Drug eruption

March 25,2015

Outline

- Clinical features
- Pathogenesis
- How to approach?
- Management?

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 Anaphylaxis	<10 30	Minutes to hours Minutes to hours	0 5	Penicillins Cephalosporins NSAIDs Monoclonal antibodies Contrast media
Fixed drug eruption	100	First exposure: 1–2 weeks Re-exposure: <48 hours, usually within 24 hours	0	TMP-SMX NSAIDs Tetracyclines 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)†	70–90	15–40 days	5–10	Anticonvulsants Sulfonamides Allopurinol Minocycline Lamotrigine (especially in combination with valproate)
Stevens–Johnson syndrome (SJS)	70–90	7–21 days	5	Sulfonamides Anticonvulsants NSAIDs Allopurinol
Toxic epidermal necrolysis (TEN)			30	

*Non-pigmenting.
†Also referred to as hypersensitivity syndrome.

TABLE 40-1
Clinical Features of Selected Cutaneous Reactions to Drugs

Clinical Presentation	Drug Eruption	Fever	Internal Organ Involvement	Arthralgia	Lymphadenopathy	Implicated Drugs
Hypersensitivity syndrome reaction	Exanthem, exfoliative dermatitis, pustular eruptions, SJS/TEN	Present	Present	Absent	Present	Aromatic anticonvulsants (e.g., phenytoin, phenobarbital, carbamazepine), sulfonamide antibiotics, dapsone, minocycline, allopurinol, lamotrigine
Serum sickness–like reaction	Urticaria, exanthem	Present	Absent	Present	Present	Cefaclor, cefprozil, bupropion, minocycline, infliximab, rituximab
Drug-induced lupus	Usually absent	Present/absent	Present/absent	Present	Absent	Procainamide, hydralazine, isoniazid, minocycline, acebutolol
Drug-induced subacute cutaneous lupus erythematosus	Papulosquamous or annular cutaneous lesion (often photosensitive)	Absent	Absent	Absent	Absent	Thiazide diuretics, calcium channel blockers, ACE inhibitors
Acute generalized exanthematous pustulosis	Non-follicular pustules on an edematous erythematous base	Present	Absent	Absent	Absent	β Blockers, macrolide antibiotics, calcium channel blockers

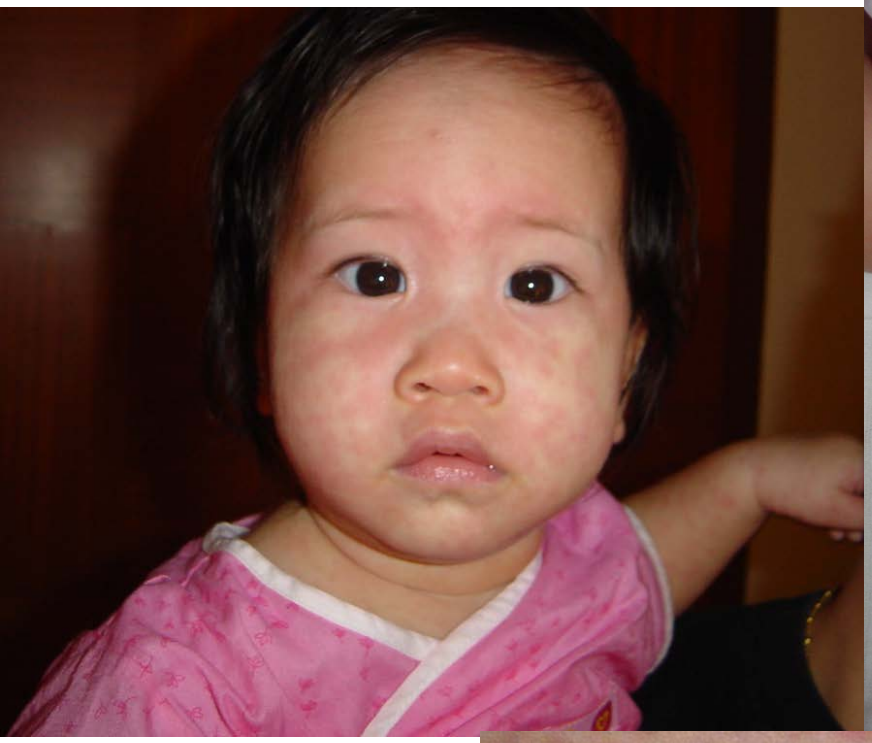
TABLE 40-2
Drug Eruptions Mimicry

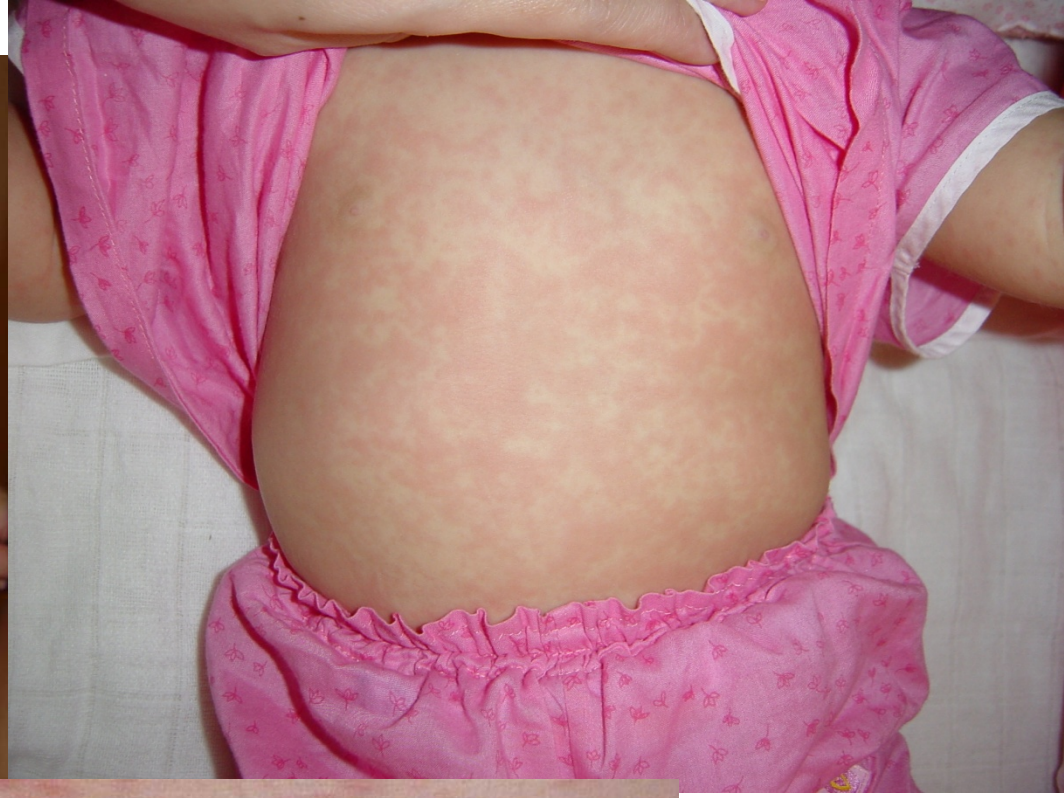
Clinical Presentation	Pattern and Distribution of Skin Lesions	Mucous Membrane Involvement	Implicated Drugs	Treatment
Stevens-Johnson syndrome	Atypical targets, widespread	Present	Aromatic anticonvulsants,[a] lamotrigine, sulfonamide antibiotics, allopurinol, piroxicam, dapsone	IVIg, cyclosporine, supportive care
Toxic epidermal necrolysis	Epidermal necrosis with skin detachment	Present	As above	IVIg, cyclosporine, supportive care
Pseudoporphyria	Skin fragility, blister formation in photodistribution	Absent	Tetracycline, furosemide, naproxen	Supportive care
Linear IgA disease	Bullous dermatosis	Present/absent	Vancomycin, lithium, diclofenac, piroxicam, amiodarone	Supportive care
Pemphigus	Flaccid bullae, chest	Present/absent	Penicillamine, captopril, piroxicam, penicillin, rifampin, propranolol	Supportive care
Bullous pemphigoid	Tense bullae, widespread	Present/absent	Furosemide, penicillamine, penicillins, sulfasalazine, captopril	Supportive care

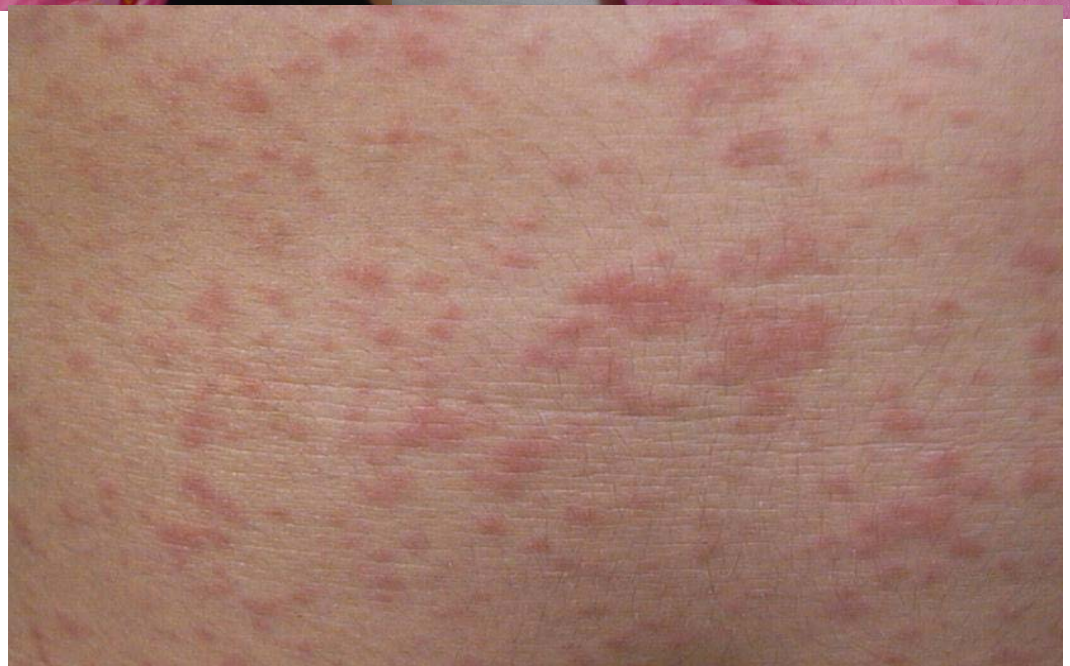
IVIg = intravenous immunoglobulin

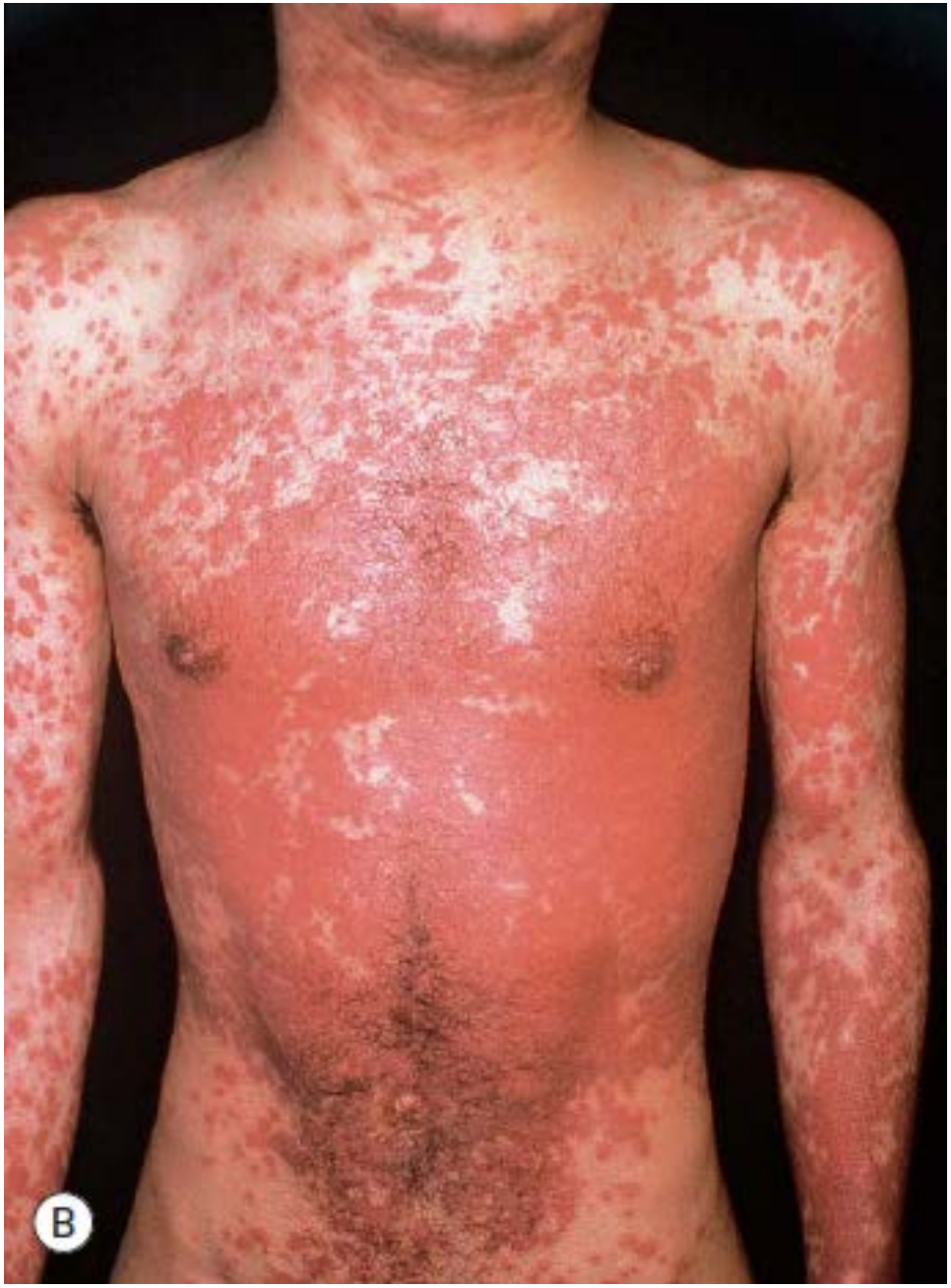
Need to know

- Urticaria
- Exanthematous rash
- DRESS
- Stevens-Johnson syndrome/TEN
- Fix drug eruptions
- Acute generalized exanthematous pustulosis
- Photoallergic/Phototoxic.
- Chemotherapy induced..





