WOLF IN SHEEP'S DRESS

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PRESENTOR:DR SHALINI.A

15 Years boy X from west bengal presented to ED with

- High grade intermittent fever for 15 days.
- Erythematous rashes all over body associated with itching 3 days after onset of fever.
- Right sided abdominal pain,non bilious vomiting,myalgia and arthralgia .
- Yellowish discolouration of sclera-7 days, High coloured urine
- Facial puffiness and swelling of legs-7 days
- No h/o abdominal distension/ LOA/LOW
- No h/o breathlessness/chest pain/palpitation
- No h/o joint swelling.

- Treated with cocktail of antibiotics (Ceftriaxone/metronidazole/ clindamycin/piperacillin/amikacin/ofloxacin/?vanco mycin)

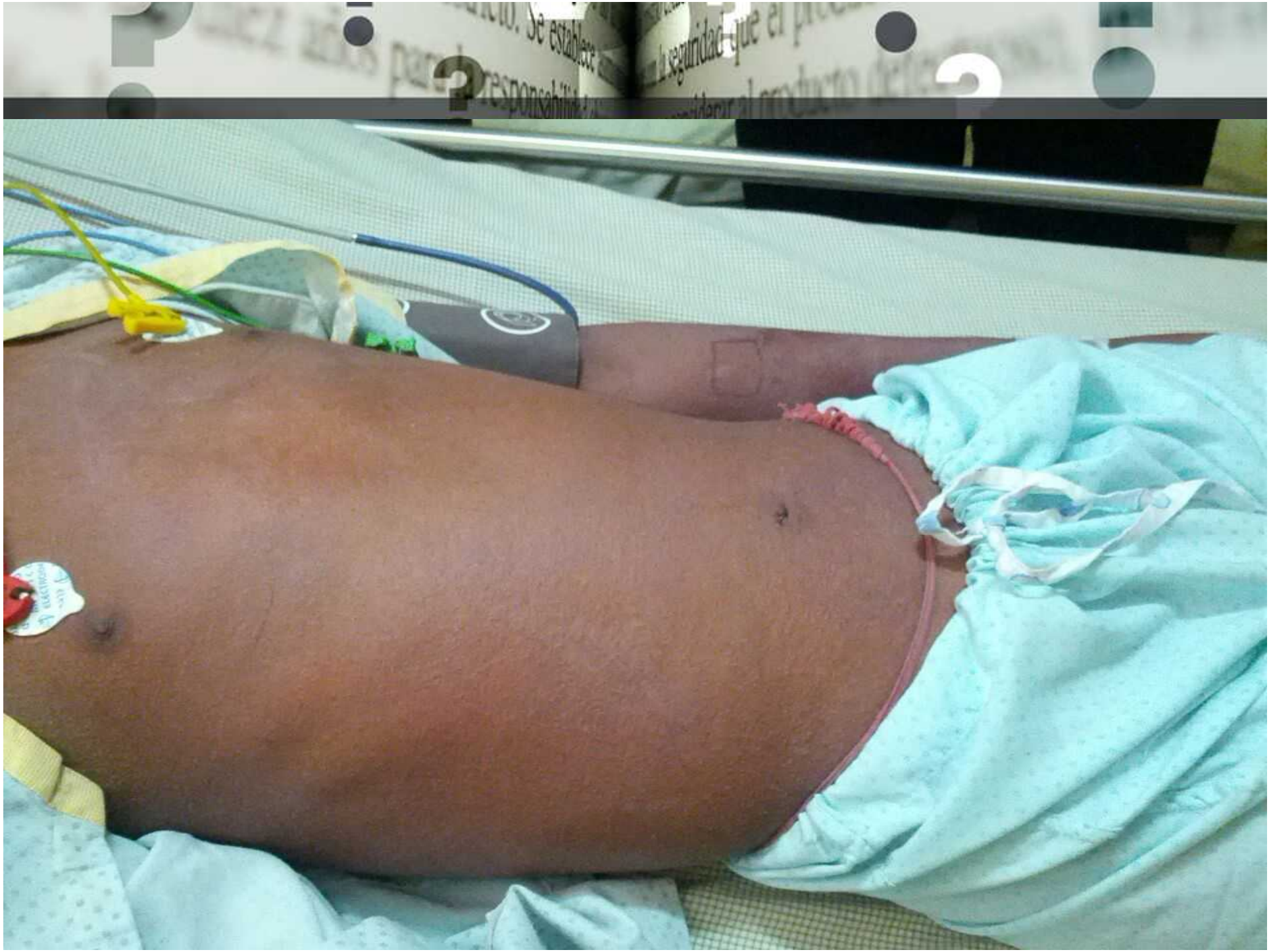
PAST HISTORY:

