent 2003	Prins 2003	Campione 2003	Al-Mutairi 2004	Shortt 2004	Tan 2005	Stella 2007	Bachot 2003	Brown 2004	Schneck 2008
Study	Prospect	Retro	Retro	Prospect	Prospect	Retro	Retro	Retro	Prospect	Retro	Retro
	NC	NC	NC	NC	NC	NC	NC	C	NC	NC	C
No. of patients	10	24	48	10	12	16	12	23	34	24	75
Detachment of epidermis (% BSA)	39	44	45	49	58	"65"	—	—	19	49	—
Dose of IVIg (g/kg)*	3	4	3	2	2–5	2.8	2	—	2	1.6	1.9 (0.7–2.3)
Predicted mortality (scoring system)	—	33% (SCORTEN)	—	35% (SCORTEN)	—	38% (APACHE)	—	36% (SCORTEN)	24% (SCORTEN)	29% (SCORTEN)	25% (SCORTEN)
Actual mortality	6%	4%	12%	10%	0%	25%	8%	26%	32%	42%	34%

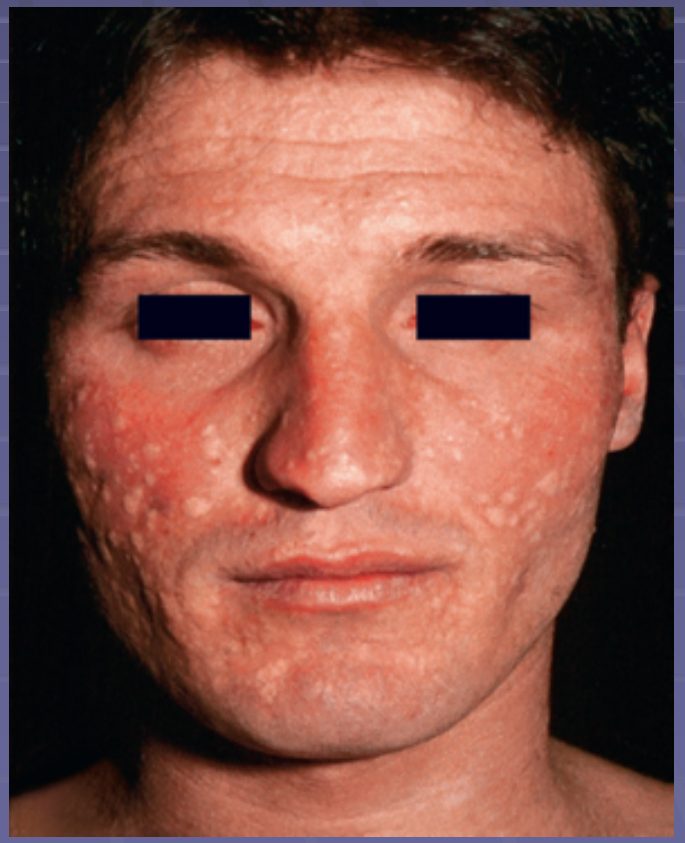
*Usually administered over 3-4 days

TEN

Before IVIG



After IVIG



Corticosteroid:-

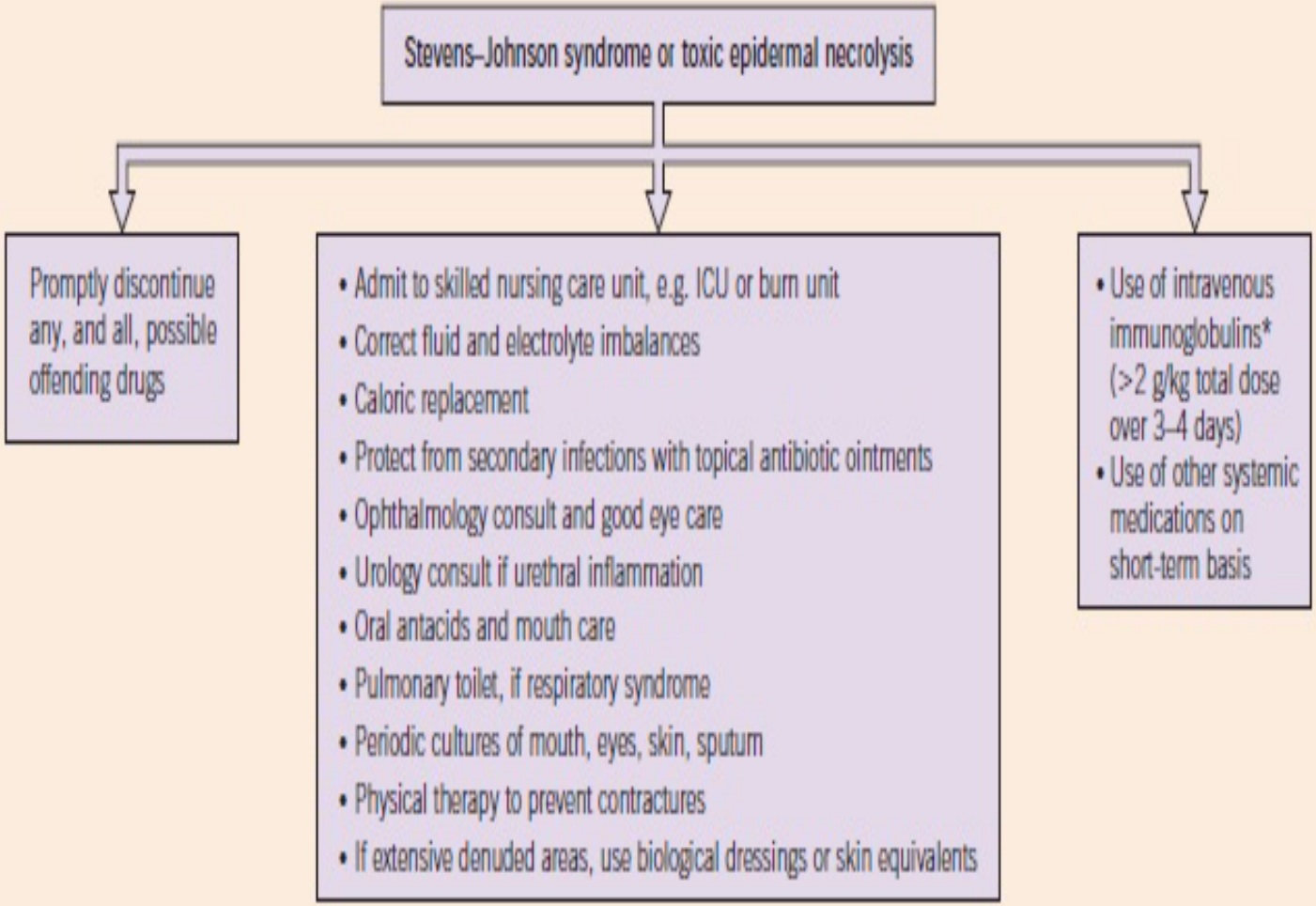
- It have been used in management of TEN for the last 30 years.
- Their use has been much debated & remains controversial.

Action:-

- Anti-inflammatory.
- Immunosuppressant.
- Anti-apoptotic

- One series (n=44) reported excessive mortality associated with prolonged use of systemic steroid therapy.
- The balance of available evidence suggests that, corticosteroid have no significant beneficial effect on TEN.
- Corticosteroid can not be recommended as a therapy for TEN.
- (British journal of dermatology 2005. 153, pp 241-253).

APPROACH TO THE PATIENT WITH STEVENS–JOHNSON SYNDROME OR TOXIC EPIDERMAL NECROLYSIS



* according to evidence from non-controlled studies performed to date (see section on therapy)

TAKE HOME MESSAGES

- Prodrome of URT symptoms, fever and painful skin
- SJS and TEN are two rare, potentially fatal, adverse cutaneous drug reactions of differing severity, characterized by mucocutaneous tenderness and erythema as well as extensive exfoliation.
- SJS is characterized by <10% body surface area of epidermal detachment, SJS–TEN overlap by 10–30%, and TEN by >30%