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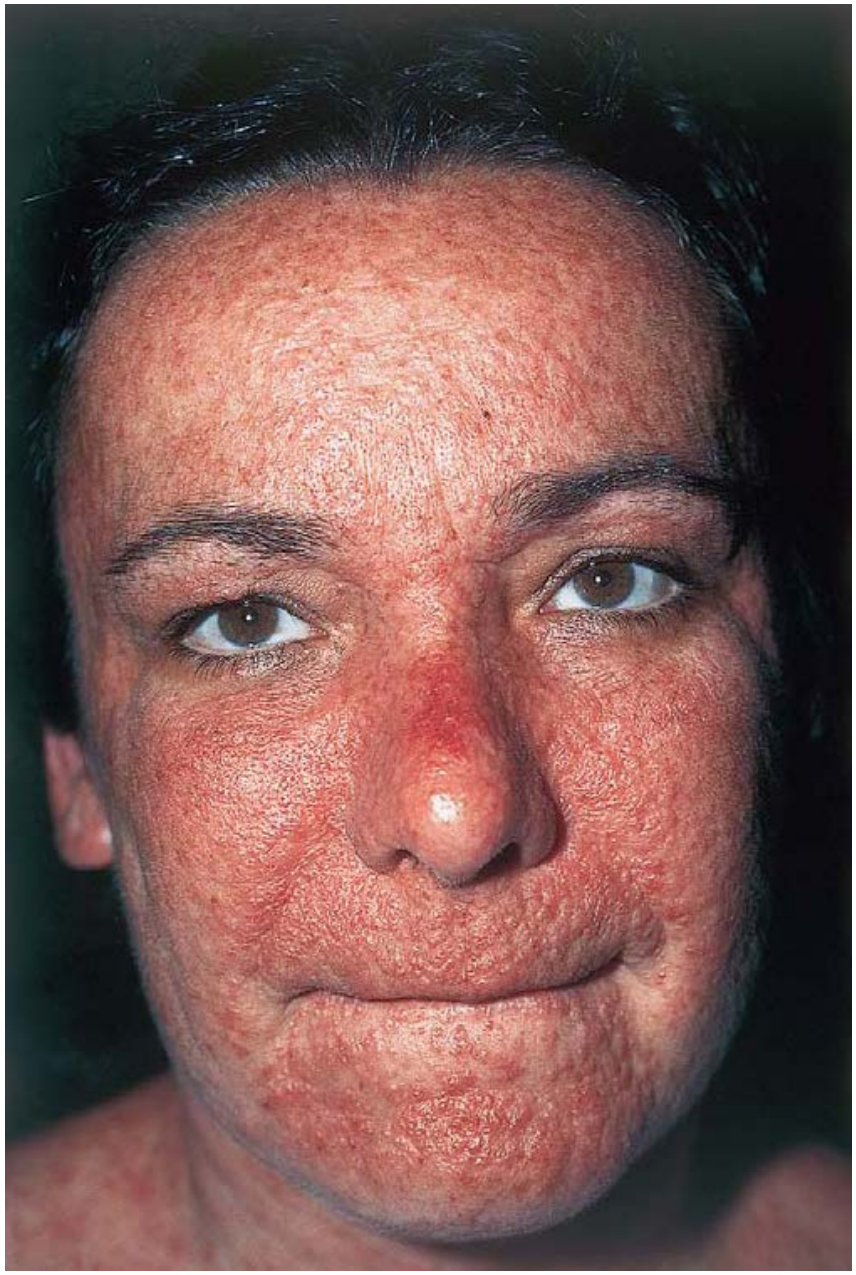
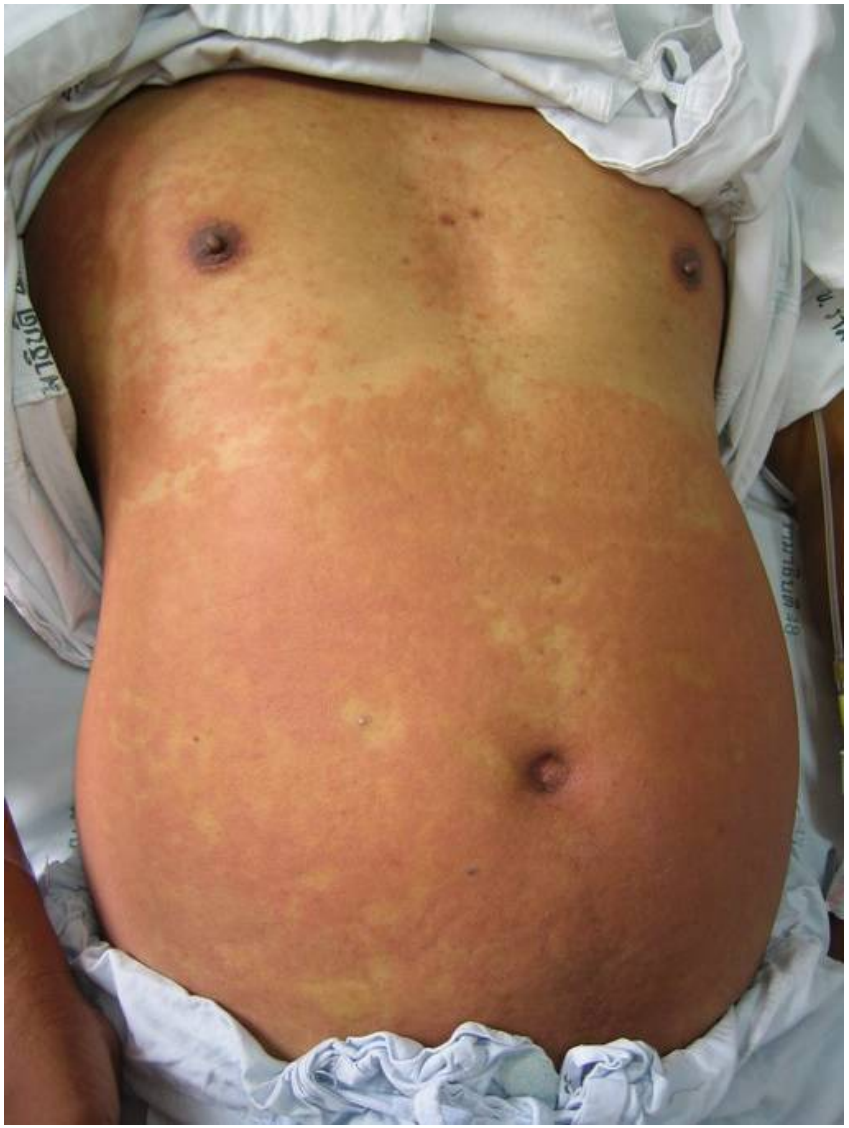
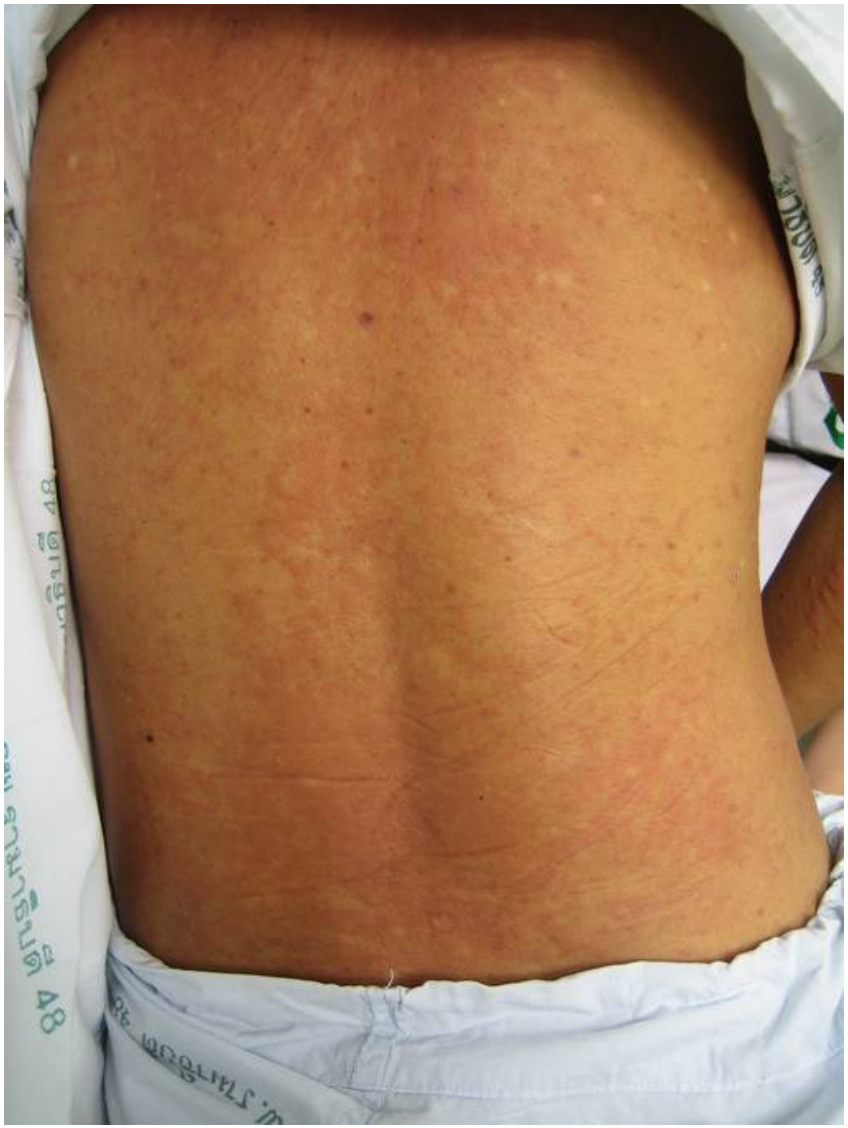
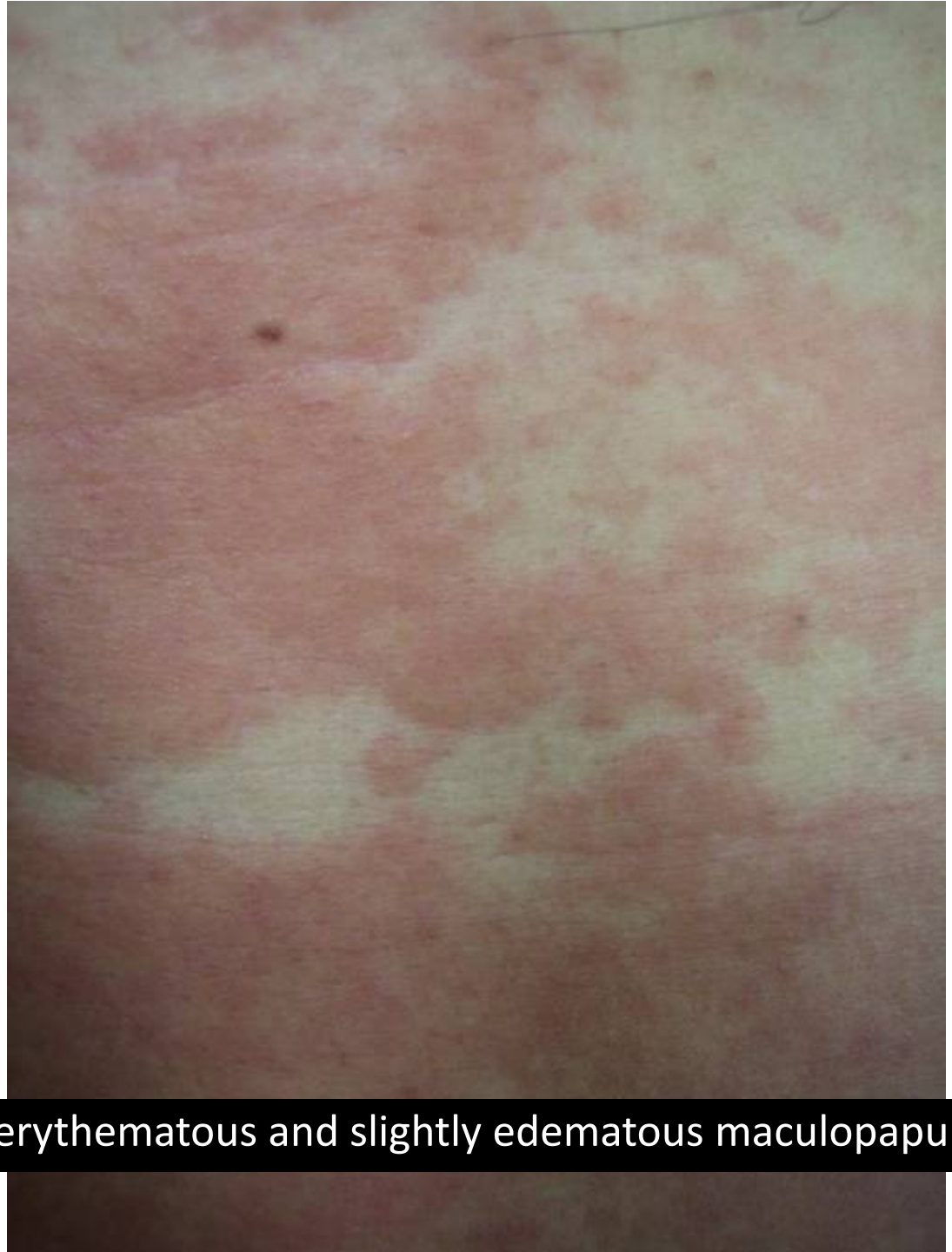
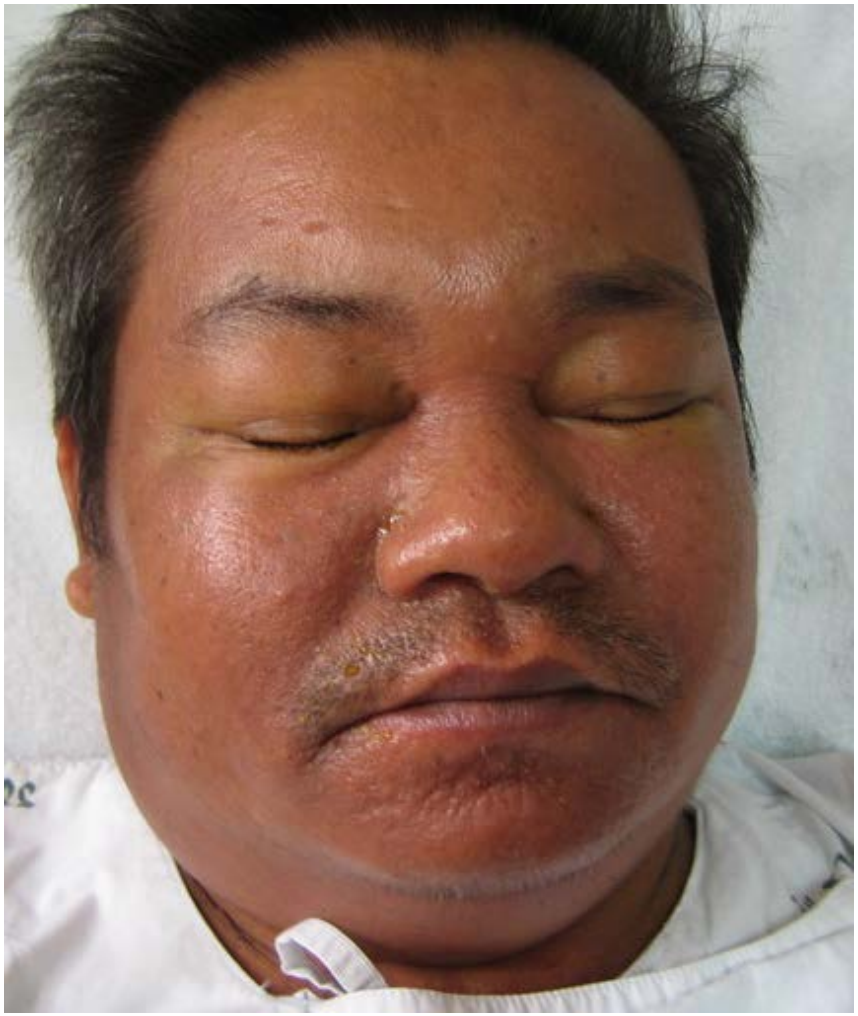


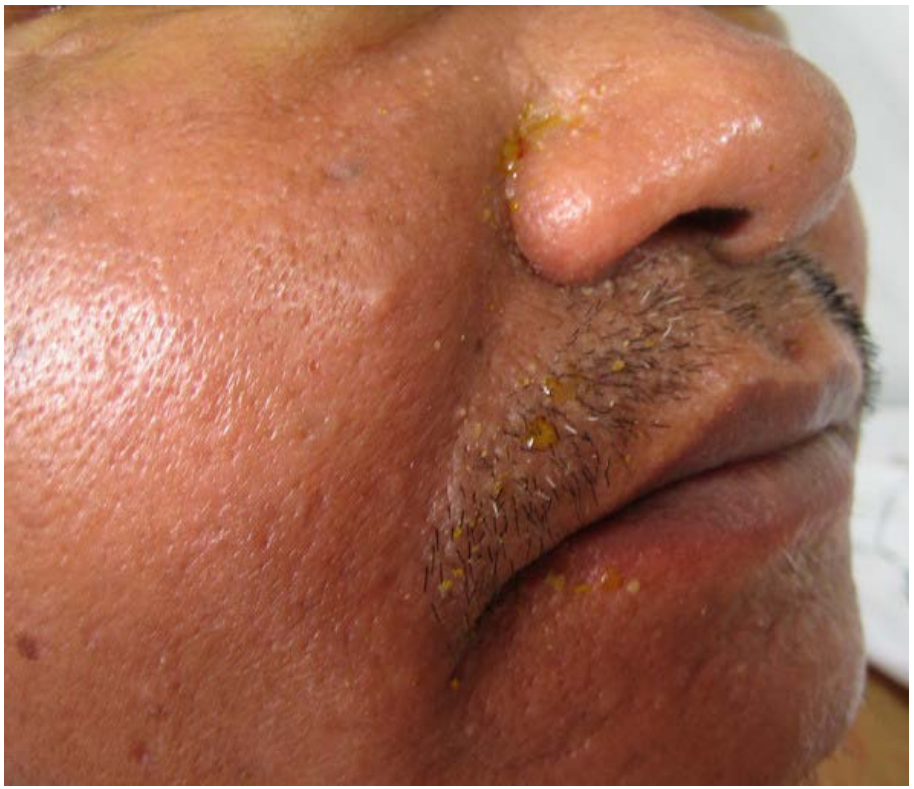






Generalized erythematous and slightly edematous maculopapular rashes





Erythema and edema of face and periorbital area

Investigations

	28/8/47	30/8/47	2/9//47
Total Eosinophil	1110	1690	2024
SGOT	42	98	69
SGPT	130	108	88

Your Dx is

D R E S S → ?

Drug Rash with Eosinophilia and Systemic Symptoms

Table II. Proposed criteria of the diagnosis for Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) [reproduced from Bocquet et al.,[51] with permission]

Cutaneous drug eruption[a]
Hematologic abnormalities[a]
Eosinophilia ≥1.5 10^9/L or
Presence of atypical lymphocytes
Systemic involvement[a]
Adenopathies ≥2cm in diameter or
Hepatitis (liver transaminases values ≥2 N) or
Interstitial nephritis or
Interstitial pneumonitis or
Carditis

a The proposed classification is based on three criteria. A person shall be said to have DRESS if three criteria are present.

- Aromatic antiepileptic agents (phenytoin, carbamazepine, phenobarbital)
- Sulfonamides, allopurinol, gold salts, dapsone, and minocycline.

Table III. Differential patterns of selected severe drug cutaneous adverse reaction (reproduced from Bocquet et al.,[51] with permission)

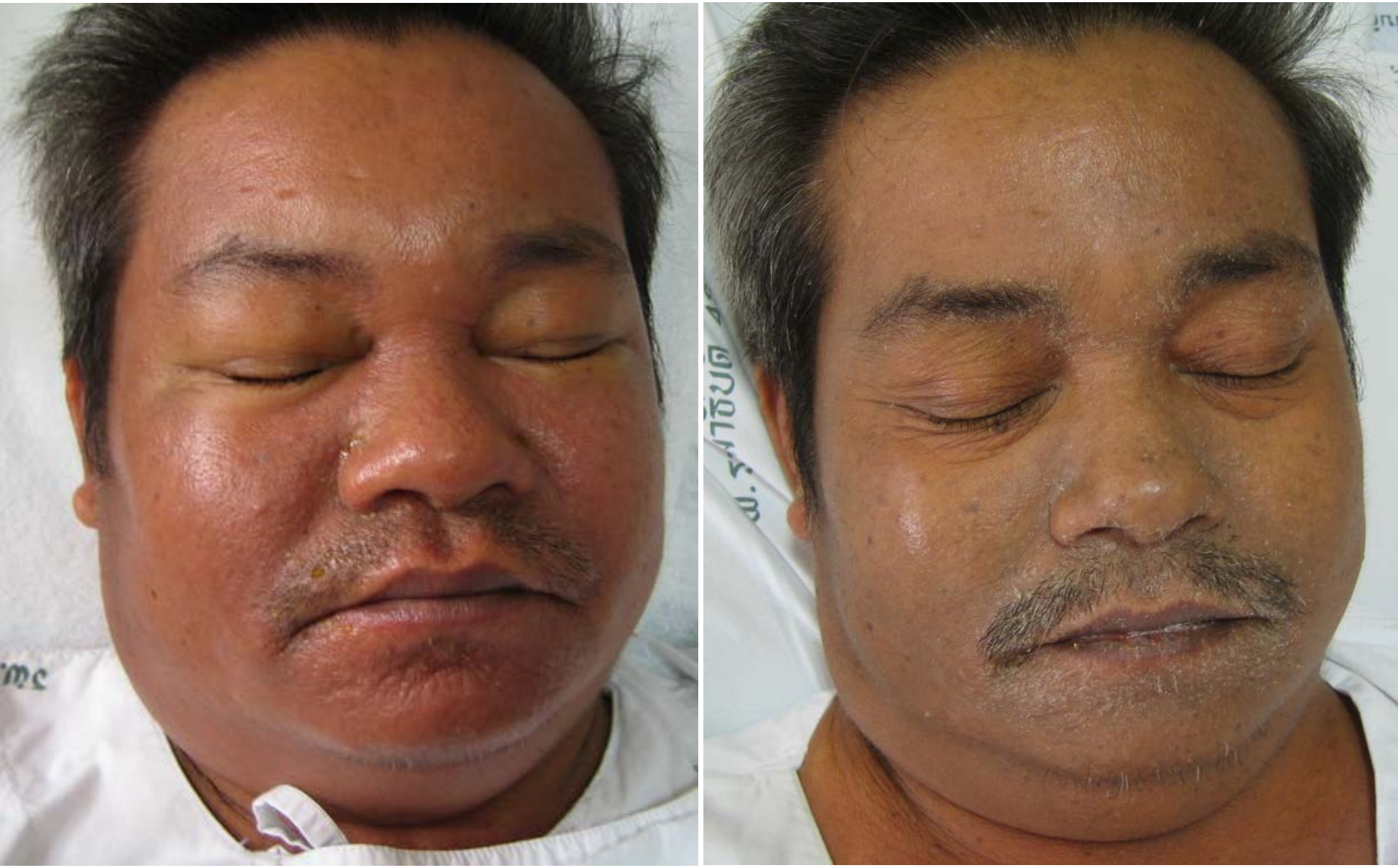
	DRESS	SJS/TEN	AGEP
Clinical signs			
Typical onset of eruption	2–6 weeks	1–3 weeks	48 hours
Typical duration of eruption	Several weeks	1–3 weeks	<1 week
Fever	+++	+++	+++
Infiltrated papules	+++	–	++
Facial edema	+++	–	++
Pustules	+	–	+++
Blisters	+[a] if edema is present	+++	+[a] if edema is present
Atypical target	+	+++	Rarely
Mucous membrane involvement	Cheilitis	+++	–
Lymph node enlargement	+++	–	+
Other organ involvement	+++[b]	+++[c]	+
Histological pattern			
Histological pattern of the skin	Lymphocytic infiltrate	Epidermal necrolysis	Subcorneal pustules
Histology of lymph nodes	Lymphoid hyperplasia pseudolymphoma	NA	NA
Laboratory values			
Hepatitis	+++	+	+
Neutrophil count	NI or ↑	↓	↑↑↑
Eosinophil count	↑↑↑	NI	↑
Atypical lymphocytes	++	–	+

a Tight blisters.

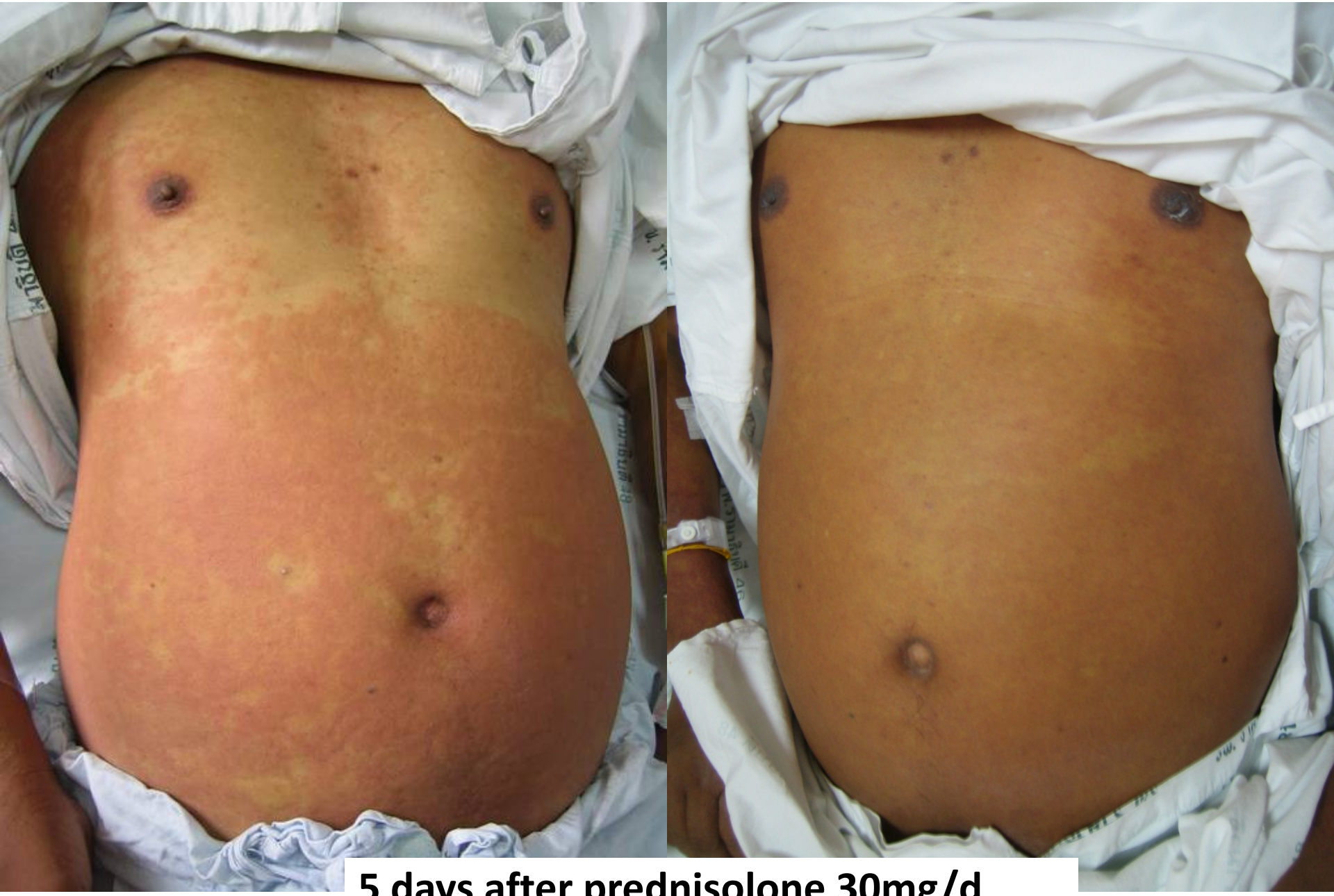
b Interstitial nephritis, interstitial pneumonitis, carditis, thyroiditis.

c Tracheobronchial necrosis, tubular nephritis.

