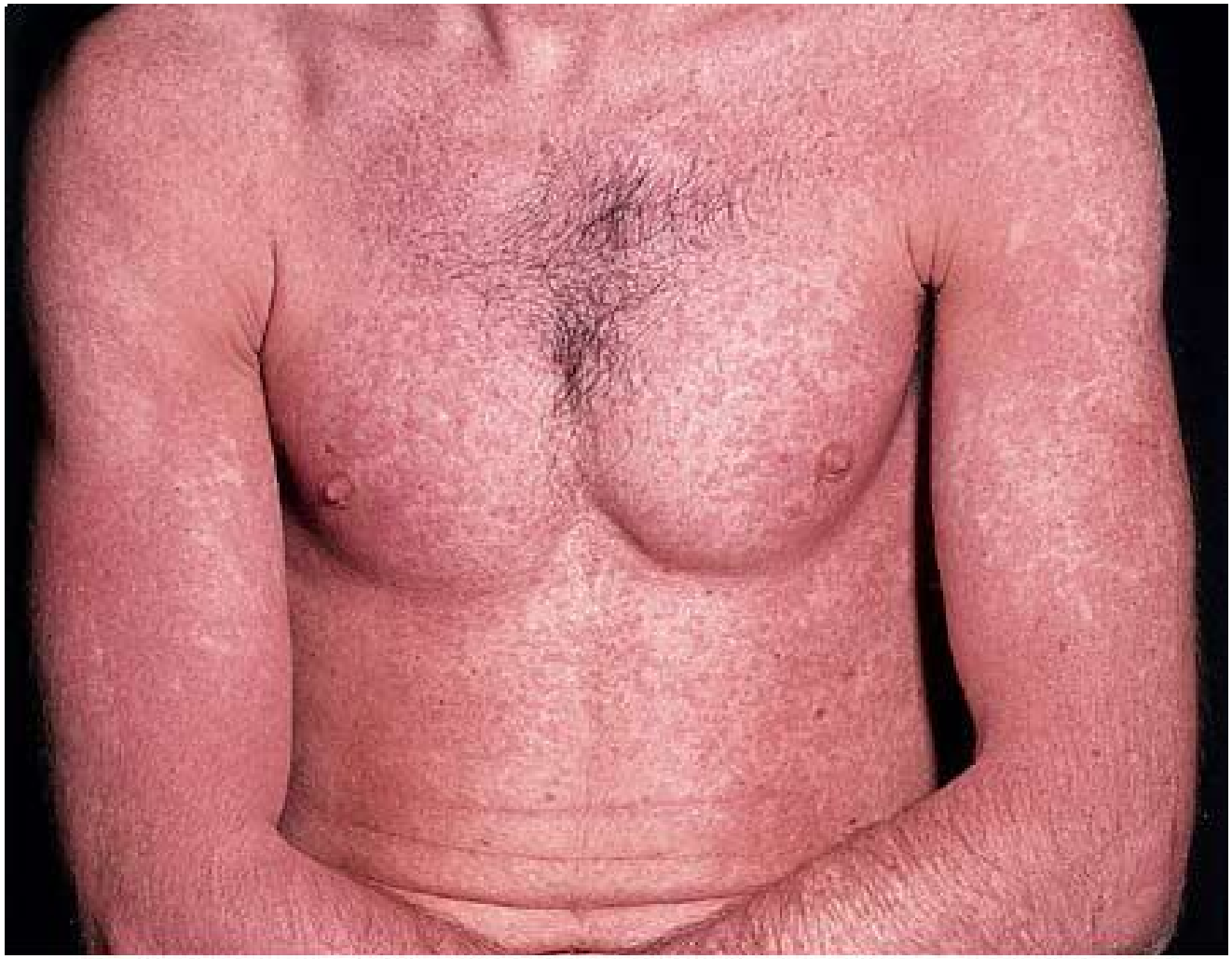
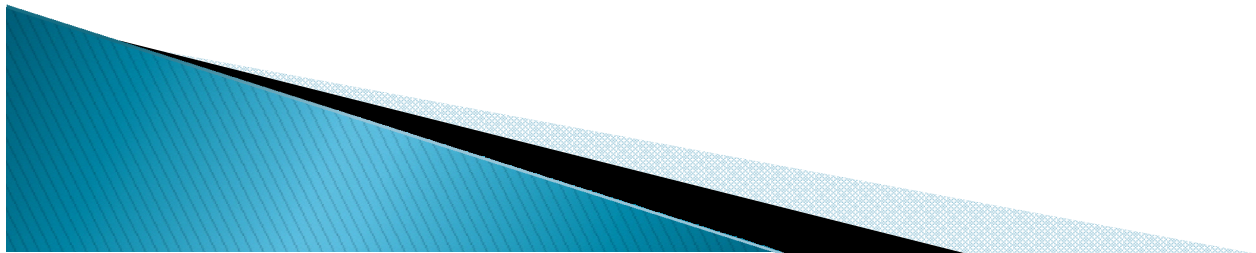