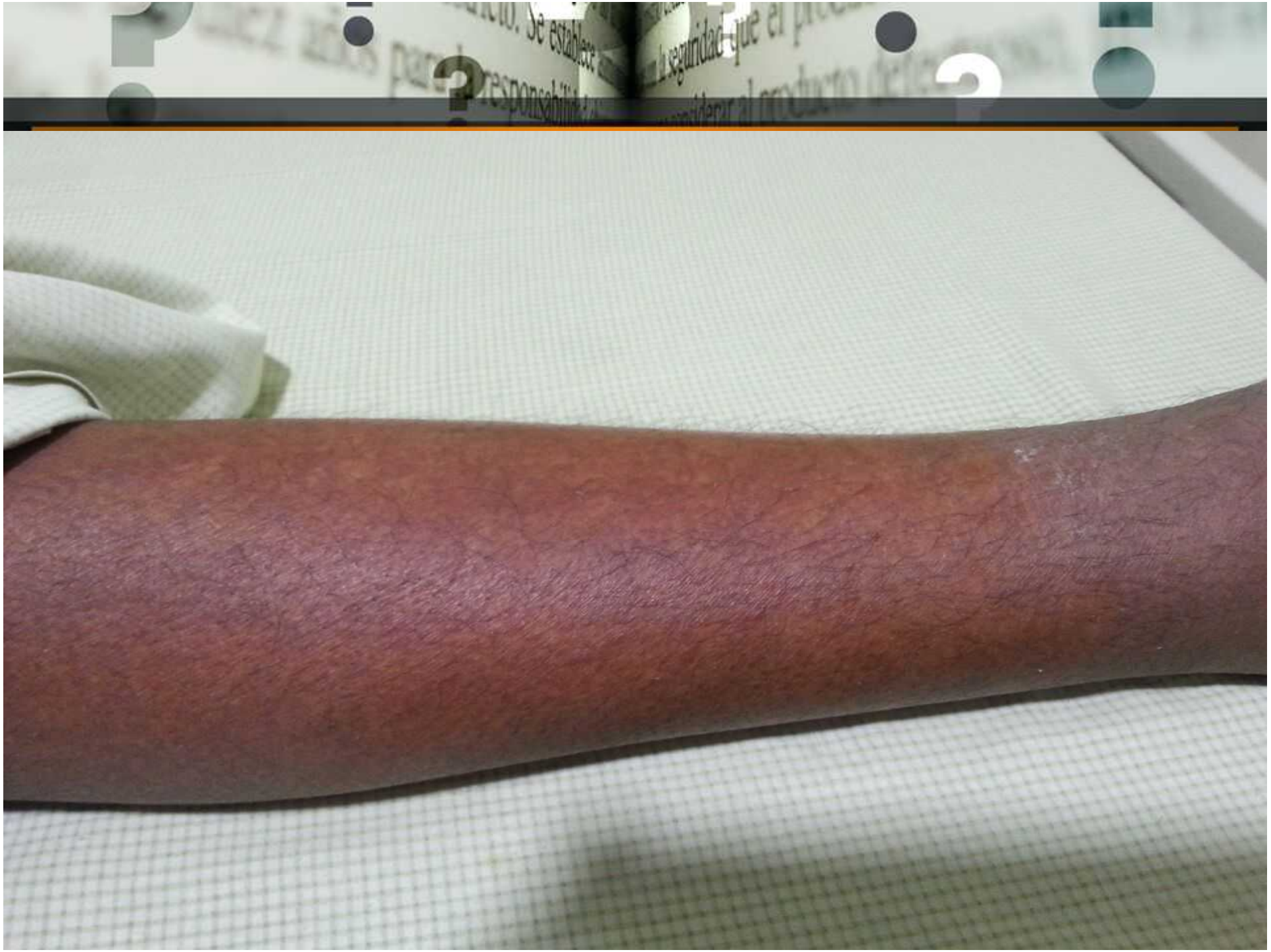
No h/o contact with TB

2 Months before, had oral ulcer for 7 days treated with oral medication.

O/E

- No pallor/Cyanosis
- Icterus present.
- Tender cervical,axillary and inguinal lymphadenopathy.
- Facial puffiness +,Bilateral pitting pedal odema +,generalised maculopapular rashes
- P/A:Ascites+,Tender hepatomegaly (4cm RCM),spleen tip palpable
- Cardiovascular,Respiratory and central nervous system normal





FEVER +ERYTHEMATOUS RASHES+ICTERUS+ANASARCA+TENDER LYMPHADENOPATHY+TENDER HEPATOMEGALY

DD???????????

- INFECTIOUS CAUSE
- CONNECTIVE TISSUE DISORDERS
- HEMATOLOGICAL MALIGNANCY

INVESTIGATIONS(OUTSIDE)

HEMO GLOBIN	11/2/15 11.8	13/2/15 11.2	14/2/15 10.6	17/2/15 8.7
TOTAL COUNTS	21,600 (N65L30E3M1)	29,700 (N60L25E2M8)	33,600	32,100
PLATELETS	1,74,000	1,52,000		
ESR	47	5		

INVESTIGATIONS IN ACH

HEMOGLOBIN	19/2/2015 10.5	21/2/2015 9.7