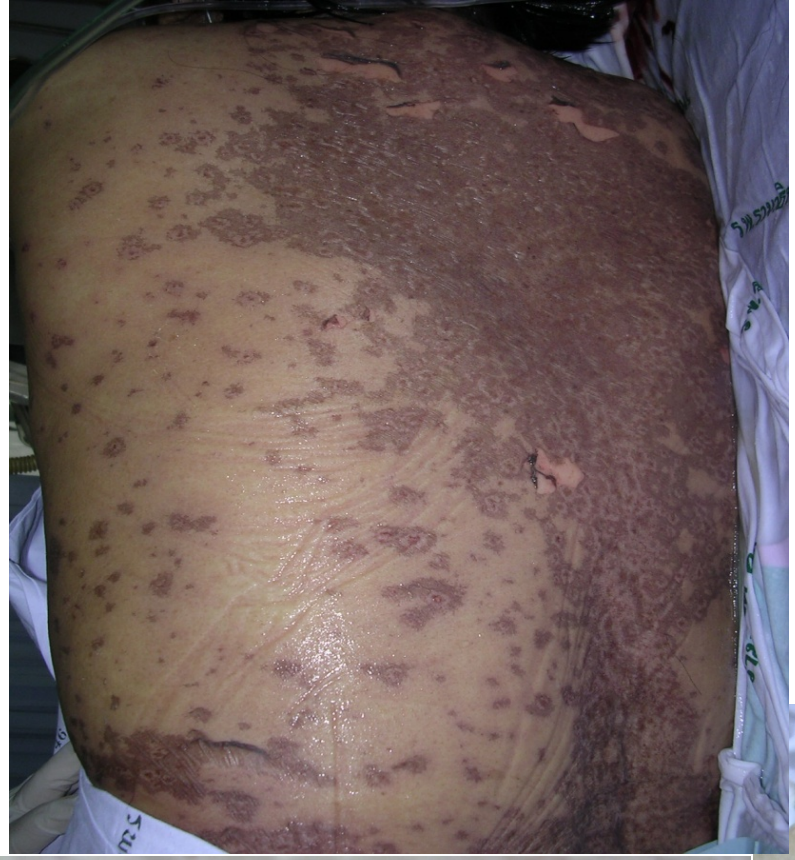
AGEP = acute generalized erythematous pustulosis; DRESS = drug rash with eosinophilia and systemic symptoms; NA = not applicable; NI = normal; SJS = Stevens-Johnson Syndrome; TEN = toxic epidermal necrolysis; + indicates the presence of the symptom, with the number of plus signs indicating the degree of severity of that symptom; – indicates that the symptom is not present; ↑ indicates elevation, with the number of arrows indicating the extent of the elevation; ↓ indicates a reduction.

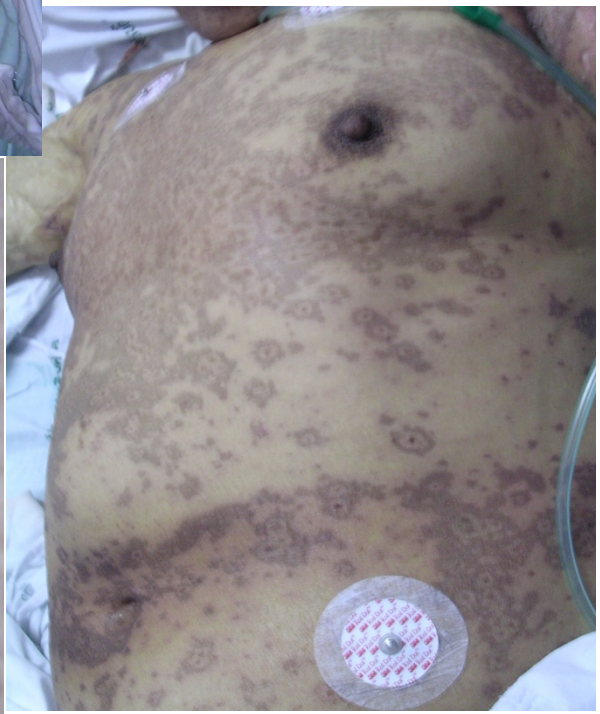


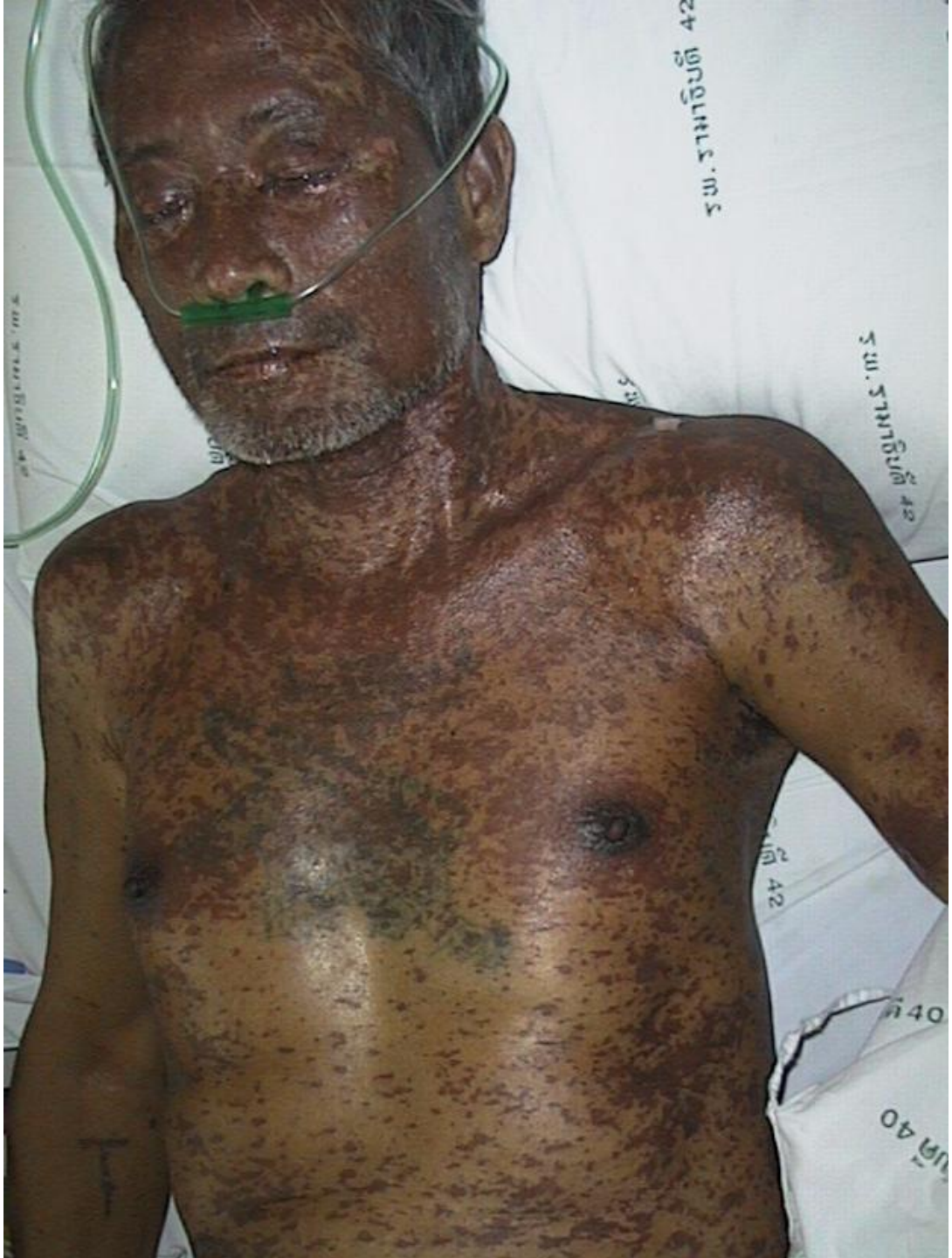
5 days after prednisolone 30mg/d



5 days after prednisolone 30mg/d







Gout after 2 weeks of allopurinol

Toxic Epidermal Necrolysis

allopurinol

Medications and the Risk of Epidermal Necrolysis

High Risk	Lower Risk	Doubtful Risk
Allopurinol	Acetic acid NSAIDs (e.g., diclofenac)	Paracetamol (acetaminophen)
Sulfamethoxazole	Aminopenicillins	Pyrazolone analgesics
Sulfadiazine	Cephalosporins	Corticosteroids
Sulfapyridine	Quinolones	Other NSAIDs (except aspirin)
Sulfadoxine	Cyclins	Sertraline
Sulfasalazine	Macrolides	
Carbamazepine		
Lamotrigine		
Phenobarbital		
Phenytoin		
Phenylbutazone		
Nevirapine		
Oxicam NSAIDs		
Thiacetazone		

Approach to the Acute Generalized Blistering Patient

History **New Drug**

Physical examination :

Investigation :

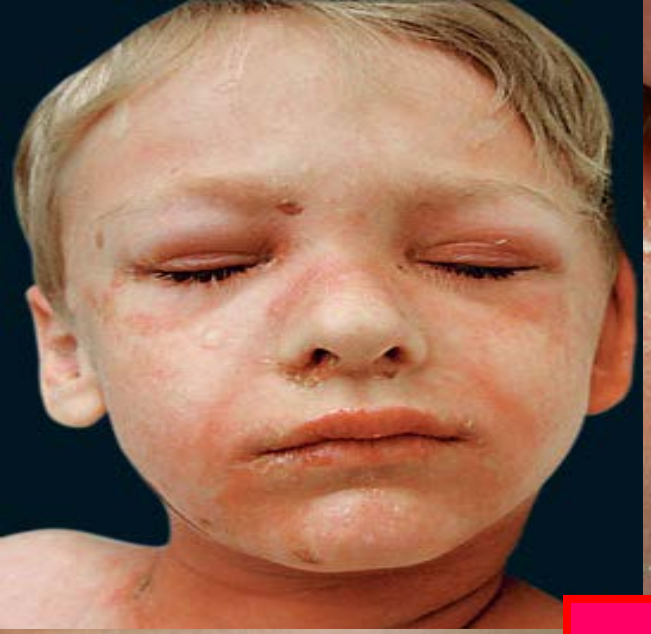
Table 1 Differential Diagnosis of the Acute, Generalized Blistering Patient

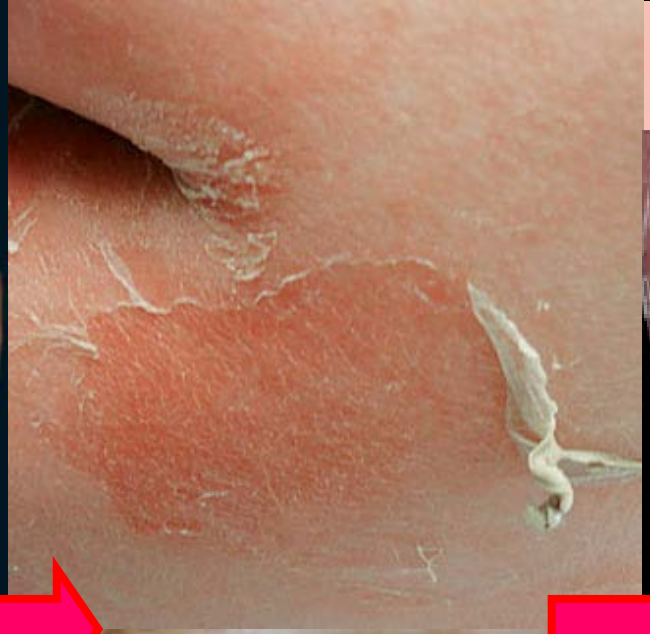
Disease	Mucosal Involvement	Acute/ Insidious	Lesions	DIF	Other Salient Features
Stevens-Johnson syndrome/Toxic epidermal necrolysis	Yes (usually >2 mucosal surfaces involved)	Acute	Initial lesions are macular; can progress to targetoid lesions that may form flaccid bullae (generally monomorphous).	–	Prodromal flu-like symptoms; likelihood of drug reaction increases with increasing severity
Staphylococcal scalded skin syndrome	No	Acute	Initially tender erythema that progresses to generalized desquamation/blistering.	–	Abrupt constitutional symptoms: fever, erythema, skin tenderness. More common in neonates and young children, possible sign of renal disease/immunodeficiency if in an adult.
Pemphigus vulgaris	Yes (usually abscent in drug-induced)	Variable	Flaccid, easily-ruptured bullae with a positive Nikolsky sign. Oral involvement first in 60%.	+	Often presents in middle age. May be mucous membrane predominate or mucocutaneous. Also drug-induced and drug-triggered PV variant.
Pemphigus foliaceus	No	Variable	Lesions begin as small bullae that erode easily and become chronic. Crusting of the lesions is common. No mucous membrane involvement.	+	Often presents in middle age. These patients usually are not severely ill and lesional symptoms are the primary concern.
Paraneoplastic pemphigus	Yes (usually severe)	Insidious	Typified by painful mucous membrane ulcerations and a polymorphous skin eruption.	+	Most often >60 years old. Develops in presence of a neoplasm, especially leukemia, lymphoma and Castleman's tumor.
Bullous pemphigoid	Sometimes-20% (rare in drug-induced)	Insidious	Subepidermal blisters that present as tense blistering of the skin, often accompanied by erythema and urticarial plaques	+	Predilection for intertriginous areas, trunk, thighs and forearm flexor surfaces. May arise in areas of trauma (in psoriasis, irradiated skin). Also drug-induced BP variant.
Acute Graft-vs-host disease	Yes (most commonly conjunctival)	Acute	Morbilliform rash; may be preceded by pruritis or burning. Often begins with folliculocentric punctate lesions.	–	May be accompanied by gastrointestinal and liver involvement. Most commonly seen after allogenic hematopoietic stem cell transplantation.
Linear IgA dermatosis	Yes (50% of idiopathic, rare in drug-induced)	Acute	Presentation can vary from urticarial plaques, to vesicles, to bullae, to generalized exfolation.	+	Drug-induced most common with vancomycin (5/7 cases presenting as TEN associated with vancomycin).

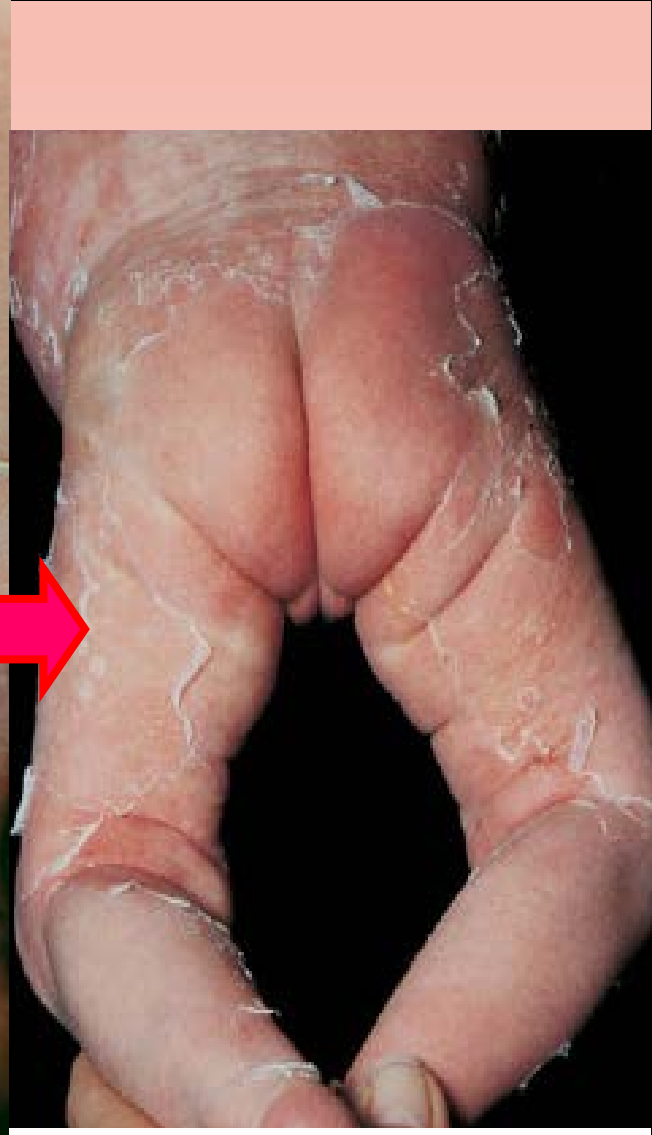
Table II. Differential diagnosis of TEN

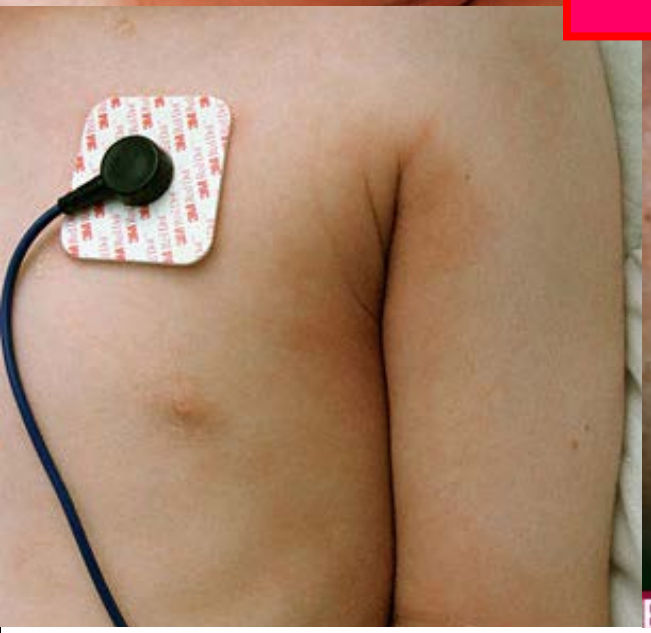
Bullous disease	Fever	Mucositis	Morphology	IF	Onset	Miscellaneous features
Drug-induced pemphigoid	No	Rare	Tense bullae (sometimes hemorrhagic)	+	Acute	Diuretics a common cause, especially spironolactone; often pruritic
Staphylococcal scalded skin syndrome	Yes	Absent	Erythema, skin tenderness, periorificial crusting	−	Acute	Affects children under 5, adults on dialysis, and those on immunosuppressive therapy
Drug-induced pemphigus	No	Usually absent	Erosions, crusts, patchy erythema (resembles pemphigus foliaceous)	±	Gradual	Commonly caused by penicillamine and other "thiol" drugs; resolves after inciting agent is discontinued
Drug-triggered pemphigus	No	Present	Mucosal erosions, flaccid bullae	+	Gradual	Caused by "non-thiol" drugs; persists after discontinuation of drug; may require long-term immunosuppressive therapy
Paraneoplastic pemphigus	No	Present (usually severe)	Polymorphous skin lesions, flaccid bullae	+	Gradual	Resistant to treatment; associated with malignancy, especially lymphoma
Acute graft-versus-host disease	Yes	Present	Morbilliform rash, bullae and erosions	−	Acute	Closely resembles TEN
Acute generalized exanthematous pustulosis	Yes	Rare	Superficial pustules (resembles pustular psoriasis)	−	Acute	Self-limiting on discontinuation of drug
Drug-induced linear IgA bullous dermatosis	No	Rare	Tense, subepidermal bullae (resembles pemphigoid)	+	Acute	Vancomycin most commonly implicated drug; pruritus often present