- The average mortality rate is 1–5% for SJS and 25–35% for TEN; it can be even higher in elderly patients and in those TEN pts with a very large surface area of epidermal detachment
- Optimal medical management of SJS and TEN requires early diagnosis, immediate discontinuation of the causative drug(s), and rapid initiation of supportive care and specific therapy
- Specific therapies that have the potential to selectively block keratinocyte apoptosise.g high-dose IVIg, may provide added benefit over supportive care alone

Thank you

1. **In the pathogenesis of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis(TEN) which of the following is the best answer?**

A. The circulating autoantibodies are directed against keratinocyte cell surfaces.

B. Impaired capacity to detoxify reactive intermediate drug metabolites

C. Staphylococcus aureus producing epidermolytic toxin A and epidermolytic toxin B

D. It is Type I immunoglobulin E (IgE)–dependent drug reaction

2. **Which of the following is/are clinical features of toxic epidermal necrolysis (TEN)?**

A. Auspitz sign is positive

B. Tense blisters over the trunk and flaccid bullae over palms

C. Nikolsky sign is positive

D. The eruption starts at the distal portions of the arms and legs.

3. Regarding prognosis of toxic epidermal necrolysis (TEN) which of the following factors indicate poor outcome?

A. Children and young adults

B. Low serum glucose level

C. Low neutrophils count

D. Mucous membranes erosions

4. In the treatment of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) which of the following is the best answer?

A. Early use of systemic antibiotic as prophylactic for skin and systemic infections

B. Thalidomide is effective in blocking epidermal detachment and decrease mortality rate

C. High dose of intravenous immunoglobulins (IVIg) is associated with high mortality rate

D. Early diagnosis, immediate discontinuation of the causative drug(s) and supportive care