Drug Hypersensitivity syndrome

- idiosyncratic adverse drug reaction that begins acutely in the first 2 months after initiation of drug
- fever, severe disease, infiltrated papules and facial edema or an exfoliative dermatitis,
- lymphadenopathy, hematologic abnormalities (eosinophilia, atypical lymphocytes), and organ involvement (hepatitis, carditis, interstitial nephritis, or interstitial pneumonitis).



- The mortality rate is 10% if unrecognized and untreated.
- *Synonym*: Drug rash with eosinophilia and systemic symptoms (DRESS).

Etiology

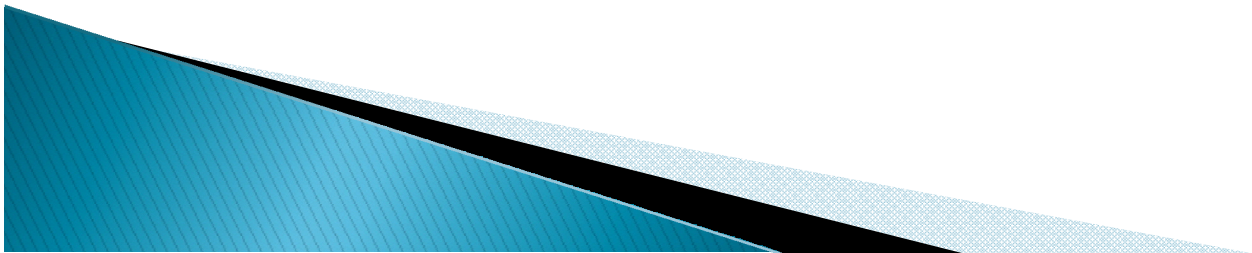
Most commonly:

antiepileptic drugs (phenytoin, carbamazepine, phenobarbital; cross-sensitivity among the three drugs is common)

sulfonamides (antimicrobial agents, dapsone, sulfasalazine).

Less commonly:

allopurinol, gold salts, sorbinil, minocycline, zalcitabine, calcium-channel blockers, ranitidine, thalidomide, mexiletine.



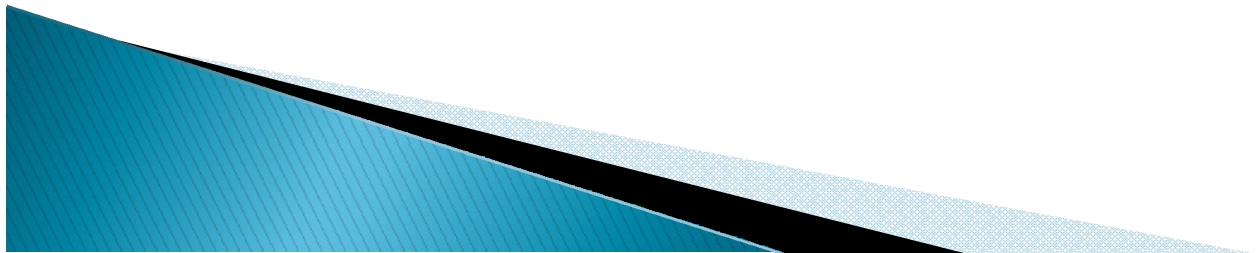
Pathogenesis

Some patients have a genetically determined inability to detoxify the toxic arene oxide metabolic products of anticonvulsant agents. Slow N-acetylation of sulfonamide and increased susceptibility of leukocytes to toxic hydroxylamine metabolites are associated with higher risk of hypersensitivity syndrome.