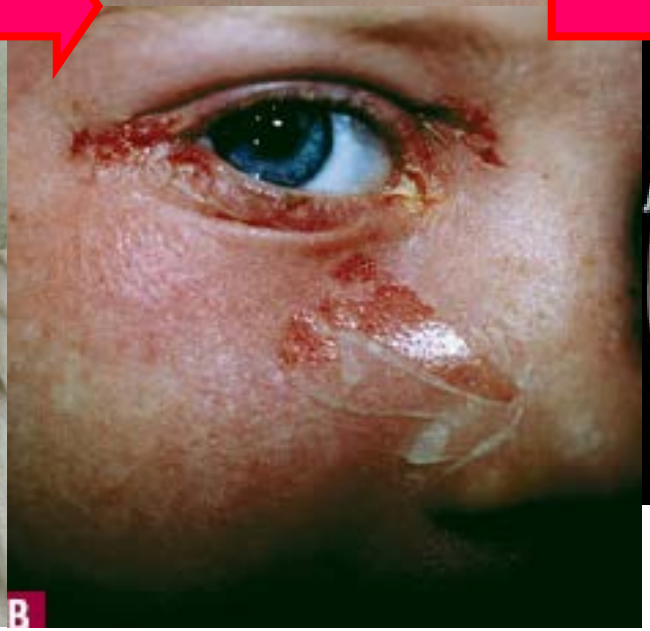
Differential diagnosis of **TEN**











Generalized exanthem
Cutaneous tenderness

→

Blistering ,denudation
Nikolsky sign +

→

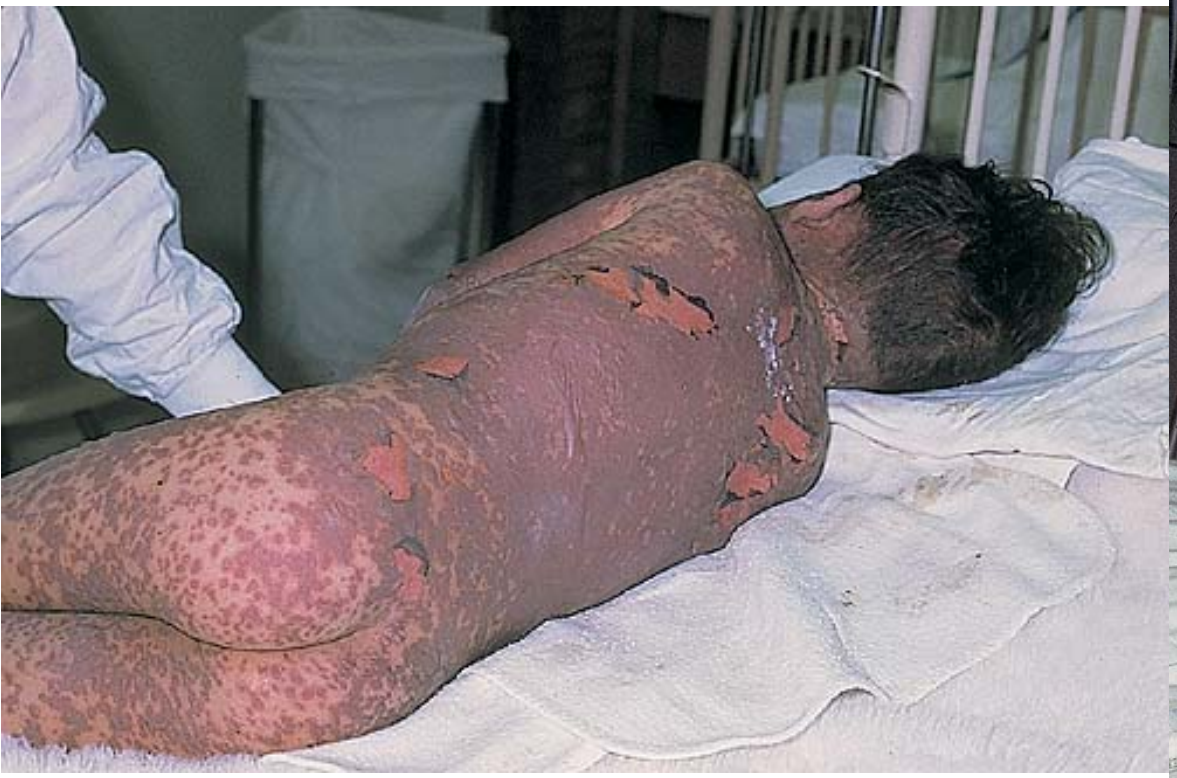
Generalized
desquamation

Apoptosis

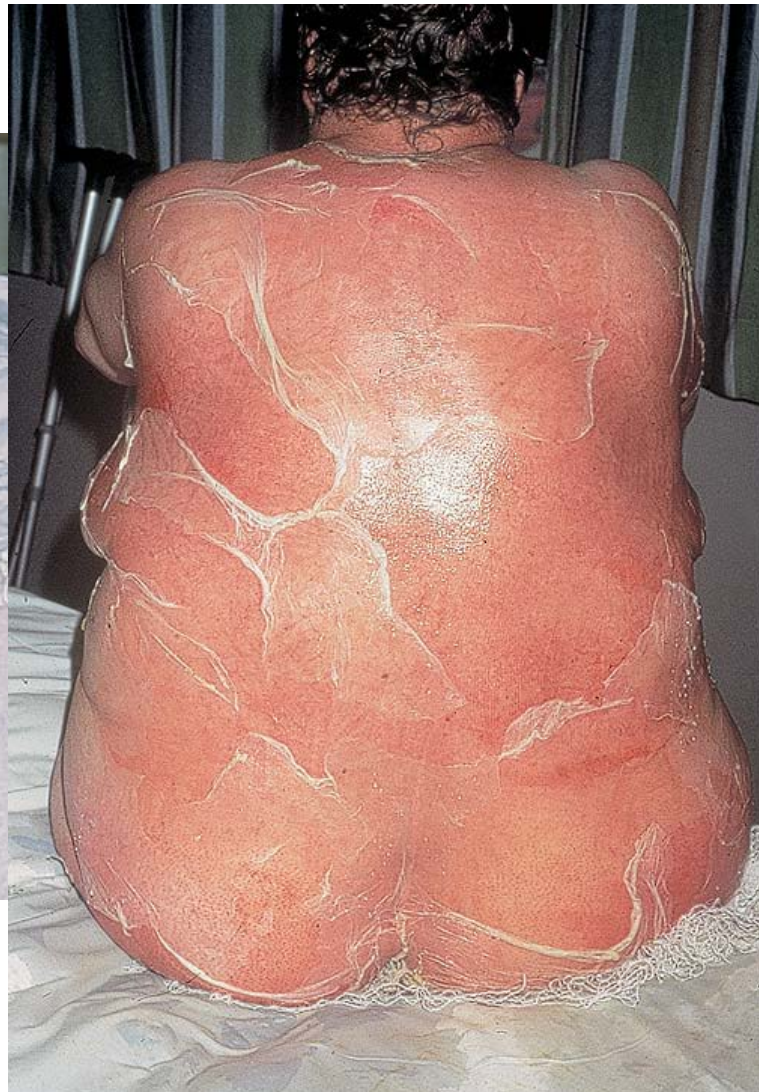
desmoglein-1

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 (-lactamase resistant) and supportive care