WBC	64,500(N59L24E12)	55,500(N51L27E16M1)
PLATELETS	2,21,000	1,33,000
CRP	8.53	

PERIPHERAL SMEAR:LEUCOCYTOSIS WITH MYELOID SHIFT,EOSINOPHILA,TOXIC CHANGES AND REACTIVE LYMPHOCYTES

SERUM BILIRUBIN	4.8(D-4.2,ID-0.6)
SERUM ALBUMIN	2.5G/DL
SERUM GLOBULIN	2.4G/dl
SGOT	1350U/L
SGPT	1075U/L
SAP	1645
GGTP	455

- BLOOD UREA-45→37→34MG/DL
- SERUM CREATININE-0.8→0.5→0.5
- SERUM ELECTROLYTES-NORMAL

COAGULATION PROFILE:

- PT-22 SECONDS
- INR-2.6
- APTT-41 SECONDS
- CPK-266U/L
- URINE AND STOOL ROUTINE-NORMAL,Urine myoglobin-negative.

- HIV/HBsAg-NEGATIVE,Anti HCV-negative
- EBV SEROLOGY:POSITIVE,CMV & Leptospirosis-negative,BRUCELLA Ig M-negative
- BLOOD & URINE CULTURE-NO GROWTH
- USG ABDOMEN:Multiple significantly enlarged mesentric lymph nodes.
- ECHO:Mild pericardial effusion,RCA & LCA 3mm

?Myocarditis.

ANA-NEGATIVE

SERUM LDH & FERRITIN-NORMAL.

DIAGNOSIS?????