History

Onset

2 to 6 weeks after drug is initially used, and later than most other serious skin reactions.



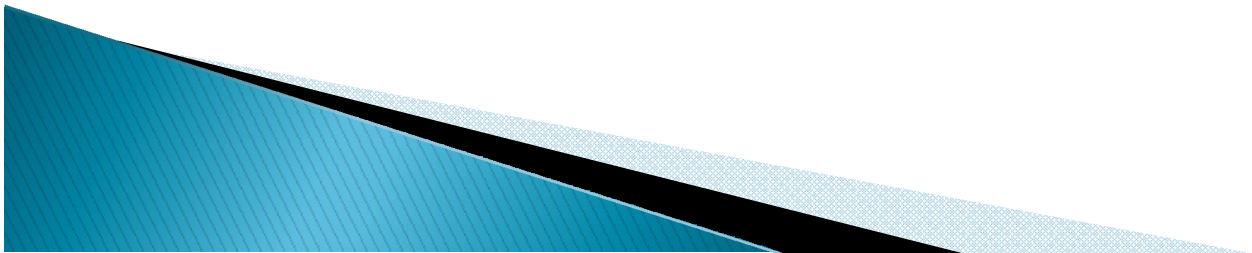
Diagnosis

Proposed Diagnostic Criteria
(1) Cutaneous drug eruption;

(2) hematologic abnormalities (eosinophilia 1500/L or presence of atypical lymphocytes);

(3) systemic involvement [adenopathies 2 cm in diameter or hepatitis (SGOT 2 *N*) or interstitial nephritis or interstitial pneumonitis or carditis].

Diagnosis is confirmed if three criteria are present.

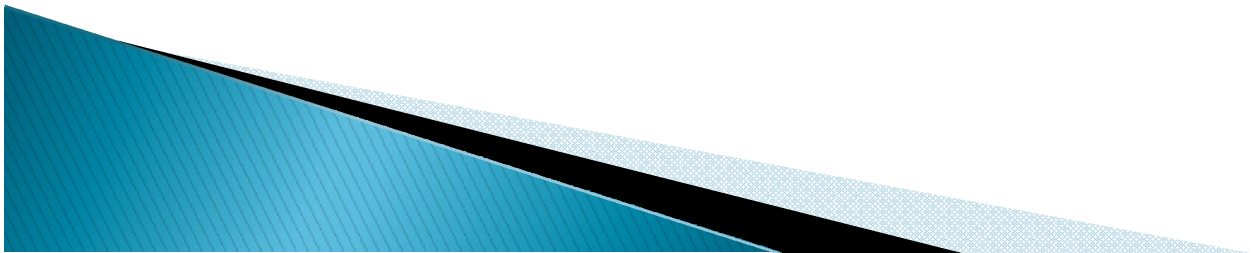


Diagnosis

- Usually made on clinical findings.
- Lesional skin biopsy is helpful in defining the type of reaction pattern occurring but not in identifying the offending drug.
- Skin tests and radioallergosorbent tests are helpful in diagnosing IgE-mediated type I hypersensitivity reactions, more specifically to penicillins.

Management

- In most cases, the implicated or suspected drug should be discontinued.
- In some, such as with morbilliform eruptions, the offending drug can be continued and the eruption may resolve.
- In cases of urticaria/angioedema or early Stevens–Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), the ACDR can be life-threatening, and the drug must be discontinued.



Findings Indicating Possible Life-Threatening ACDR[1]