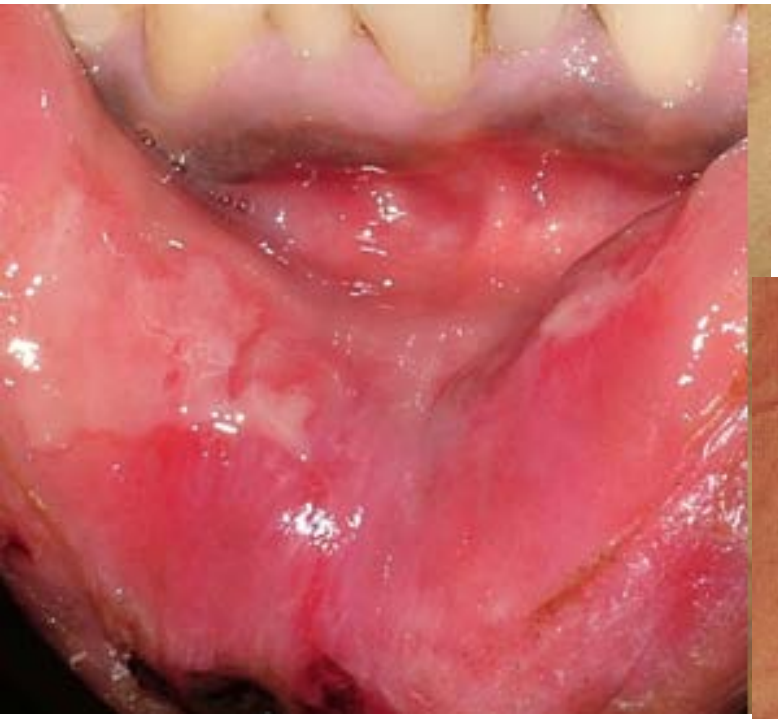
TEN

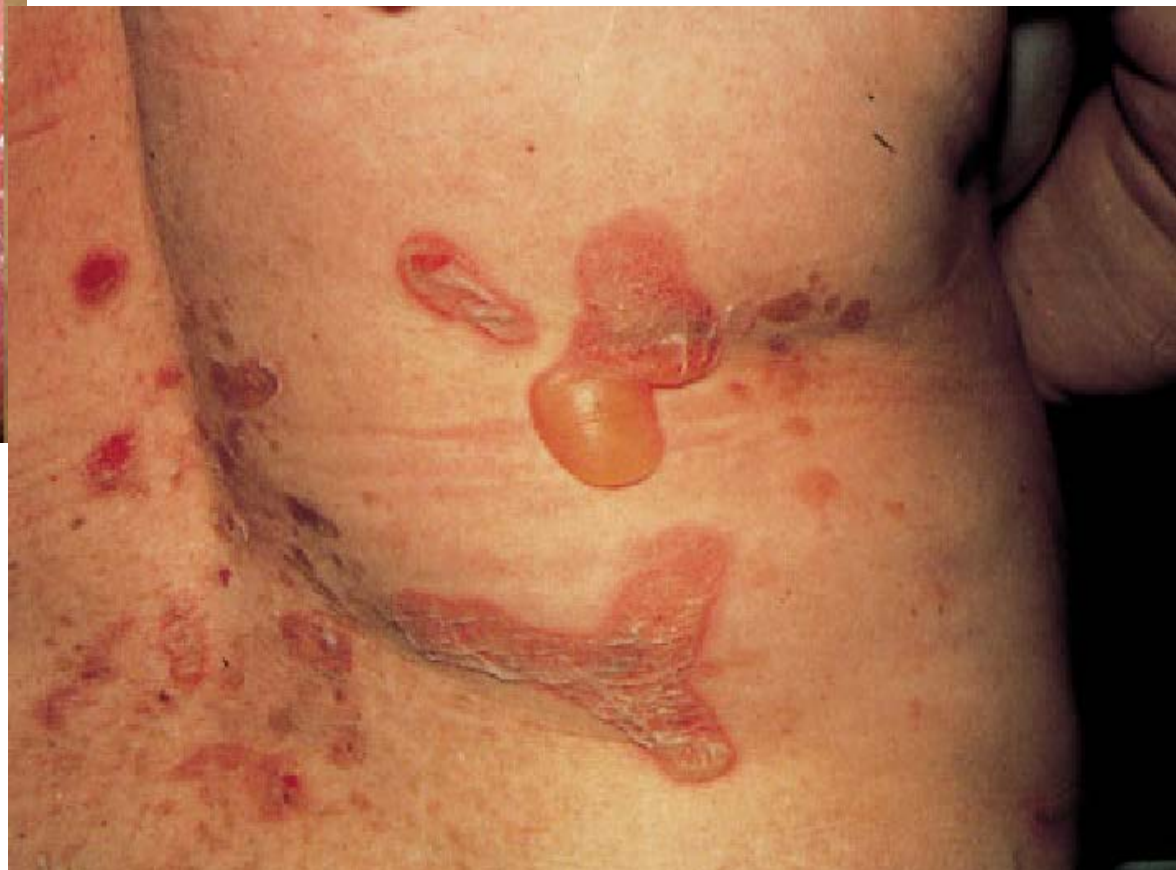


SSSS

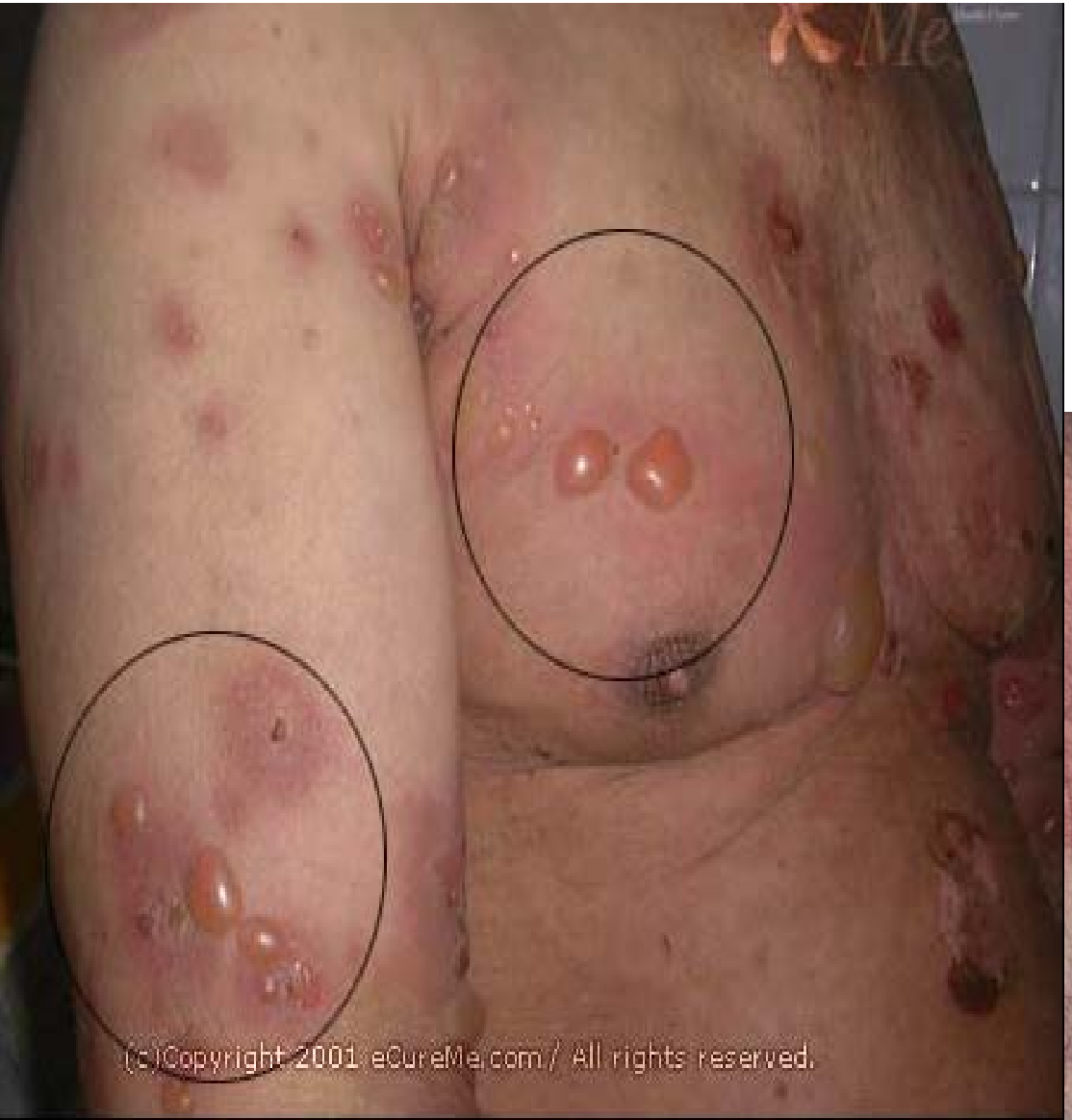


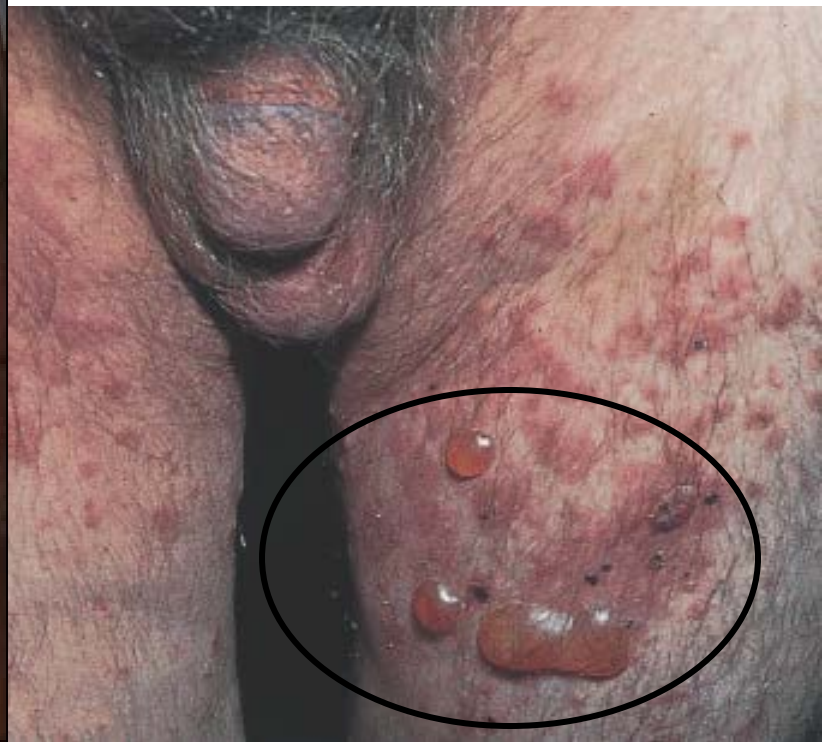
Pemphigus vulgaris



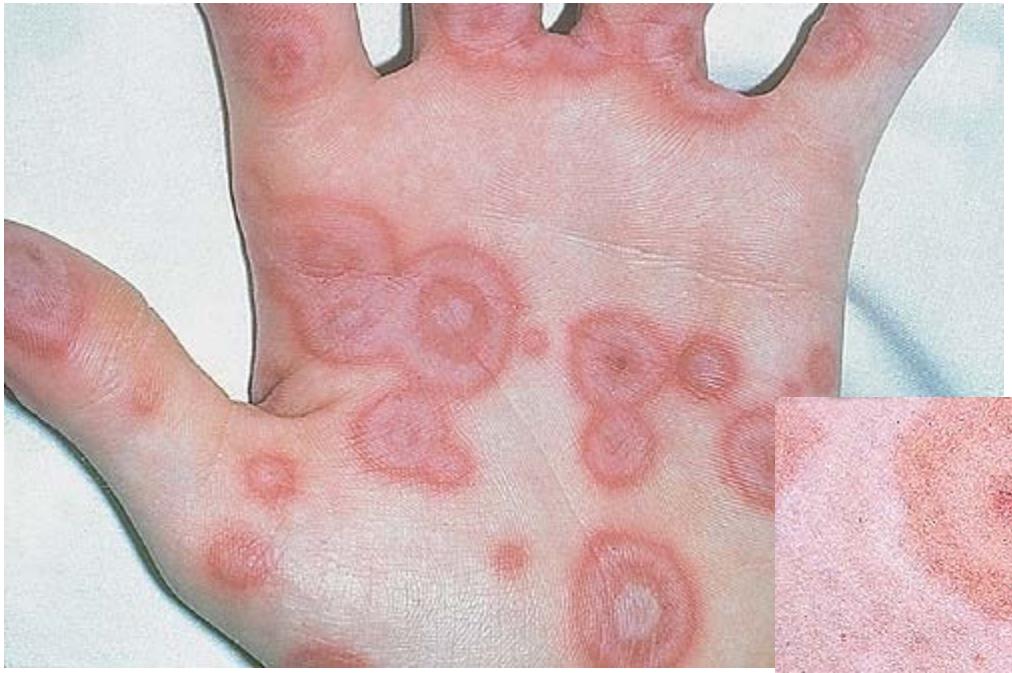


Bullous pemphigoid





Erythema multiforme



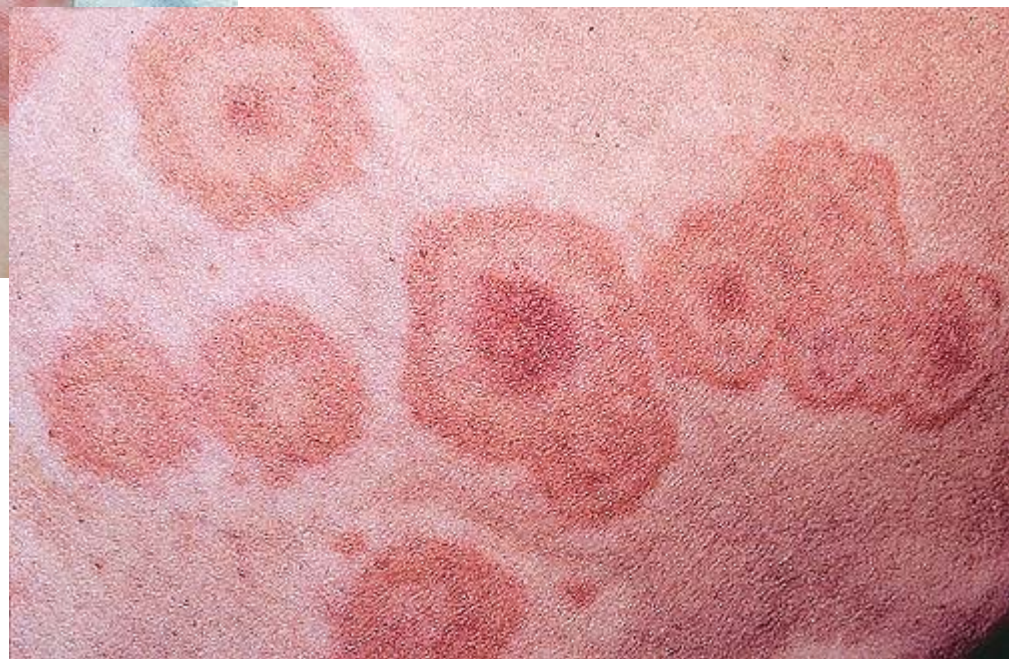
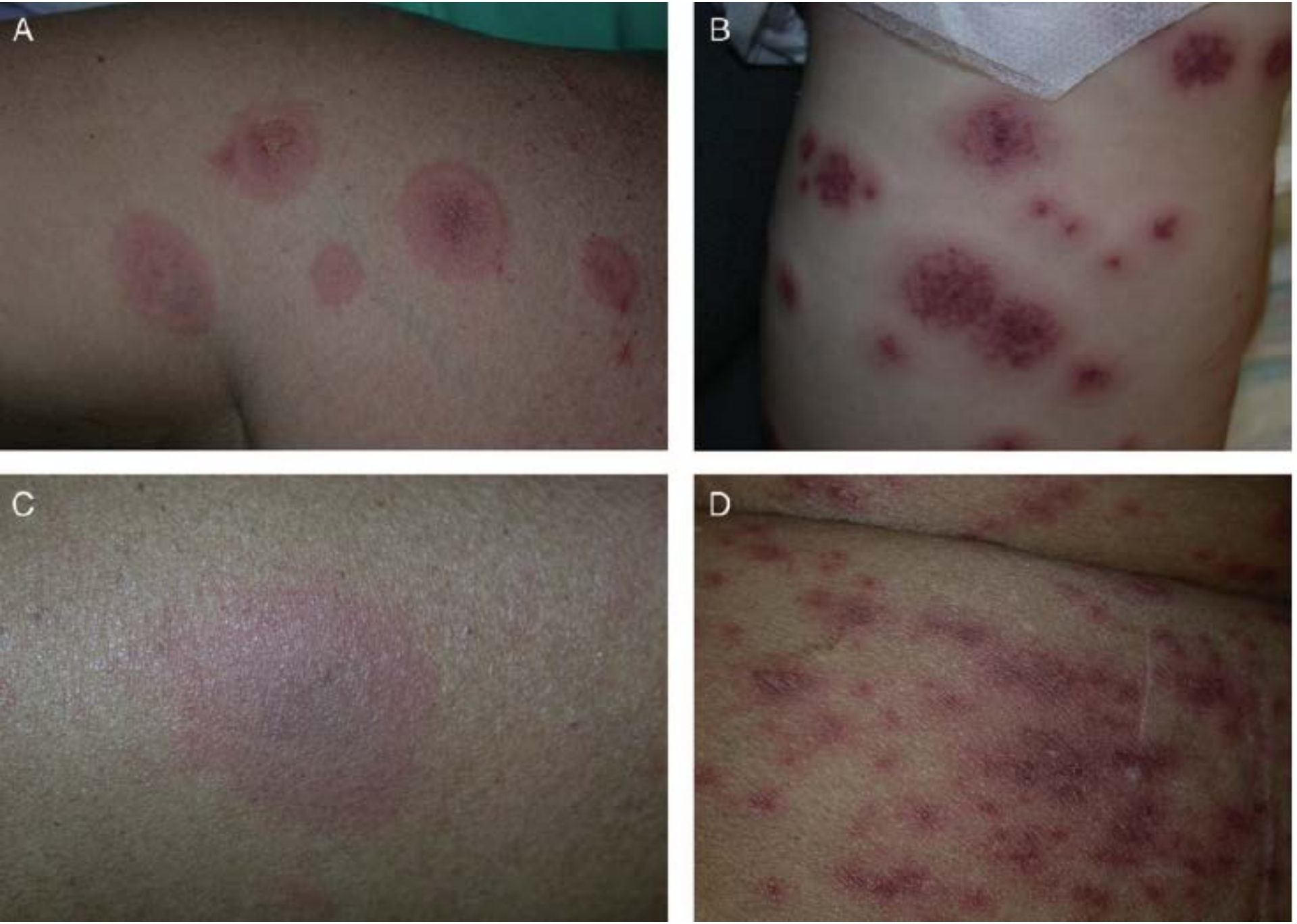


Table 2. Differentiating factors between erythema multiforme and Stevens–Johnson syndrome/toxic epidermal necrolysis

	Erythema multiforme	SJS/TEN
Lesion morphology	Typical three zone targets and raised atypical two-zone targets	Flat atypical two-zone targets and macules
Percent detachment	<10%	<10%–>30%
Distribution	Acral and extremities	Widespread and truncal
Underlying erythema	Localized	Diffuse
Etiology	Herpes simplex virus and other infections, rarely drugs	Drugs (small percentage of cases secondary to infection)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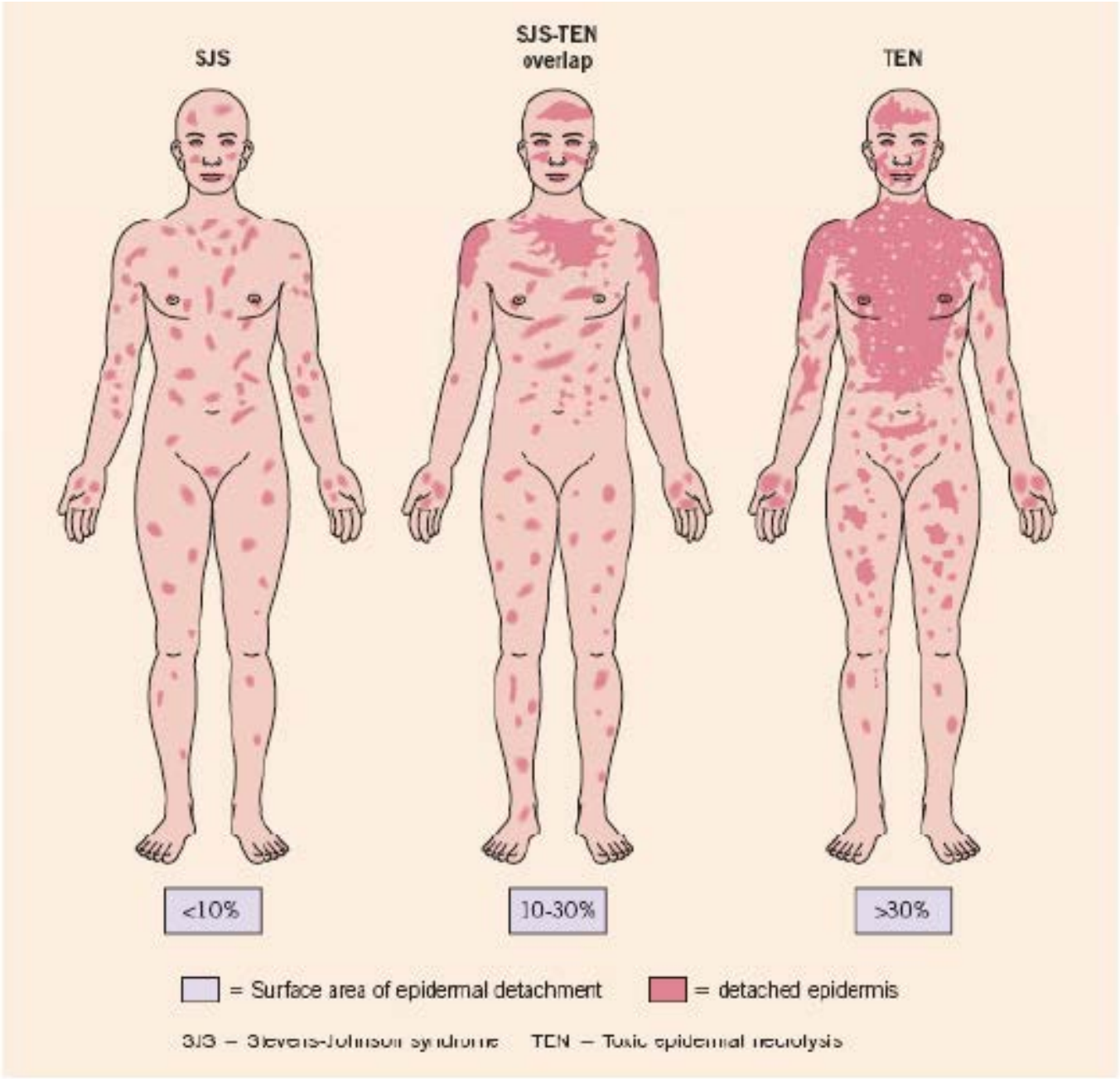
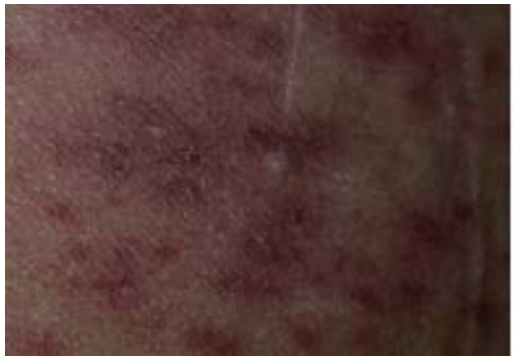
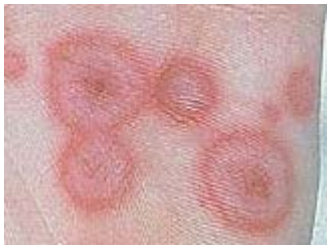

SJS
SJS-TEN overlap
TEN
<10%
10-30%
>30%
= Surface area of epidermal detachment
= detached epidermis
SJS – Stevens-Johnson syndrome
TEN – Toxic epidermal necrolysis

Take home pictures

- **SJS/TEN** : atypical target,

  drug >>other



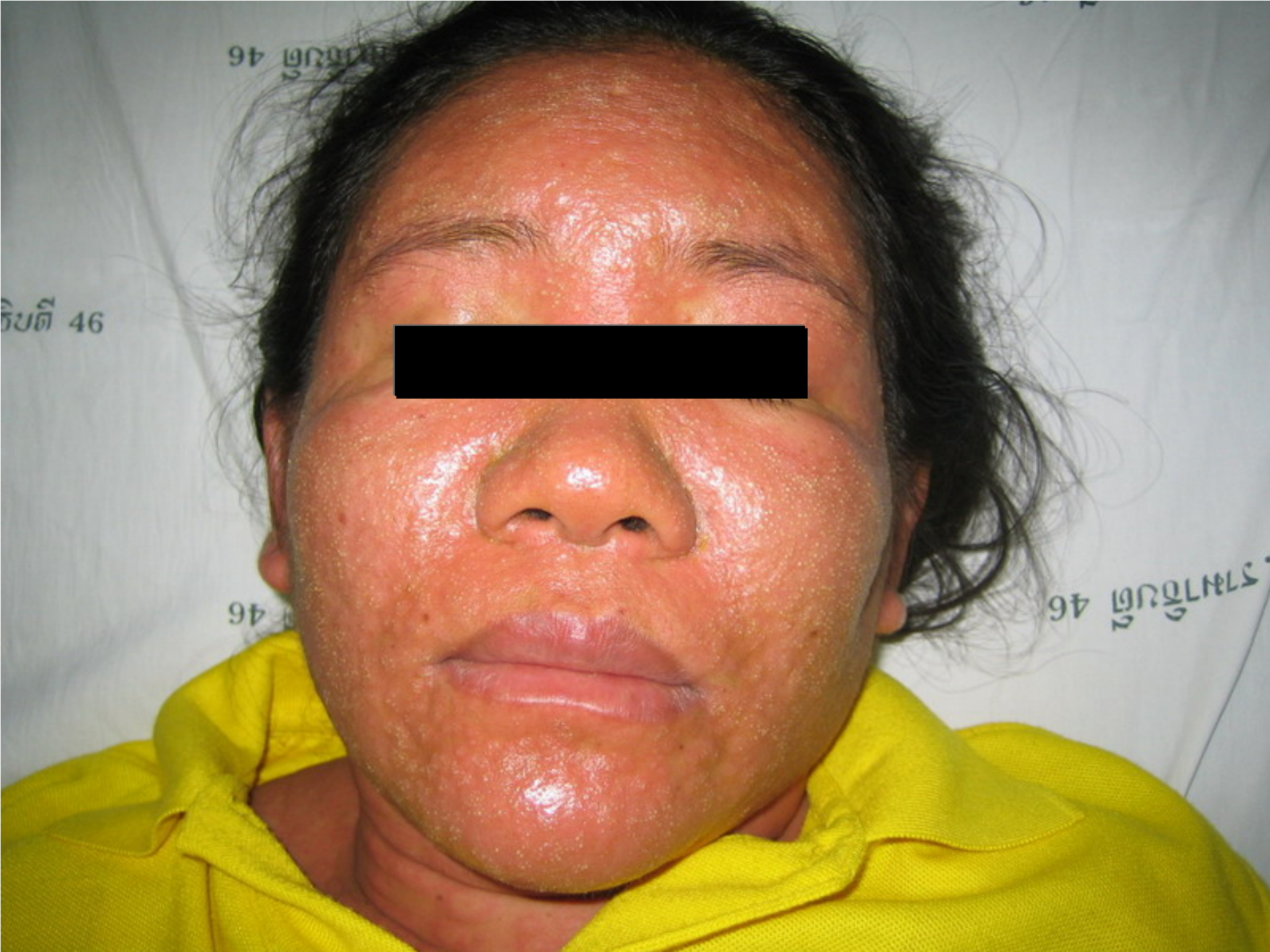


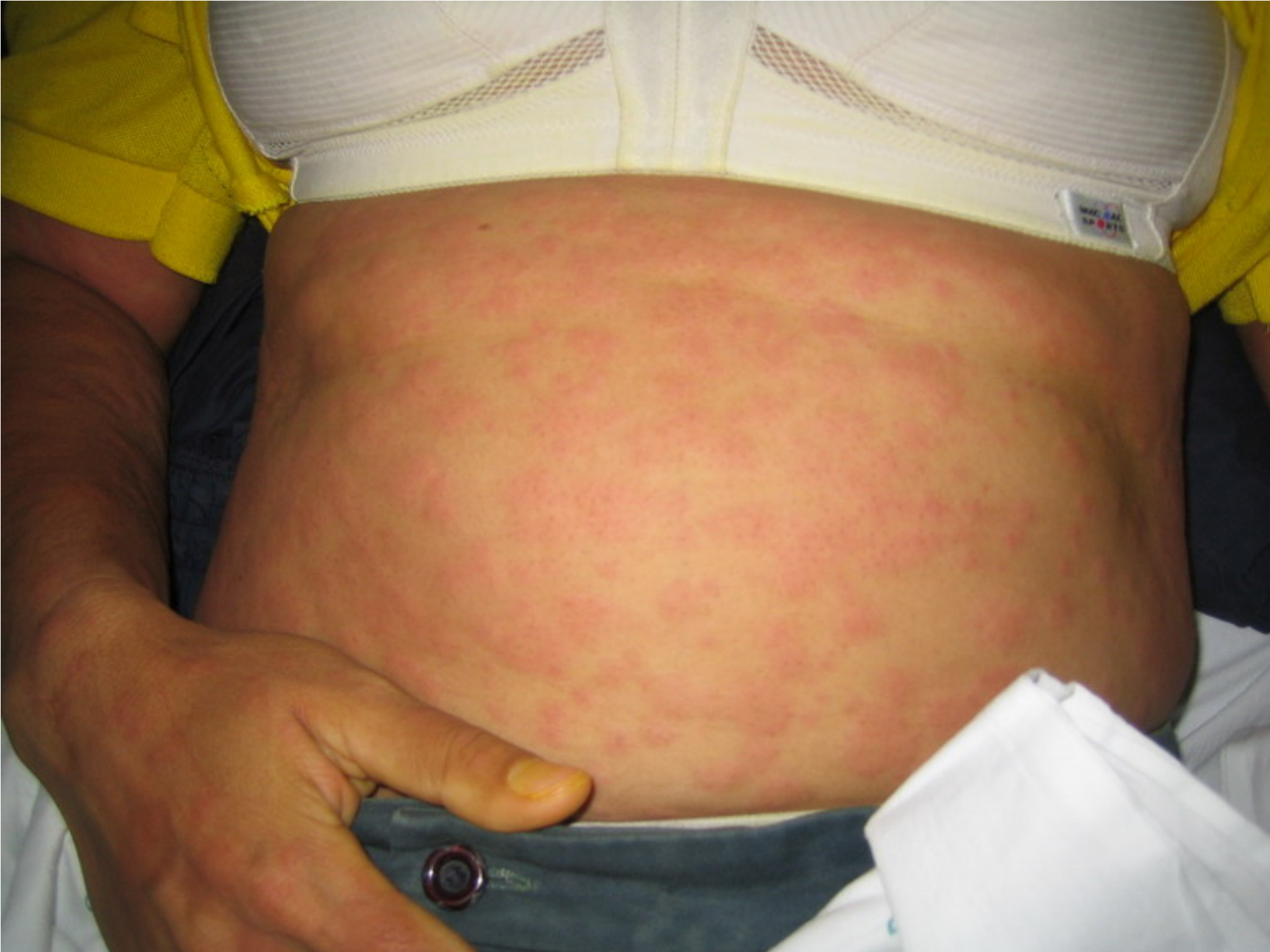
- **Erythema multiforme** : typical target

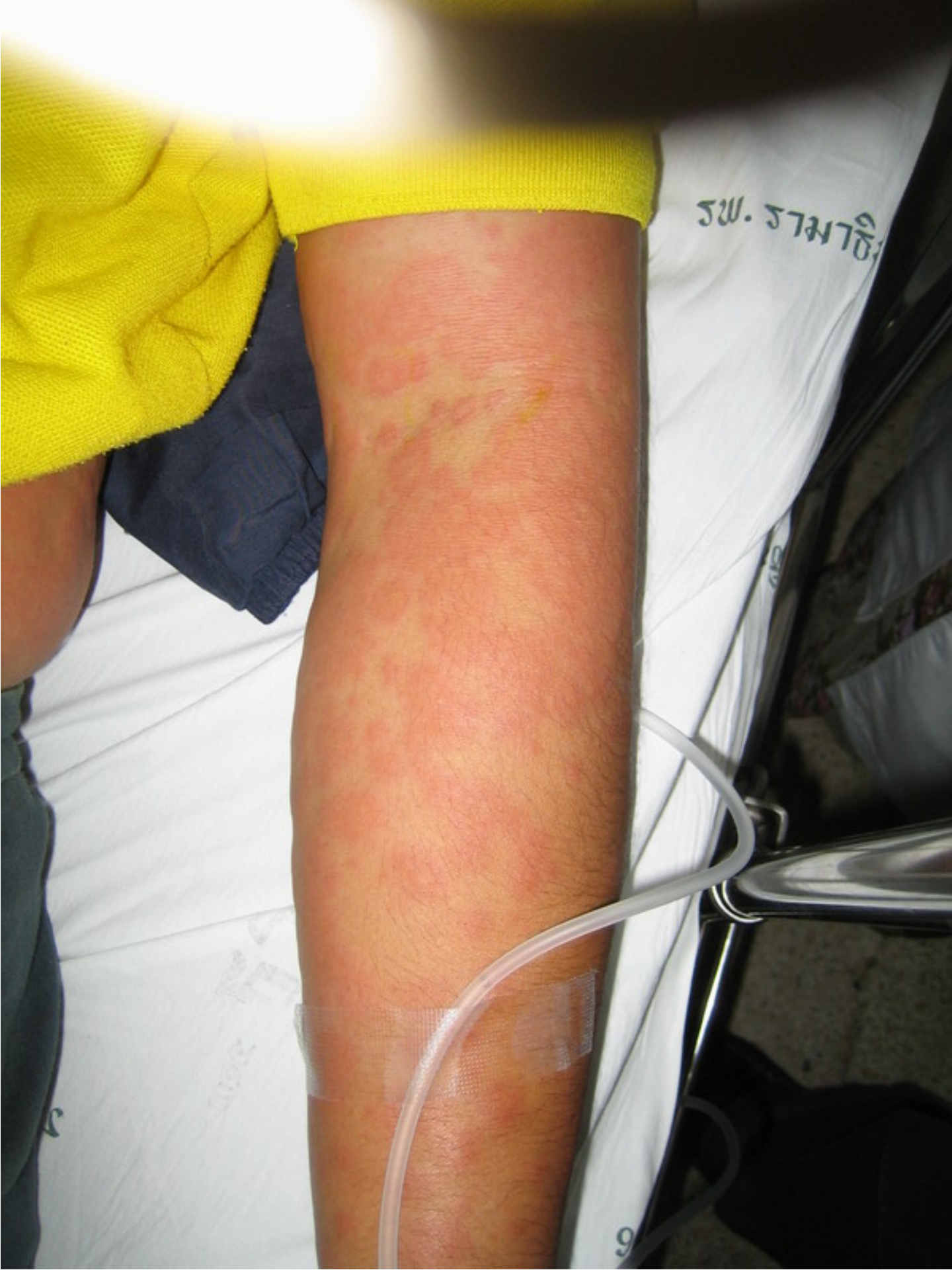
TABLE 40-3

Clinical Features That Warn of a Potentially Severe Drug Reaction

- Systemic
  - Fever and/or other symptoms of internal organ involvement such as pharyngitis, malaise, arthralgia, cough, and meningism
  - Lymphadenopathy
- Cutaneous
  - Evolution to erythroderma
  - Prominent facial involvement ± edema or swelling
  - Mucous membrane involvement (particularly if erosive or involving conjunctiva)
  - Skin tenderness, blistering or shedding
  - Purpura