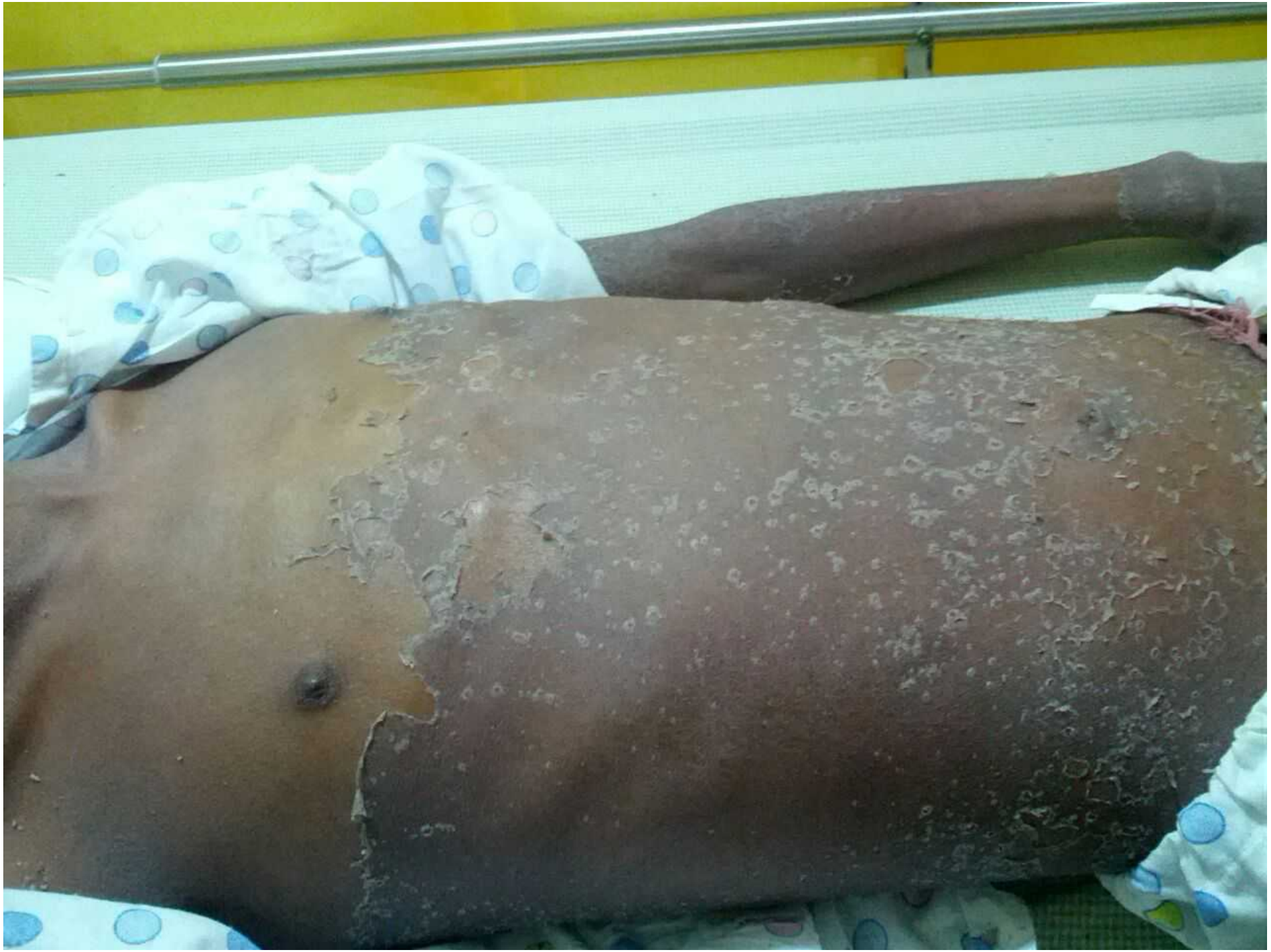
- INFECTIVE
- DRUG INDUCED

DAPSONE WAS GIVEN FOR ORAL ULCER

DRESS

TREATMENT

- Hydration
- Intravenous steroids(dexamethasone)given.
- Intravenous NAC given.
- Liver supportives(udiliv)



FOLLOW UP

SERUM BILIRUBIN	4.4
SERUM ALBUMIN	2.1
SERUM GLOBULIN	4.2
SGOT	320
SGPT	655
SAP	1510
GGTP	640

DRESS

- Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a distinct, severe, idiosyncratic reaction(type IV hypersensitivity reaction) to a drug characterized by a prolonged latency period (2 to 8 weeks).
- DRESS was coined by Bocquet in 1996.
- The estimated incidence of this syndrome ranges from 1 in 1000 to 1 in 10,000 drug exposures