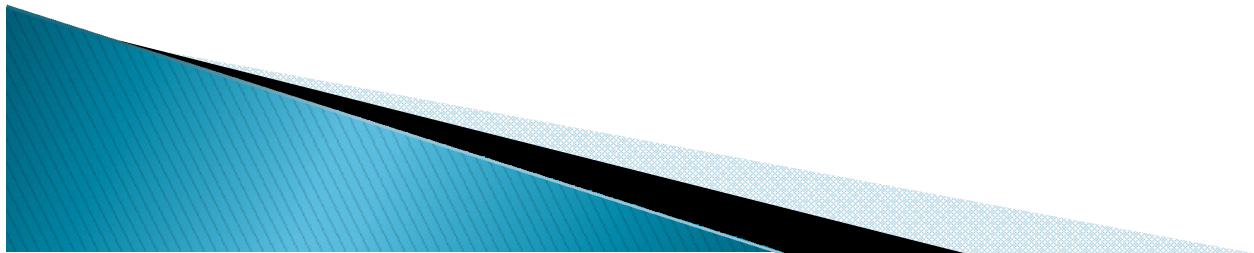
[1]Source: from JC Roujeau, RS Stern: N Engl J Med 331:1272, 1994.

Cutaneous

Confluent erythema
Facial edema or central facial involvement
Skin pain
Palpable purpura
Skin necrosis
Blisters of epidermal detachment
Positive Nikolsky's sign (epidermis separates readily from dermis with lateral pressure)
Mucous membrane erosions
Urticaria
Swelling of the tongue

General

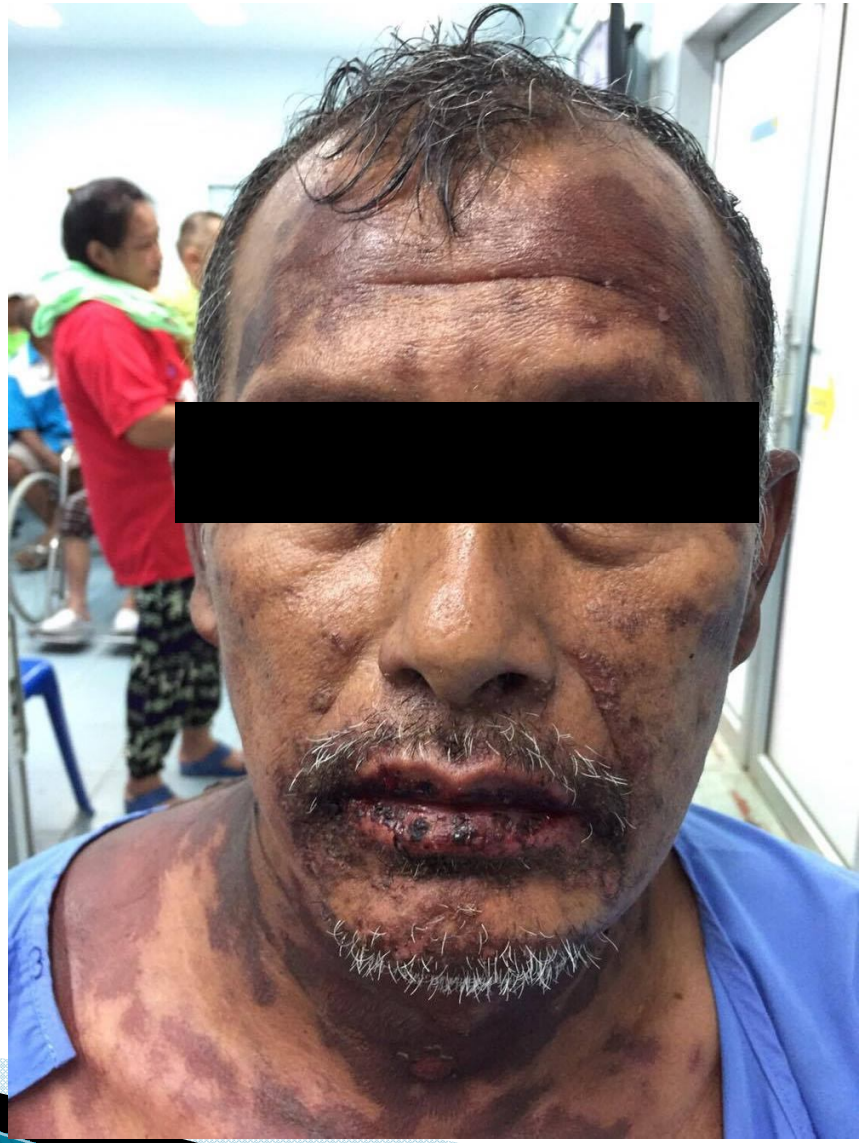
High fever (temperature >40°C)
Enlarged lymph nodes Arthralgias or arthritis
Shortness of breath, wheezing, hypotension