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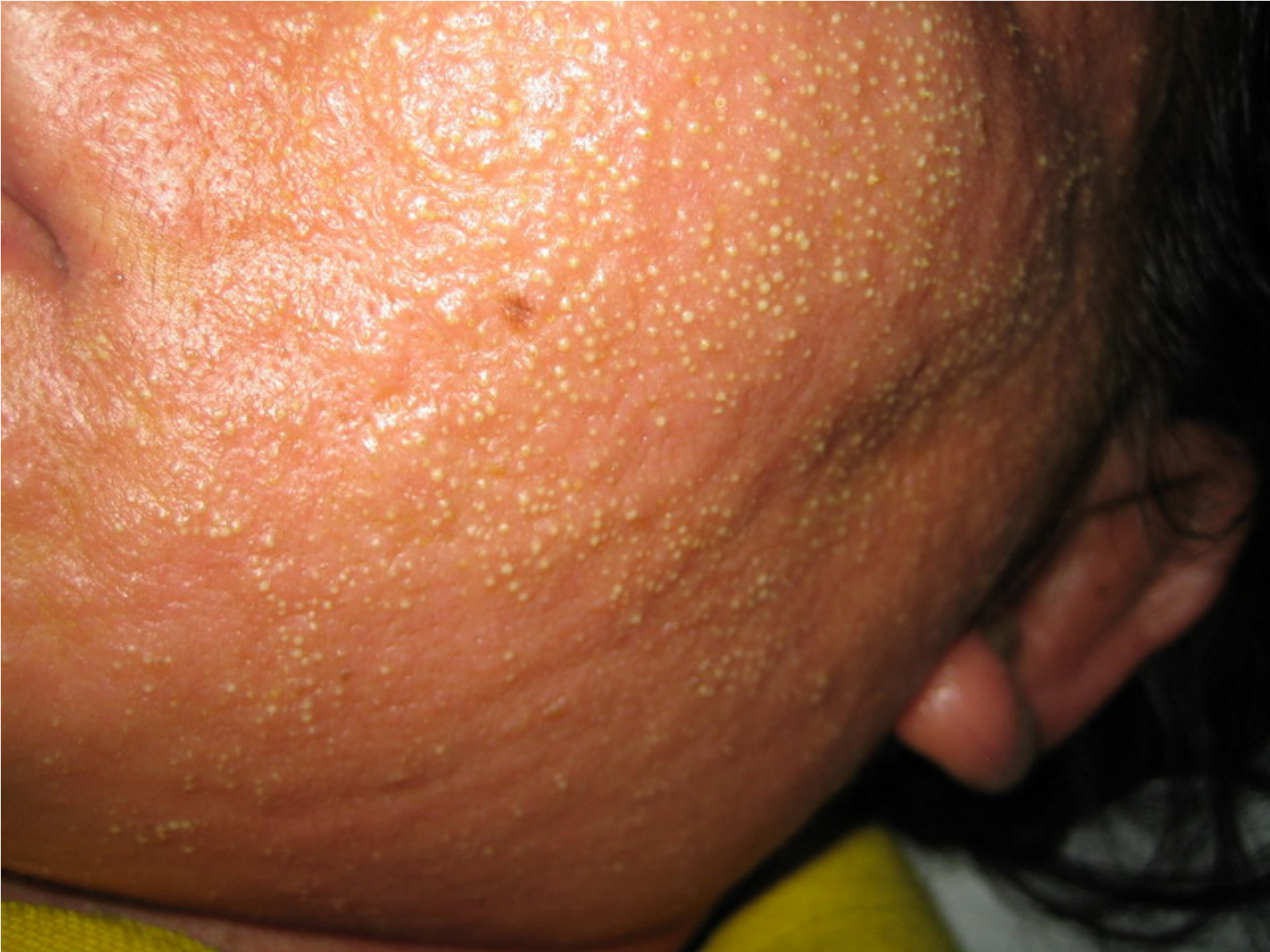


8/2 13/2

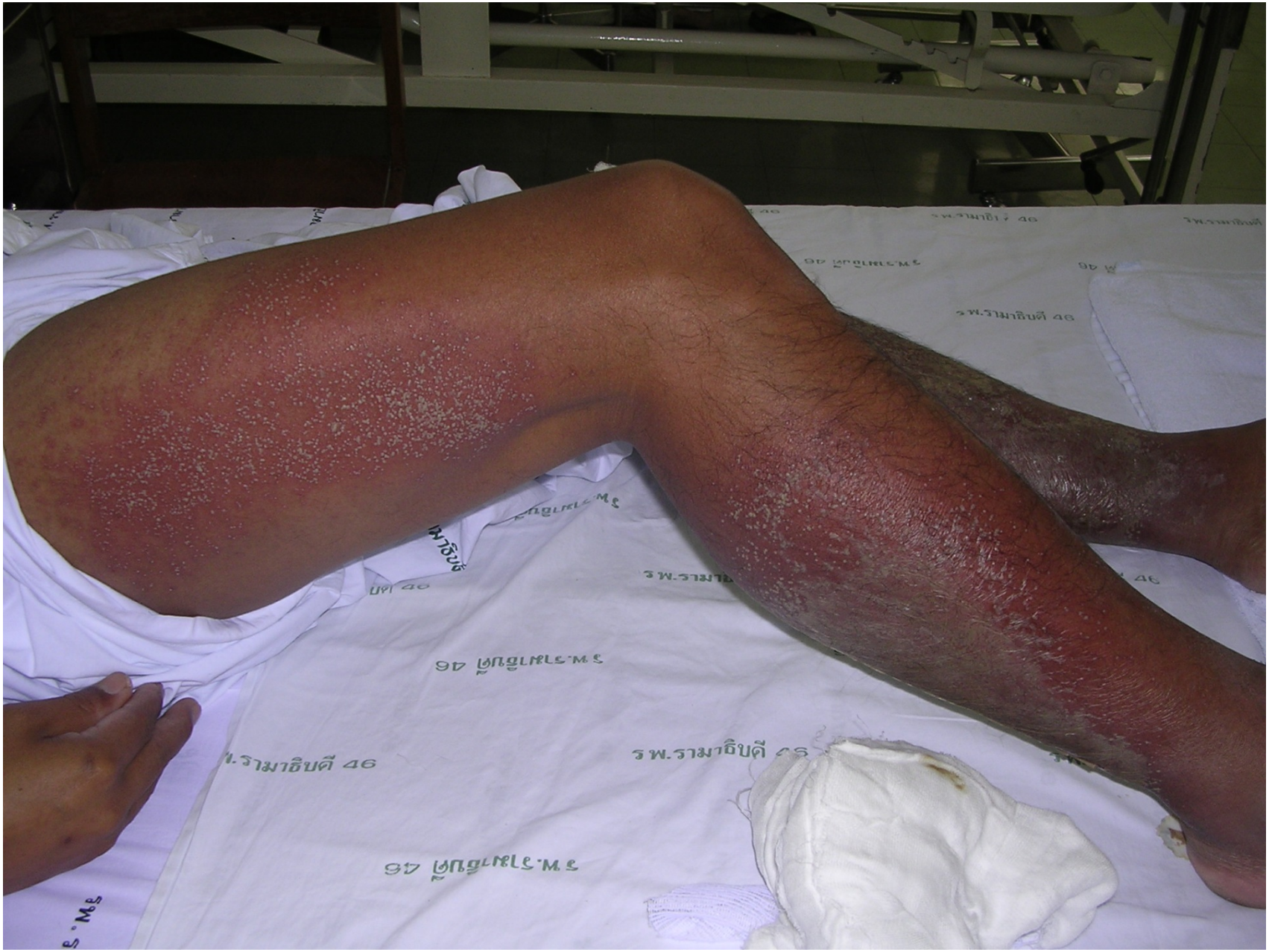
- Cephalexin
- Metronidazole
- Celecoxib

RASH

เคยได้ ampicillin 1-5 Dec 2006
cefoxitin 8-11 Jan 2007

- Dx Acute generalized exanthematous pustulosis due to?
-
- Rx D/C Cephalexin, Metronidazole, Celecoxib 0.1%
  Triamcinolone lotion bid

  Hydroxizine(10) 1*3 pc
  Prednisolone 30 mg/d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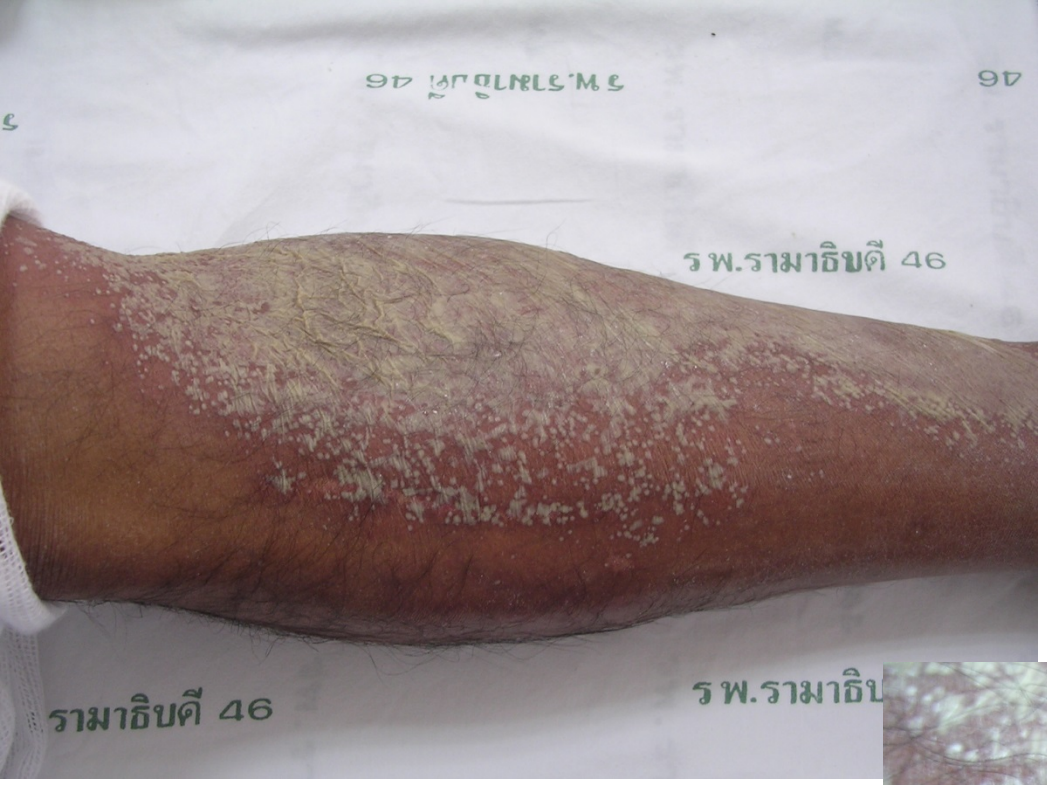
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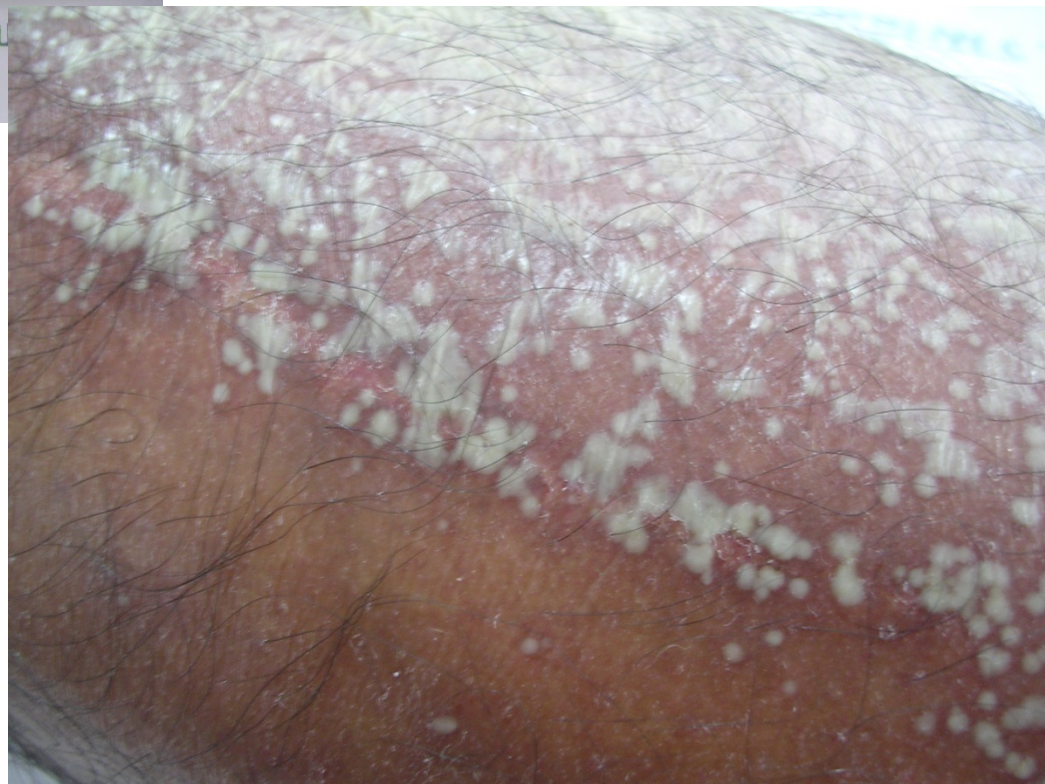
รามาธิบดี 46



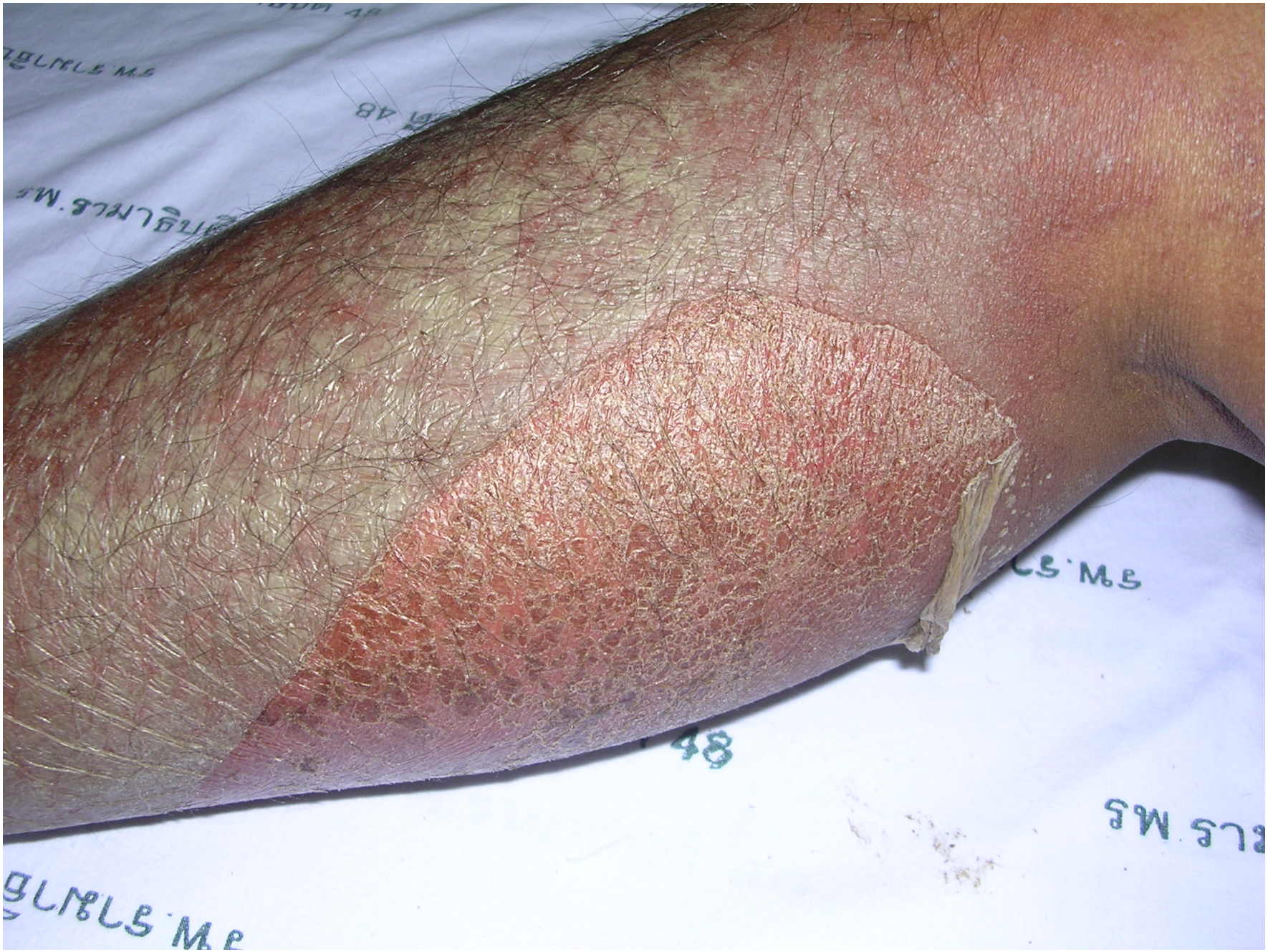


Table 1. Differentiation between generalised AGEP and GPP (10–12)

Feature	AGEP	GPP
History of psoriasis	No	Usually
History of drug reaction	Usual	Uncommon
Recent drug administration	Very frequent	Less frequent
Duration of fever	Shorter	Longer
Duration of pustules	Shorter	Longer
Arthritis	Rare	30%
Recurrence	No	Frequent
Histopathology	Cells include neutrophils and eosinophils subcorneal blisters, mild spongiosis, and a sparse infiltrate of neutrophils and eosinophils in the papillary dermis	Subcorneal and/or intraepidermal pustules, papillomatosis, acanthosis

The Journal of dermatology.vol 30:732-726,2003

AGEP validation score of EuroSCAR study group

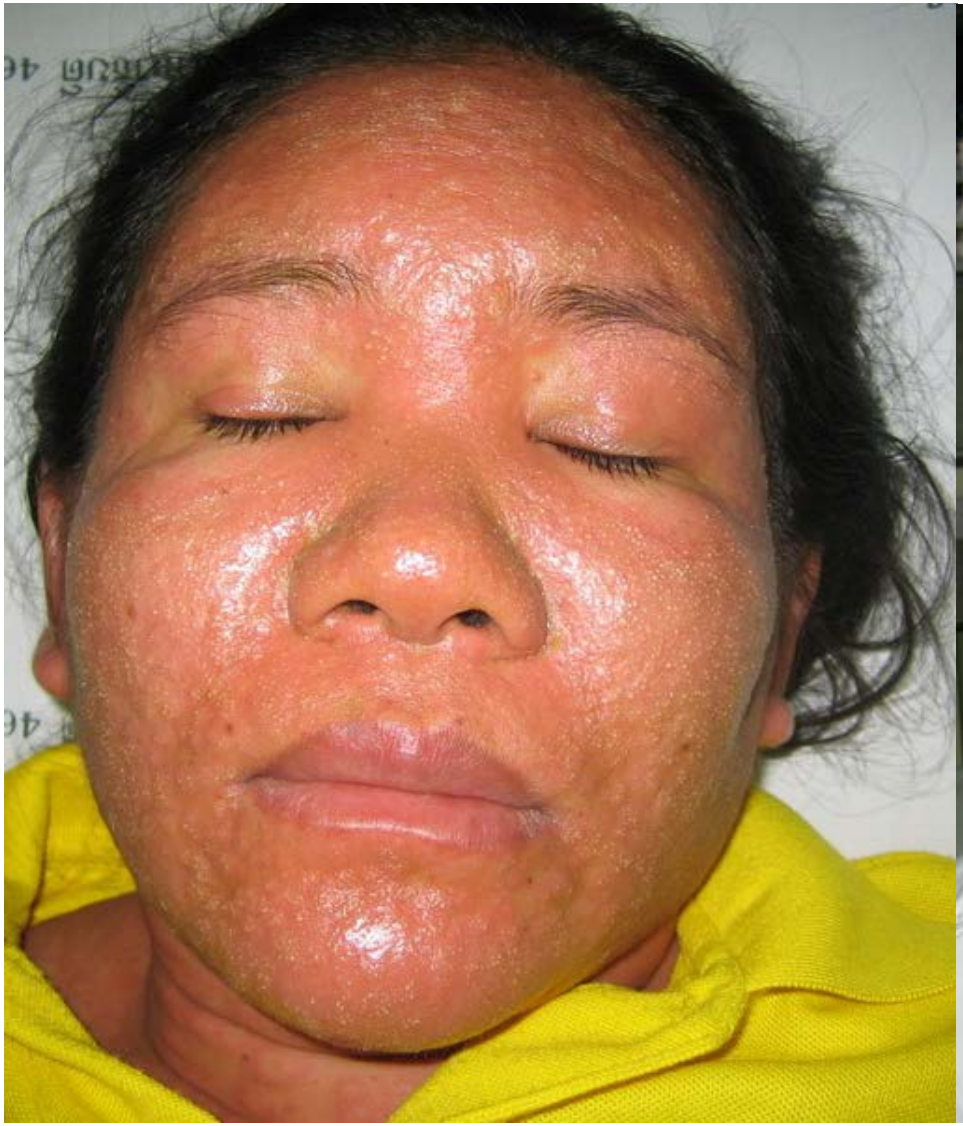
- </=0 ; no AGEP
- 1-4 ; possible
- 5-7 ; probable
- 8-12 ; definite
- exclude,only localized pustule,pustular last longer than 3 wks or clear alternative diagnosis has been made by a dermatologist