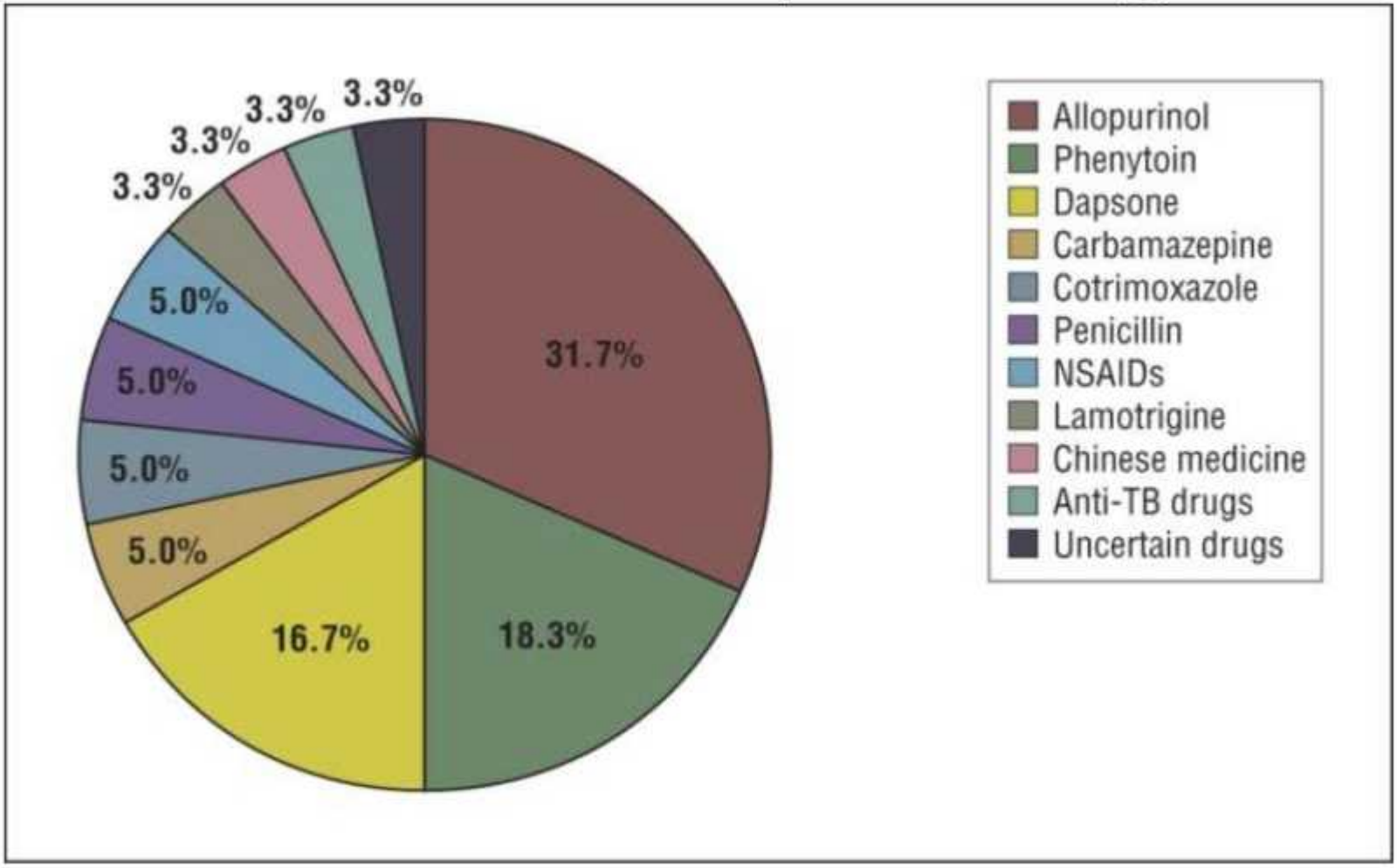
- EVOLVING NOMENCLATURE

Anticonvulsant hypersensitivity syndrome (AHS), drug-induced hypersensitivity (DIHS), drug-induced delayed multiorgan hypersensitivity syndrome (DIDMOHS) .