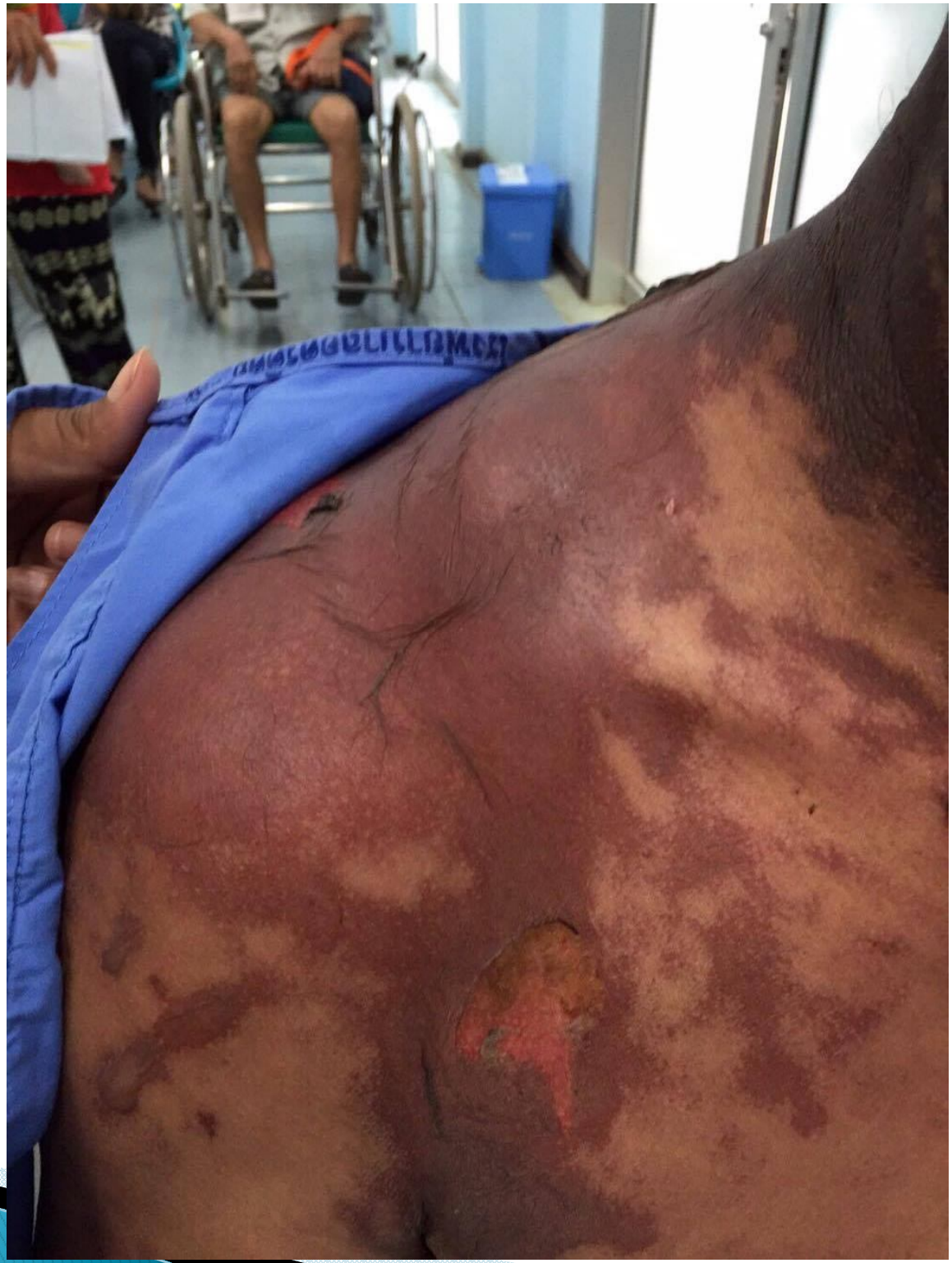