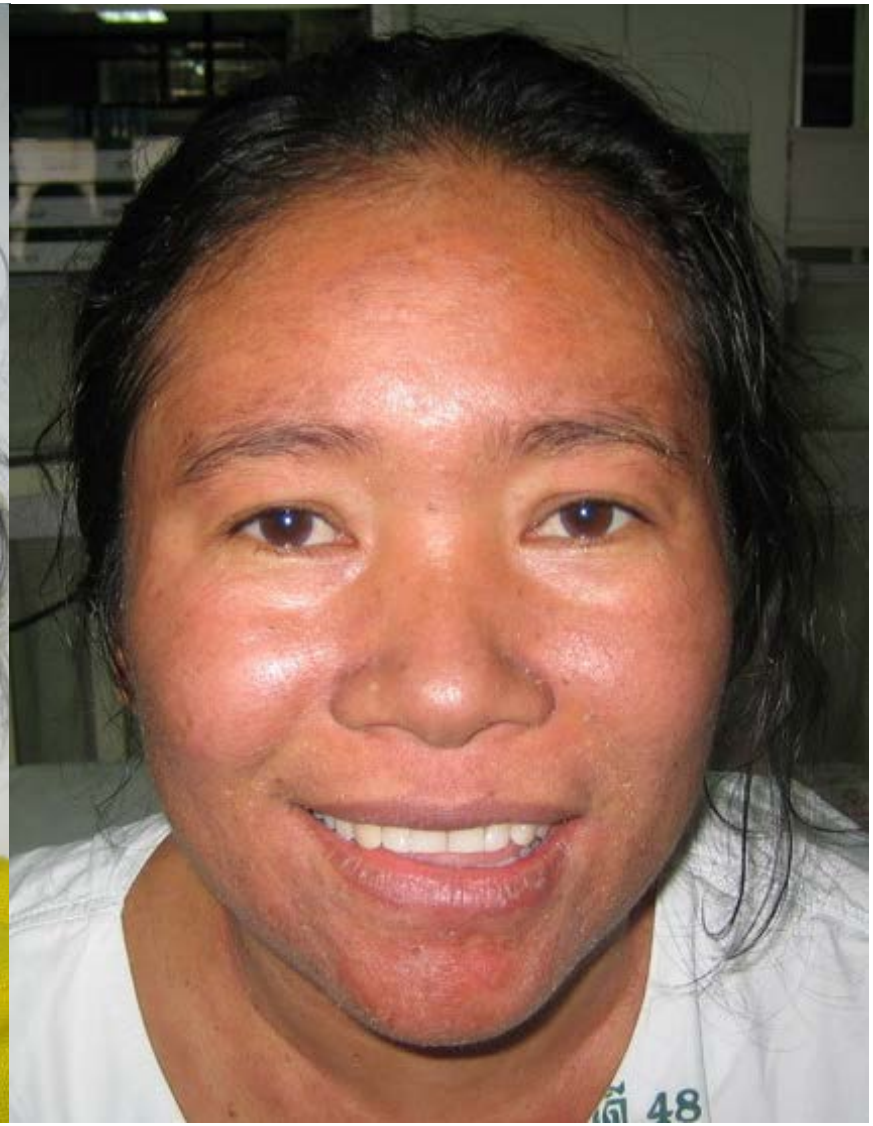
Diagnosis criteria

1.arising on edematous base

- 2.fever above 38 c
- 3.neutrophilia (>7000) with or without mild eosinophilia
- 4.subcorneal or intraepithelial or subcorneal pustules on skin biopsy
- 4.spontaneous resolution in less than 15 days

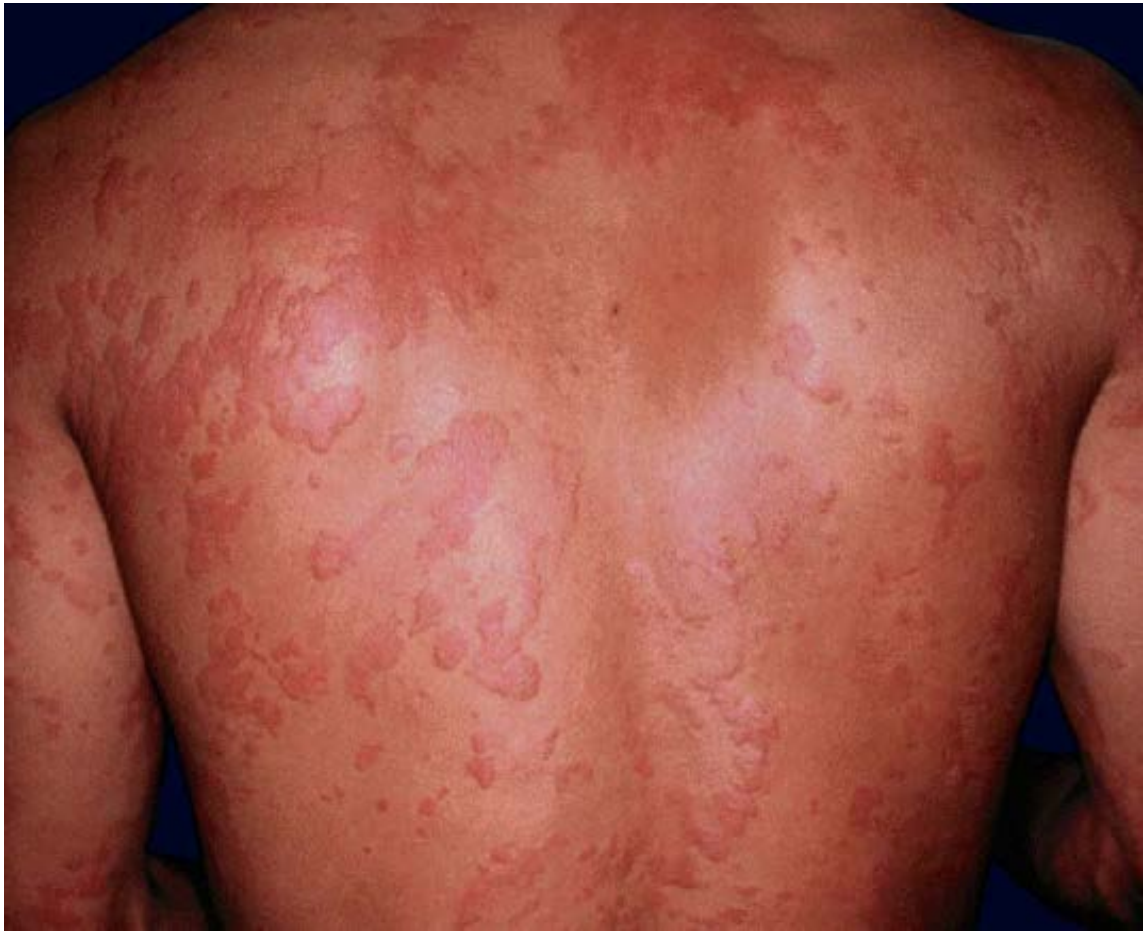
Roujeau JC et al,AGEP:analysis of 63 cases
Arch Dermatol1991;127:1333-8

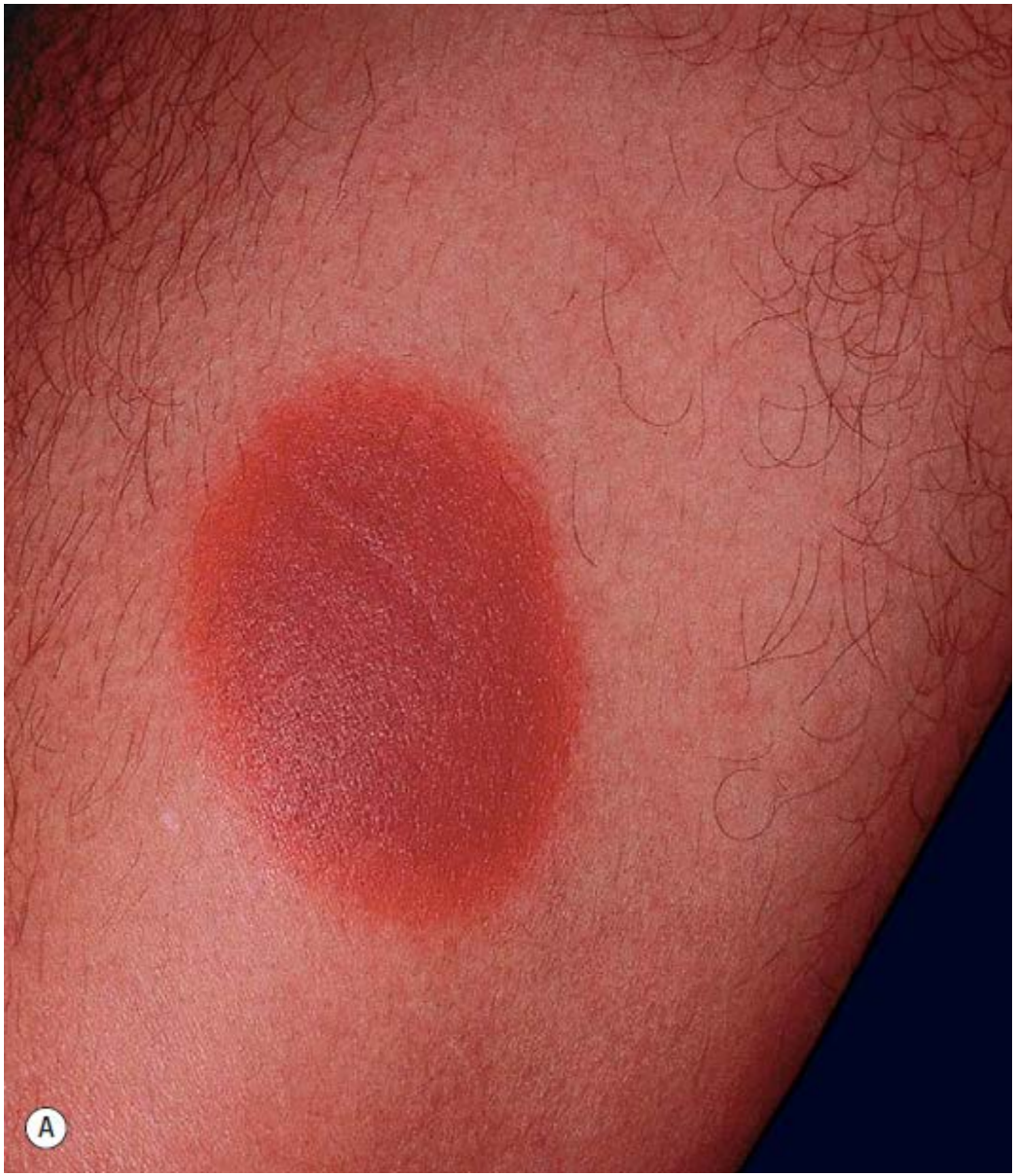




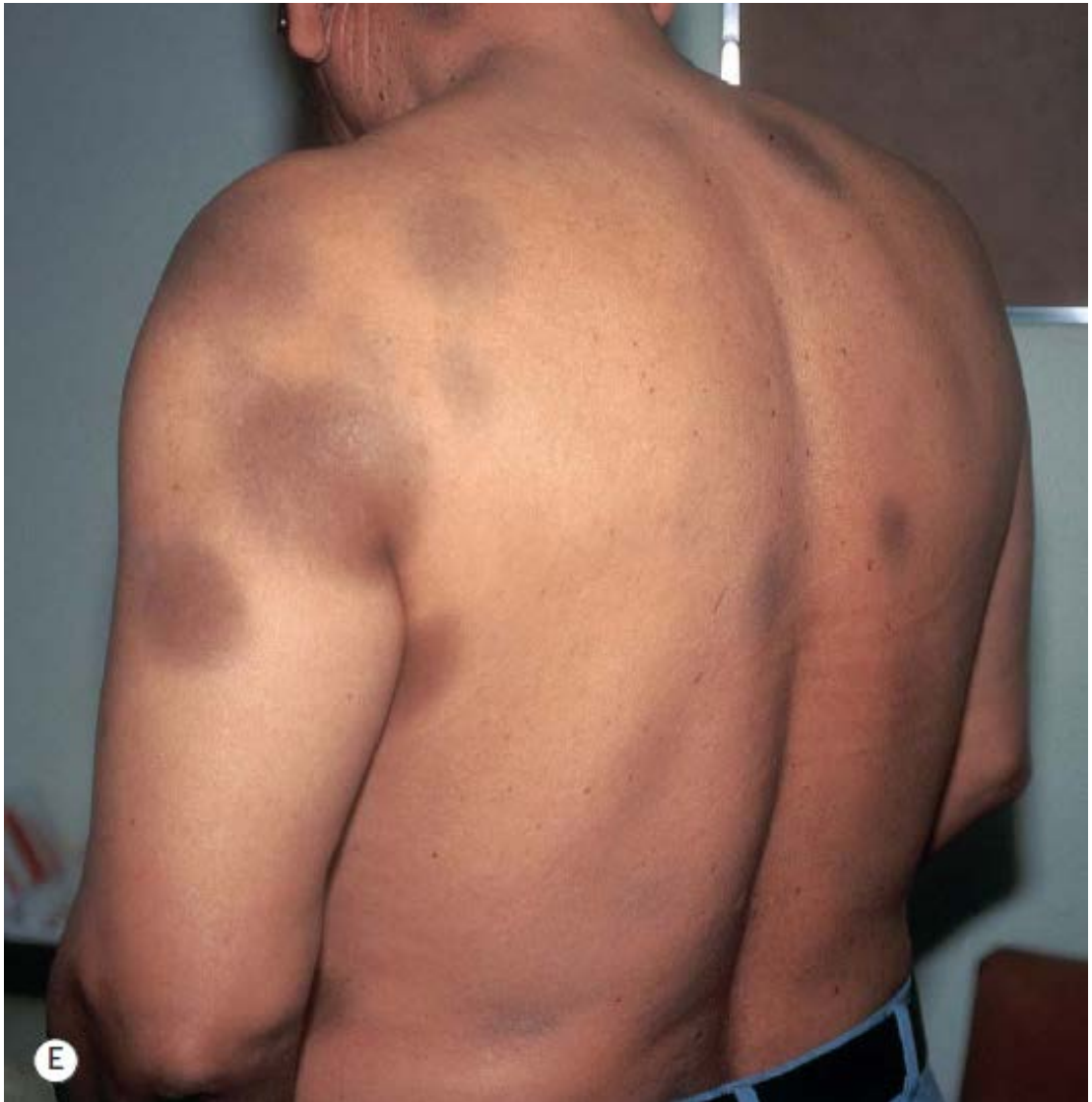
4 days after discontinuation of drug
And prednisolone 30mg/d

Urticaria

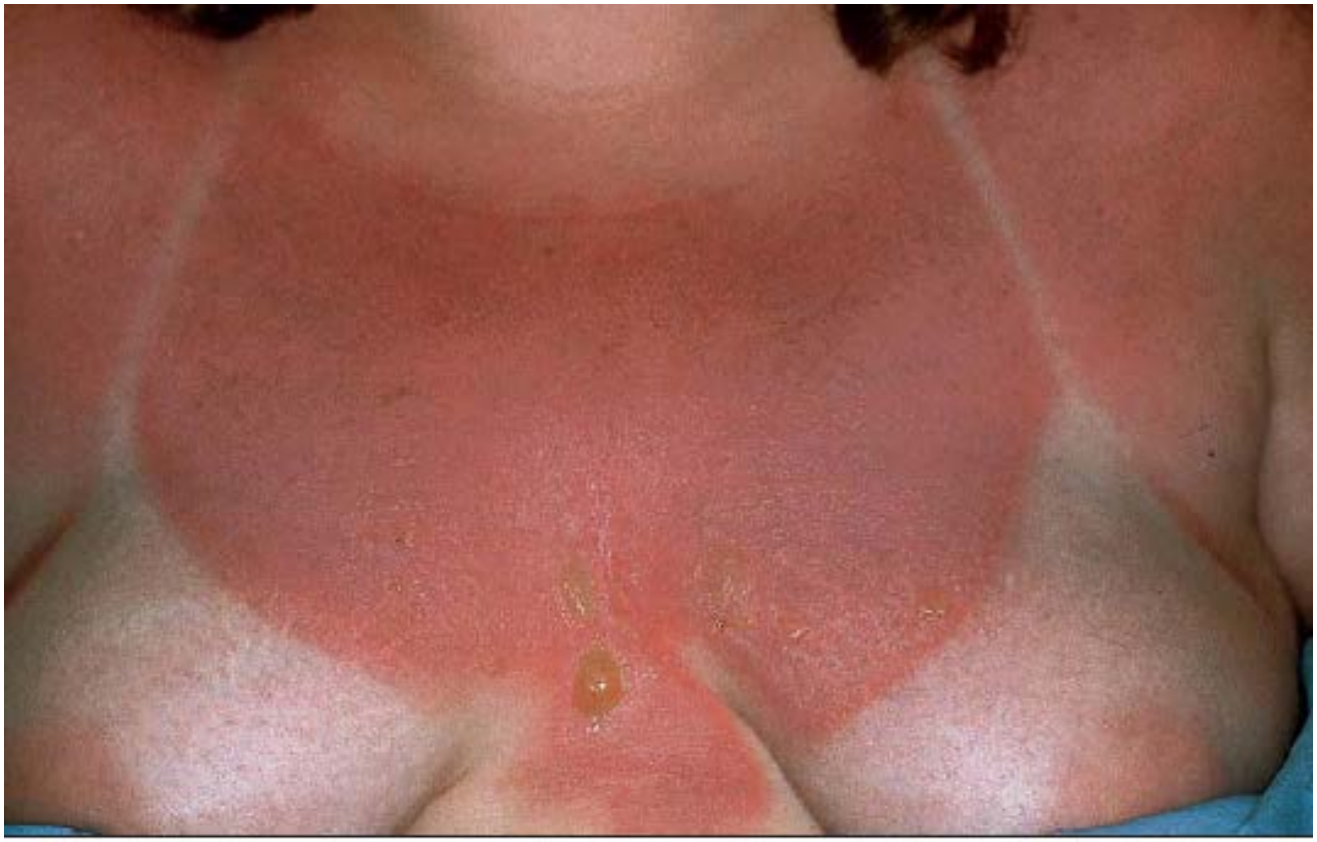



A

Fix drug eruptions



Phototoxic reaction



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 • TEN/SJS • Drug reactions in the setting of HIV infection • Drug-induced lupus

Table 22.3 Mechanisms of cutaneous drug-induced reactions. DRESS, drug reaction with eosinophilia and systemic symptoms; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

LOGICAL APPROACH TO DETERMINE THE CAUSE OF A DRUG ERUPTION	
Drug responsibility assessment	
Clinical characteristics	• Type of primary lesion • Distribution and number of lesions • Mucous membrane involvement • Associated signs and symptoms: fever, pruritus, lymph node enlargement, visceral involvement
Chronological factors	• Document all drugs to which the patient has been exposed 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 • Response to rechallenge*
Literature search	• Bibliographic research (e.g. Medline) • Drug Alert Registry or Medwatch • Data collected by pharmaceutical companies • In the case of recently released medications, extrapolation based on the class of drug
**Often inadvertent.*	

Table 22.4 Logical approach to determine the cause of a drug eruption.