PATHOGENESIS

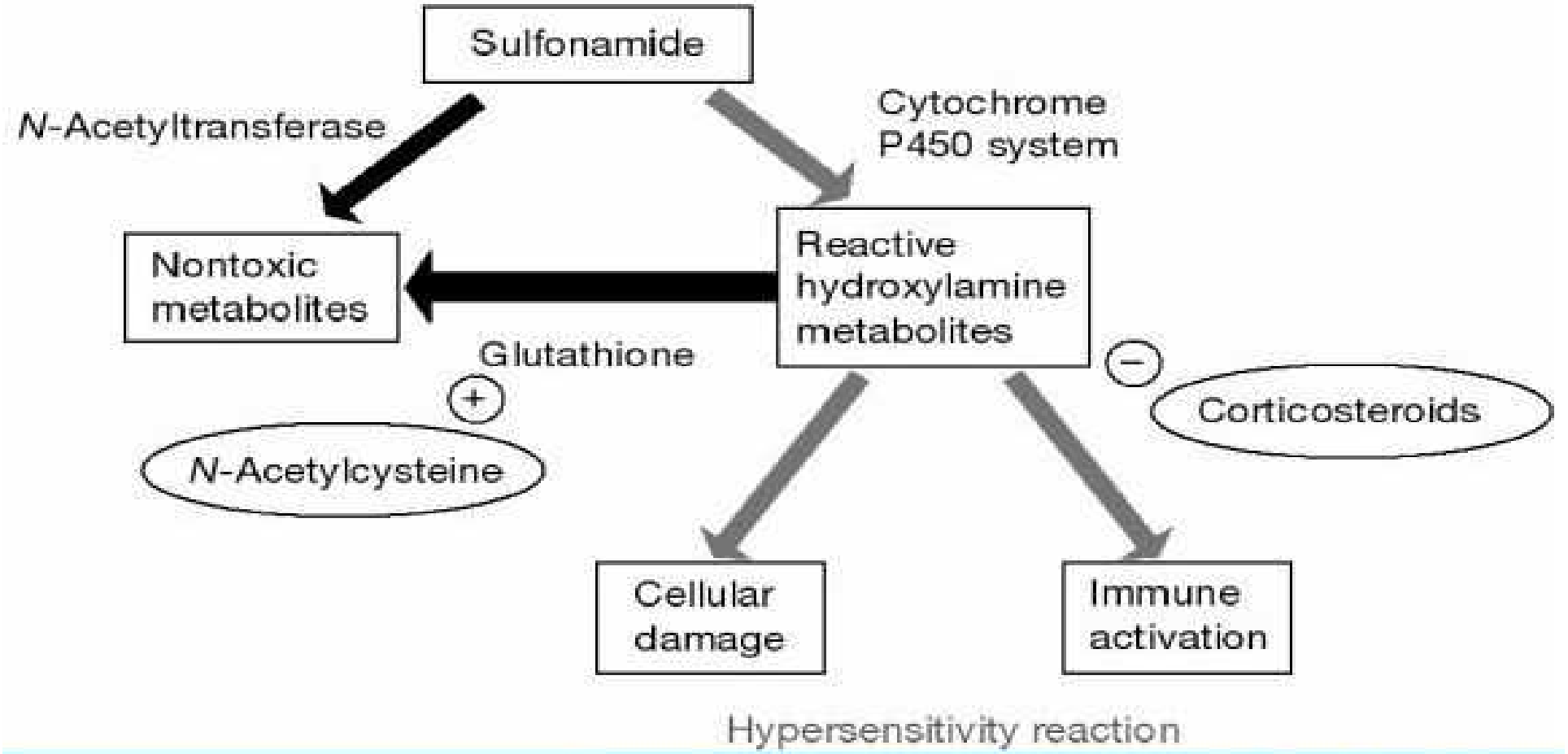
- Genetic deficiency of detoxifying enzymes leading to an accumulation of drug metabolites.
- Genetic associations between human leukocyte antigen (HLA) associations and drug hypersensitivity may occur(HLA-B*1502).
- A possible virus-drug interaction associated with viral reactivation may exist(HHV-6,HHV7,EBV)
- A total of 44drugs were described to be associated with DRESS.