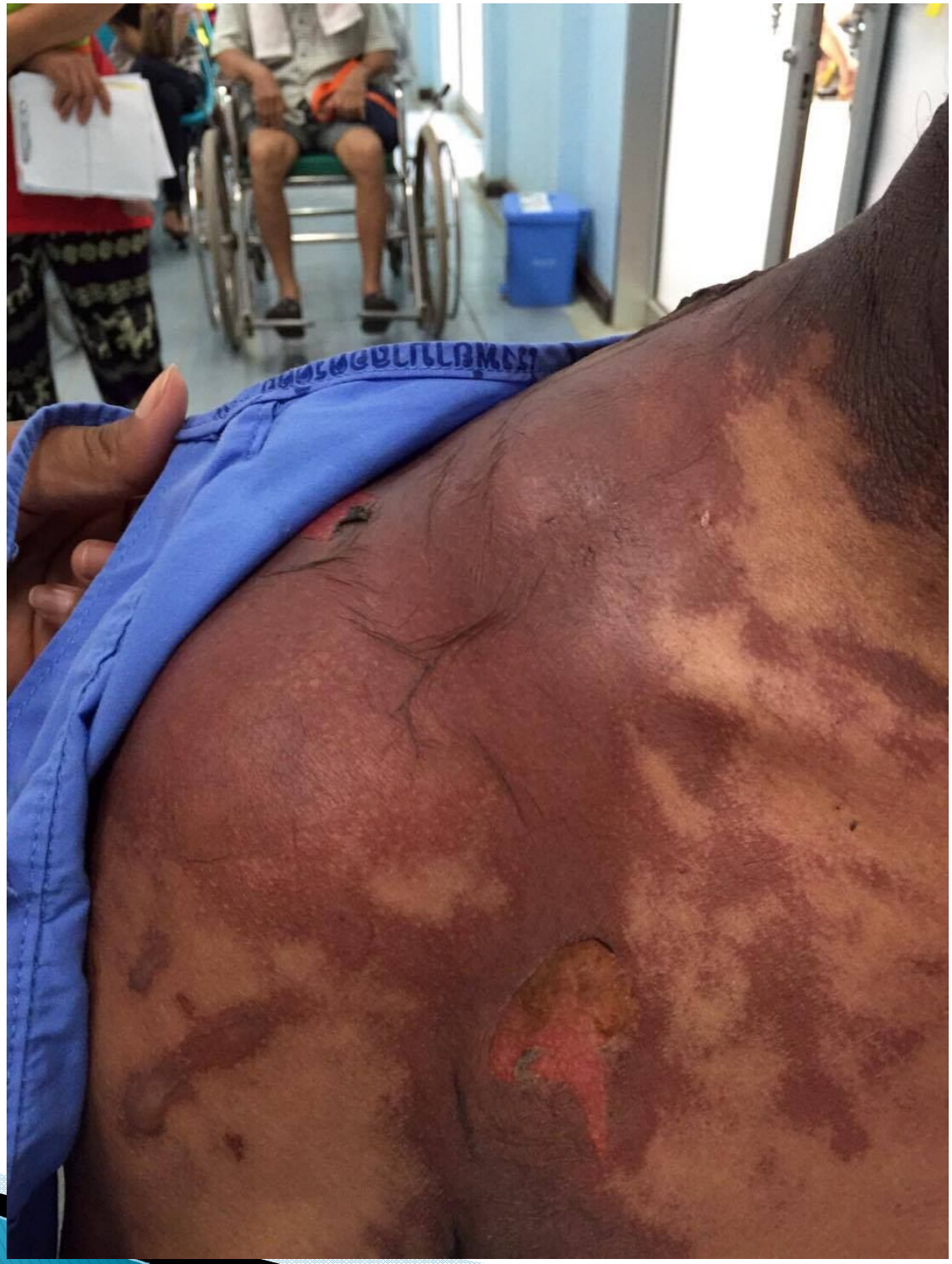
Indications for discontinuation of drugs