Diagnosis

4 Questions

1.Drugs>>reaction

2.Reaction >>Drugs

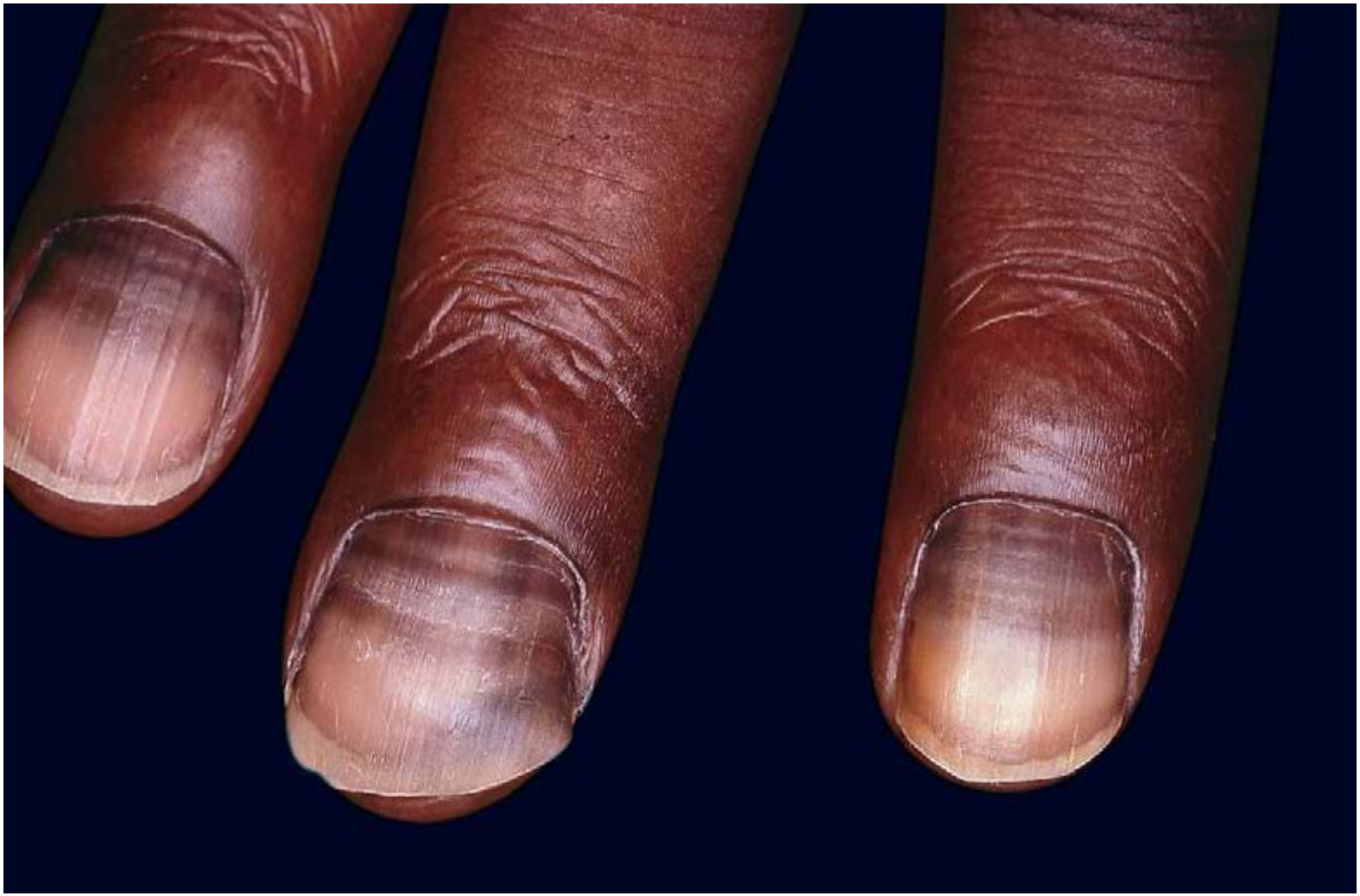
3.Dechallenge

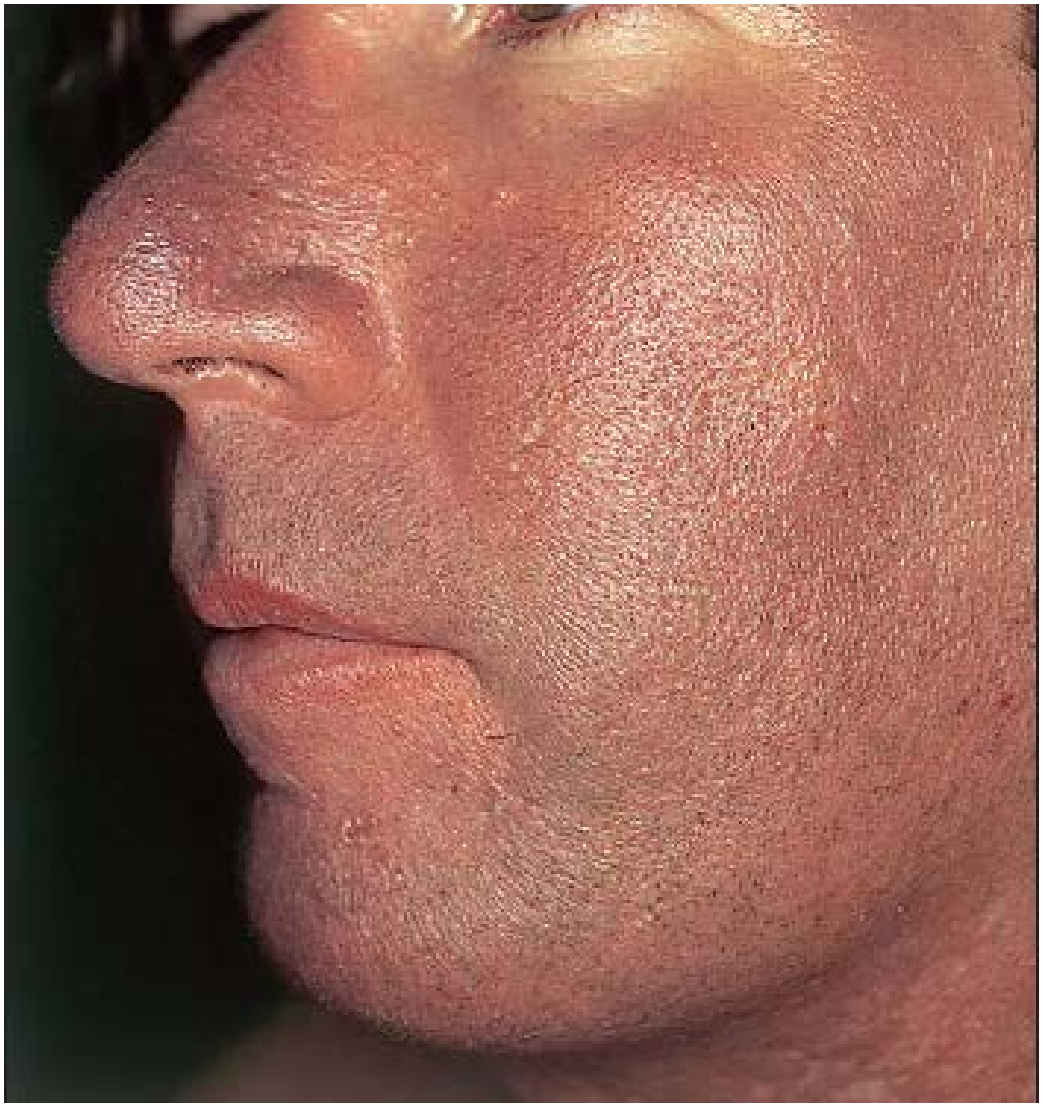
4.Rechallenge

Management

- Depend on type and severity of reaction
- Consider the need of that drugs
- Allergy CARD for patient !!
- Genetics?

The Other (should know)





DRUG-INDUCED ALOPECIA	
Telogen phase	– **Anticoagulants**: heparin > warfarin – Anticonvulsants: carbamazepine, valproic acid, phenytoin – Antidepressants: imipramine, desipramine, maprotiline, fluoxetide – Antihypertensive agents: **β-blockers**: acebutolol, propanolol ACE inhibitors: captopril, enalapril Diuretics: spironolactone – Antimicrobials: gentamicin, thiamphenicol, fluconazole – Antithyroid drugs: carbimazole, thiouracils – Colchicine – Interferons – Lipid-lowering agents: clofibrate, cholestyramine – **Lithium** – NSAIDs: piroxicam, naproxen, indomethacin, ibuprofen – Oral contraceptives – **Retinoids** – Others: allopurinol, cimetidine, L-dopa, amphetamines, pyridostigmine, bromocriptine
Anagen phase	– Antineoplastic agents (see Table 22.8) – Others: arsenic, bismuth, gold, thallium

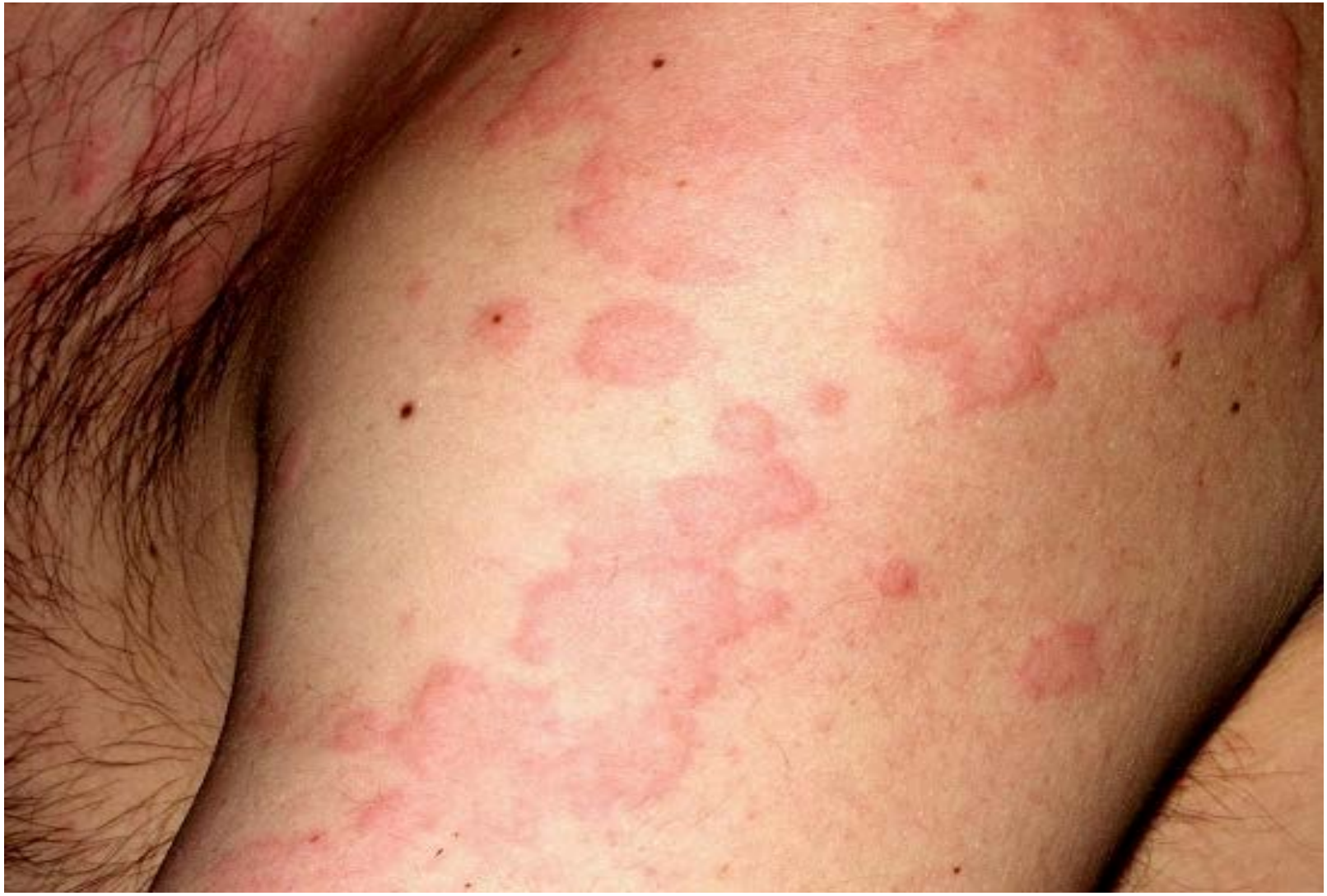
DRUG-INDUCED ERUPTIONS DUE TO CHEMOTHERAPEUTIC AGENTS

Mucocutaneous reactions	Responsible drugs
Alopecia	Alkylating agents: cyclophosphamide, ifosfamide, mechlorethamine Anthracyclines: daunorubicin, doxorubicin, idarubicin Taxanes: paclitaxel, docetaxel Etoposide, vincristine, vinblastine, topotecan, irinotecan, actinomycin D
Mucositis	Daunorubicin, doxorubicin, high-dose methotrexate, high-dose melphalan, topotecan, cyclophosphamide, continuous infusions of 5-fluorouracil and analogues of 5-fluorouracil
Extravasation reactions (e.g. chemical cellulitis, ulceration)	Anthracyclines, carmustines, 5-fluorouracil, vinblastine, vincristine, mitomycin C
Chemotherapy recall (tender sterile inflammatory nodules at sites of previous chemotherapy extravasation or administration)	5-fluorouracil, mitomycin C, paclitaxel, doxorubicin, epirubicin
Hyperpigmentation (see Ch. 66)	Alkylating agents: busulfan, cyclophosphamide, cisplatin, mechlorethamine Antimetabolites: 5-fluorouracil, methotrexate, hydroxyurea Antibiotics: bleomycin, doxorubicin
Mucosal hyperpigmentation	Busulfan, 5-fluorouracil, hydroxyurea, cyclophosphamide
Nail hyperpigmentation	5-Fluorouracil, cyclophosphamide, daunorubicin, doxorubicin, hydroxyurea, methotrexate, bleomycin
Onycholysis	Paclitaxel
Radiation recall	Doxorubicin, daunorubicin, taxanes, actinomycin D, capecitabine, gemcitabine
Radiation enhancement	Doxorubicin, hydroxyurea, taxanes, 5-fluorouracil, etoposide, gemcitabine, methotrexate
Photosensitivity	5-Fluorouracil and its analogues, methotrexate, hydroxyurea, dacarbazine, mitomycin C
Inflammation of 'keratoses'	Actinic keratoses: 5-fluorouracil and its analogues (e.g. capecitabine), pentostatin Seborrheic keratoses: cytarabine, docetaxel Squamous cell carcinoma: fludarabine
Acral erythema (erythrodysesthesia)	Cytarabine, anthracyclines, 5-fluorouracil and its analogues, taxanes, tegafur, methotrexate, cisplatin
Neutrophilic eccrine hidradenitis	Cytarabine, bleomycin, anthracyclines, cyclophosphamide, cisplatin, topotecan
Eccrine squamous syringometaplasia	Cytarabine, cyclophosphamide, busulfan, carmustine, taxanes
Ulcerations	Hydroxyurea (lower extremities)
Nodulosis	MTX (but usually in patients with rheumatoid arthritis)
Lymphoma	MTX (most commonly in patients with rheumatoid arthritis)
Squamous cell carcinoma	Fludaribine, hydroxyurea, topical BCNU
Flushing	Asparaginase, high-dose BCNU, mithramycin
Others:	Urticaria: asparaginase, bleomycin, chlorambucil, cyclophosphamide, daunorubicin Exanthematous eruption: bleomycin, carboplatin, cytarabine, methotrexate, liposomal doxorubicin, paclitaxel SJS/TEN: bleomycin, busulfan, cyclophosphamide, doxorubicin, etoposide, methotrexate Cutaneous vasculitis: gemcitabine, busulfan, cyclophosphamide, hydroxyurea, levamisole Dermatomyositis-like eruption: hydroxyurea

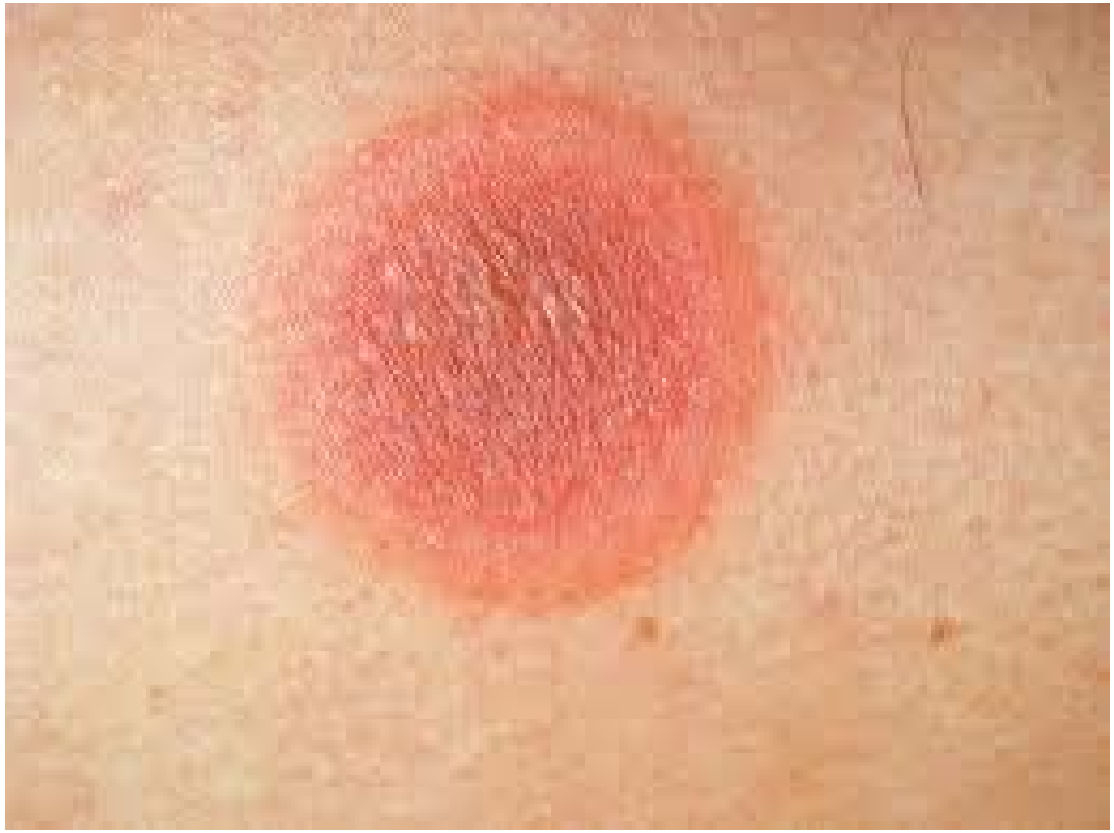
ADDITIONAL REVIEWS OF SPECIFIC TYPES OF DRUG REACTIONS	
Psoriasiform	Chapters 9 and 128
Erythroderma	Table 11.3
Lichenoid	Table 12.2
Urticaria	Chapter 19
Stevens–Johnson syndrome and toxic epidermal necrolysis	Table 21.5, Chapter 21
Warfarin and heparin necrosis	Chapter 24
Vasculitis	Table 25.4
Pemphigus and bullous pemphigoid	Chapters 30 & 31
Linear IgA bullous dermatosis	Table 32.5
Acneiform/folliculitis	Chapter 37
Hyper- and hypohidrosis	Tables 40.4 & 40.9
Lupus erythematosus (systemic and subacute cutaneous)	Chapter 42
Pseudoporphyria	Table 49.5
Hypopigmentation (skin and hair)	Tables 65.10 & 65.12
Hyperpigmentation and dyschromatosis	Tables 66.2 & 66.8
Hypertrichosis and hirsutism	Tables 69.3 & 69.5, Chapter 69
Phototoxic and photoallergic	Table 86.5

END

1. What is the clinical diagnosis?

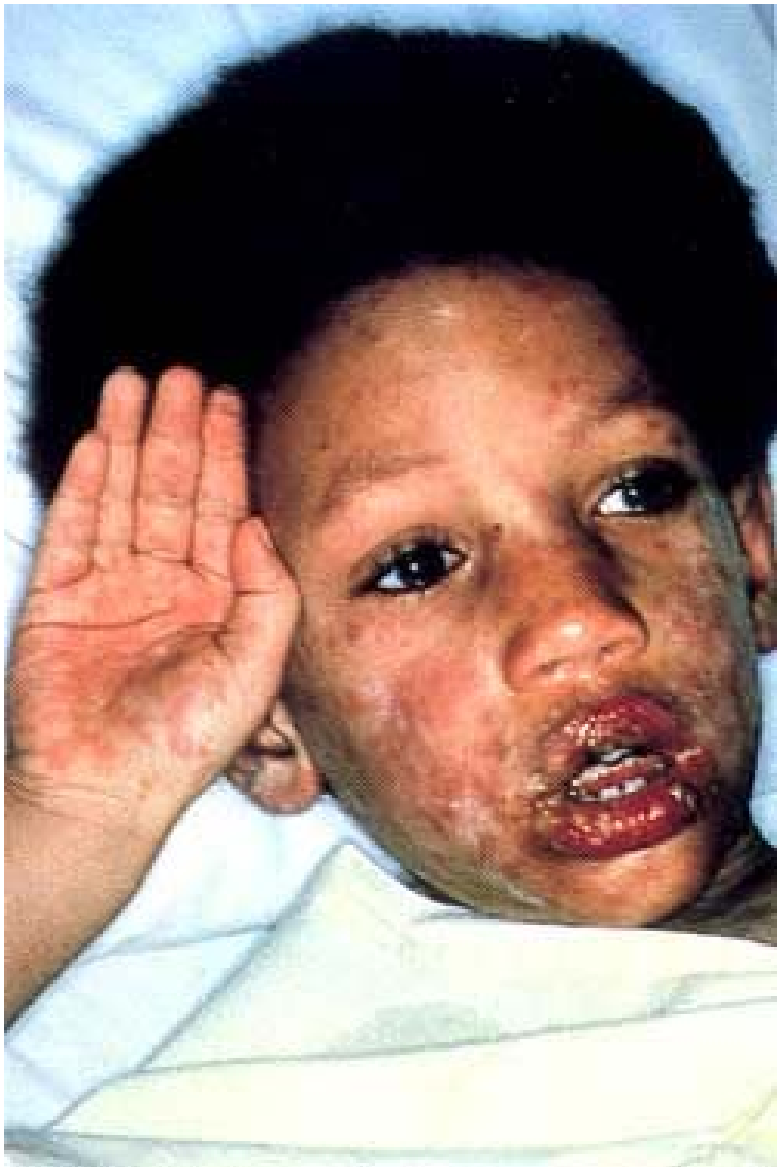


2. What is the clinical diagnosis?



3. Name drug that causing this condition

4. What is the diagnosis



5. Name three cause of this presentation.