Common Culprit Drugs



Chen Y C,Chiu H C & Chu C Y. **Drug Reaction With Eosinophilia and Systemic Symptoms: A Retrospective Study of 60 Cases.** *Arch Dermatol*. 2010;146(12):1373-1379

Medscape

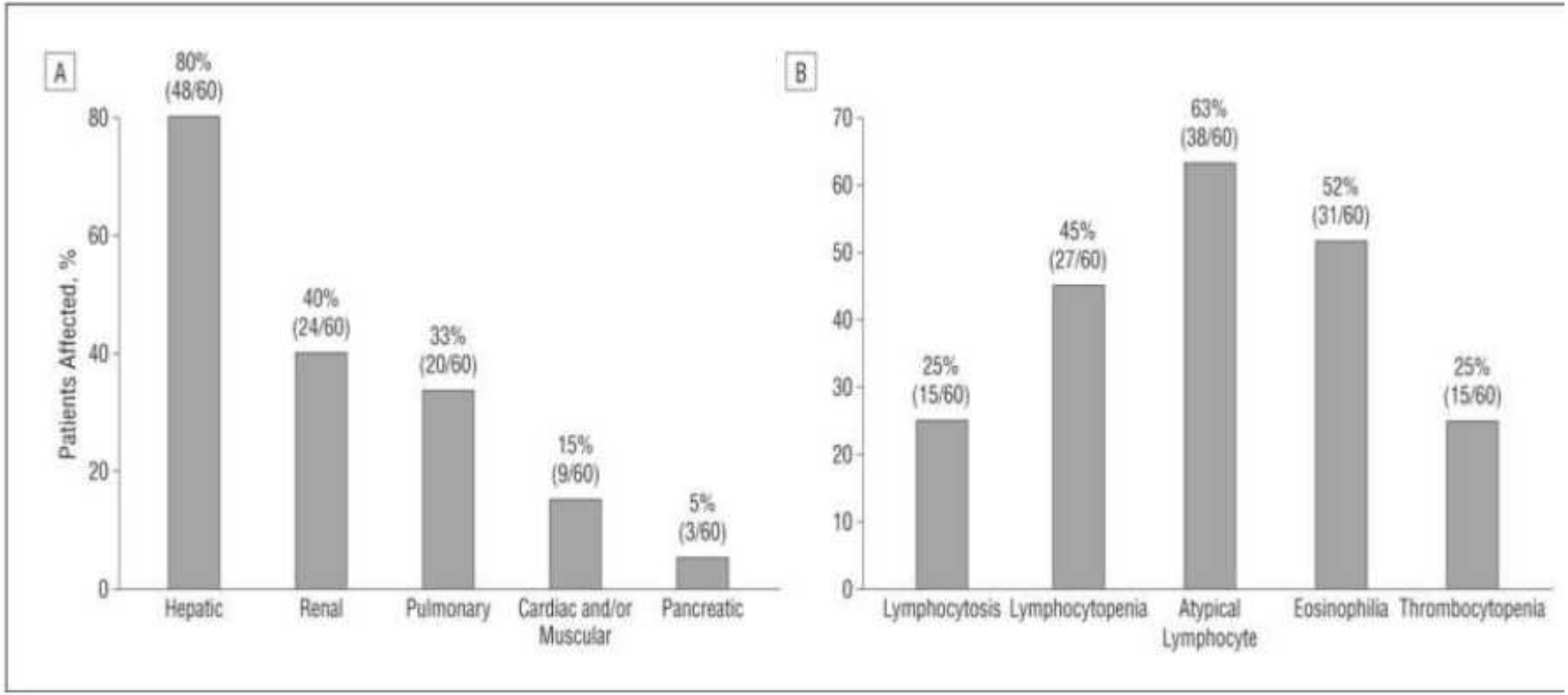


Proposed mechanism for sulfonamide-induced hypersensitivity reactions and treatment. *N*-Acetylcysteine acts by replacing stores of glutathione, an antioxidant involved in the detoxification pathway. Corticosteroids act by inhibiting the activity of reactive hydroxylamine metabolites.

CLINICAL FEATURES

- Fever
- The cutaneous manifestations typically consist of an urticarial, maculopapular eruption.
- Visceral involvement (hepatitis, pneumonitis, myocarditis, pericarditis, nephritis, and colitis) is the major cause of morbidity and mortality in this syndrome.
- Many cases are associated with leukocytosis with eosinophilia (90%) and/or mononucleosis (40%).