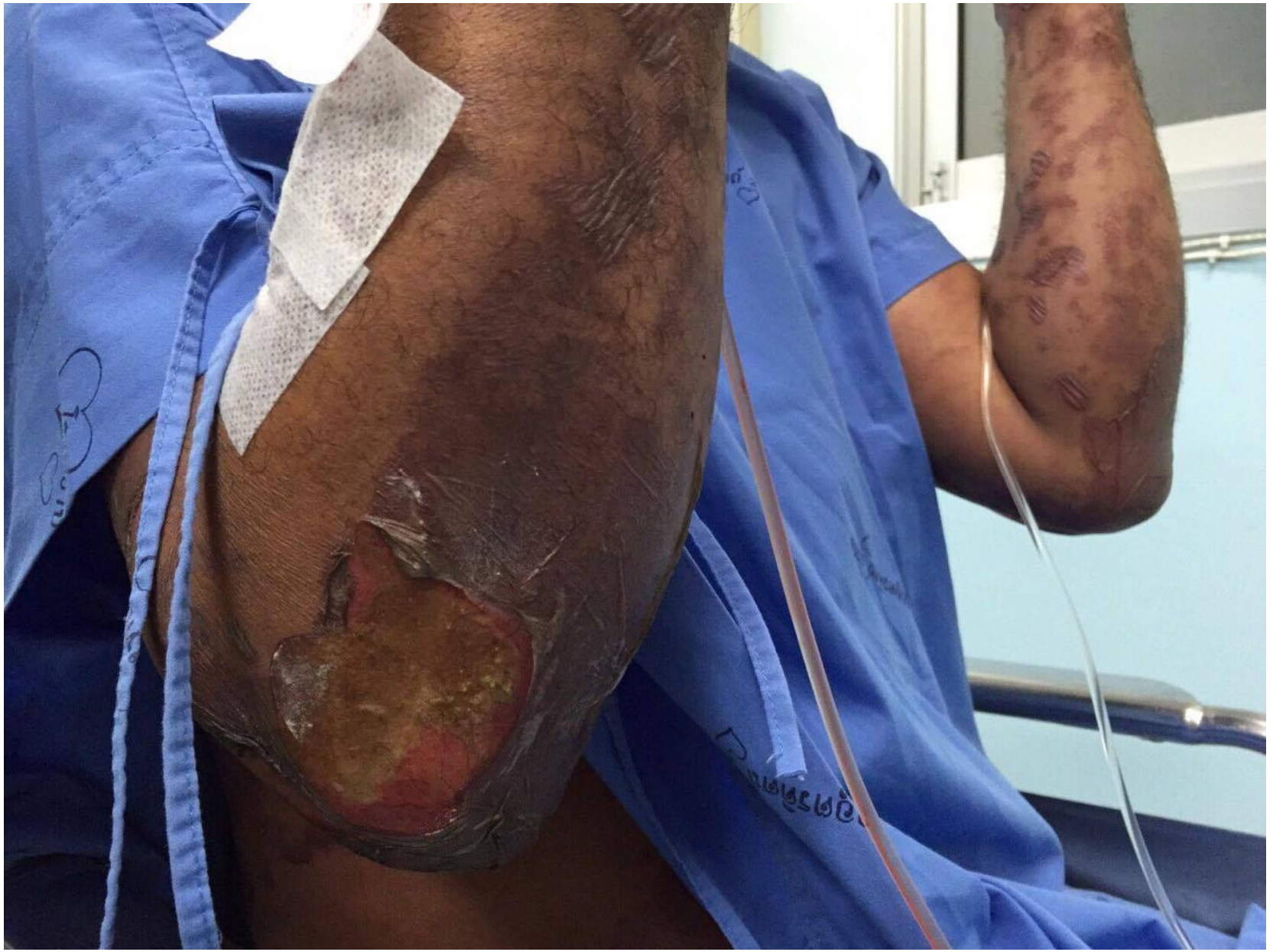
Urtricaria
Facial edema
Pain, Blisters, Mucosal inv.
Ulcers, palpable/extensive purpuric
Fever
Lymphadenopathy

CASE 1 ผู้ป่วยชายไทยคู่ อายุ 50 ปี มีอาการปวดหลัง ได้รับยา piroxicam 2 สัปดาห์









SJS – TEN from piroxicam

CASE 2 ผู้ป่วยหญิงไทยคู่ อายุ 50 ปี Case Malignant Melanoma on Vemurafenib 11 วัน หลังได้รับยา มีผื่นแดงที่หลังเท้า หน้า และแขน