Effects on internal organs (A) and blood (B) of drug reaction with eosinophilia and systemic symptoms.



Drug Reaction With Eosinophilia and Systemic Symptoms: A Retrospective Study of 60 Cases

Arch Dermatol. 2010;146(12):1373-1379. doi:10.1001/archdermatol.2010.198

REGISCAR CRITERIA

- HospitalizationReaction suspected to be drug-related.
- Acute rash,Fever >38°C.
- Enlarged lymph nodes at a minimum of 2 sites.
- Involvement of at least 1 internal organ
- Blood count abnormalities-Lymphocytes above or below normal limits,EosinophilIA(>700),Thrombocytopenia.
- Three out of four criteria are required for making the diagnosis.

Eski M,Auanore L,Musette P et al.Arch Dermatol2009;145:67-72

JAPANESE GROUP'S CRITERIA

- Maculopapular rash developing >3 weeks after starting with the suspected drug.
- Prolonged clinical symptoms 2 weeks after discontinuation of the suspected drug.
- Fever >38°C
- Liver abnormalities (alanine aminotransferase>100U/L)
- Leucocyte abnormalities:Leucocytosis,Atypical lymphocytosis (>5%),Eosinophilia .
- Lymphadenopathy
- Human Herpes 6 reactivation
- The diagnosis is confirmed by the presence of the 7 criteria

Shihara T,Iijma M.Ikezawa Z.Hashimoto K.Br J Dermatol.2007;156:1083-1084

Diagnostic Tests

Confirmation of DRESS:

- CBC with differential and peripheral blood smear.
- Testing for HHV infection.
- Skin biopsy.

Exclusion of DDx:

- Blood cultures
- Antinuclear antibodies
- Serology for viral hepatitis

Assessment of organ involvement:

- Serum creatinine and urinalysis.
- Troponin and ECG.

Table 1. DRESS syndrome: most common differential diagnoses

	DRESS syndrome	SJS/TEN	Hypereosinophilic syndrome
Cutaneomucous features	Facial oedema, morbilliform eruption, exfoliative dermatitis, tight blisters	Blisters, atypical targets, cutaneomucous erosions	Urticaria, angio-oedema, morbilliform eruption, infiltrated papules or nodules
Haematological abnormalities			
Eosinophilia	+	–	+
Presence of atypical lymphocytes	+	–	+/–
Systemic involvement			
Adenopathies	+	–	+
Hepatitis	+	+	+
Other organ involvement	Interstitial nephritis, pneumonitis, carditis	Tubular nephritis, tracheobronchial necrosis	Carditis, pneumonitis, encephalopathy, diarrhoea, vomiting or abdominal pain

+ = Usual; +/– = possible; – = very rare or absent.

MANAGEMENT

- DRESS syndrome must be recognized promptly and the causative drug withdrawn. The earlier the drug withdrawal, the better the prognosis.
- Treatment is largely supportive and symptomatic; Antihistamines,corticosteroids are often used, but the evidence regarding their effectiveness is scant.
- Other immunosuppressants, such as cyclosporin, may also be required.

MONITORING:

Monitored for new skin lesions,clinical or laboratory Abnormalities in organ.

Weekly laboratory testing is advised.

COMPLICATIONS:

Autoimmune diseases have been reported in some patients.

Chronic renal failure or lymphoma-rare complications.

PROGNOSIS:

Most patients recover within weeks or months after the drug withdrawal.

MORTALITY-10%

TAKE HOME MESSAGE

- Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) is a great CLINICAL MIMICKER and potentially life-threatening syndrome including severe skin lesion, fever, hypereosinophilia,lymphadenopathy and internal organ involvement.
- DRESS can be associated with human herpesvirus 4, 6, and 7 infections; serology of these viruses should be checked.
- The main treatment of DRESS are withdrawal of culprit drug and corticosteroid treatment.

ACKNOLEDGEMENT

- Dr Venugopal Reddy (Consultant Dermatologist)
- Dr Muralidaran(Consultant Dermatologist)
- Dr Ramagopalakrishnan(Infectious Disease Consultant)
- Dr Shymala.J(consultant pediatrician)