STANDARD TREATMENT WORKFLOW (STW)

Cutaneous Adverse Drug Reactions - B

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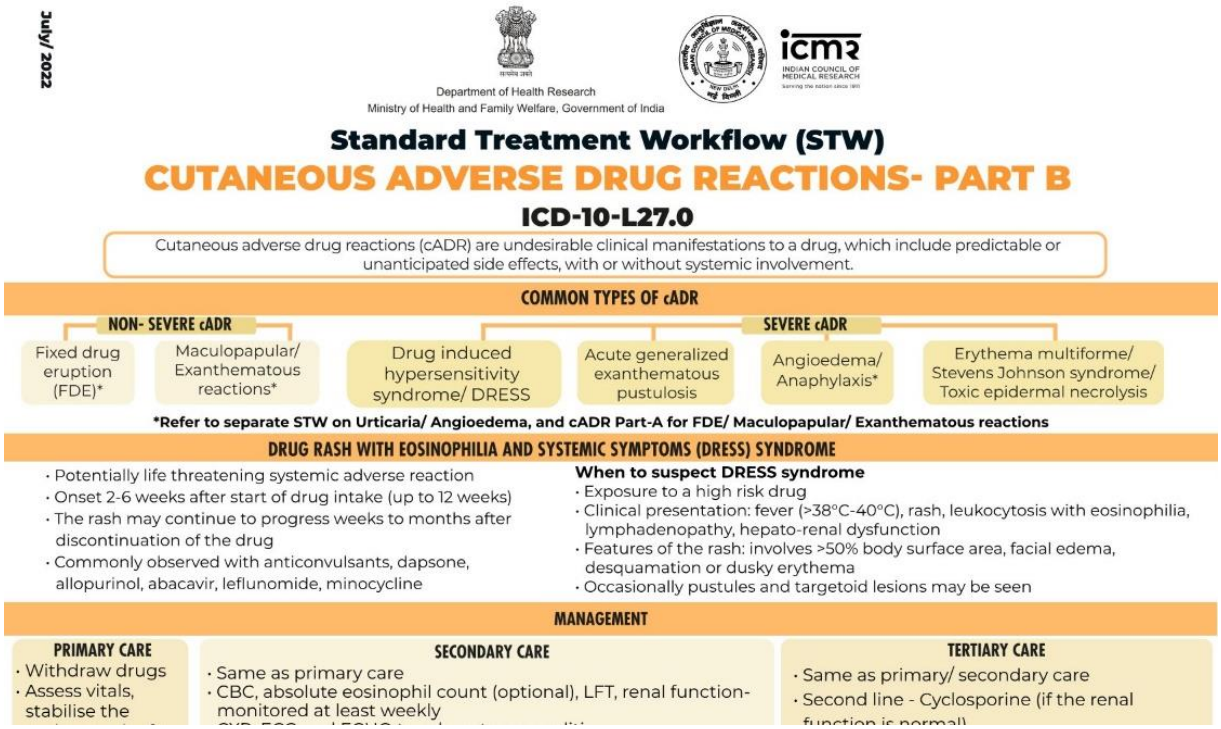

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Standard Treatment Workflow (STW)

CUTANEOUS ADVERSE DRUG REACTIONS- PART B

ICD-10-L27.0

Cutaneous adverse drug reactions (cADR) are undesirable clinical manifestations to a drug, which include predictable or unanticipated side effects, with or without systemic involvement.

COMMON TYPES OF cADR

NON- SEVERE cADR

- Fixed drug eruption (FDE)*
- Maculopapular/ Exanthematous reactions*

SEVERE cADR

- Drug induced hypersensitivity syndrome/ DRESS
- Acute generalized exanthematous pustulosis
- Angioedema/ Anaphylaxis*
- Erythema multiforme/ Stevens Johnson syndrome/ Toxic epidermal necrolysis

*Refer to separate STW on Urticaria/ Angioedema, and cADR Part-A for FDE/ Maculopapular/ Exanthematous reactions

DRUG RASH WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME

- Potentially life threatening systemic adverse reaction
- Onset 2-6 weeks after start of drug intake (up to 12 weeks)
- The rash may continue to progress weeks to months after discontinuation of the drug
- Commonly observed with anticonvulsants, dapsone, allopurinol, abacavir, leflunomide, minocycline

When to suspect DRESS syndrome

- Exposure to a high risk drug
- Clinical presentation: fever (>38°C-40°C), rash, leukocytosis with eosinophilia, lymphadenopathy, hepato-renal dysfunction
- Features of the rash: involves >50% body surface area, facial edema, desquamation or dusky erythema
- Occasionally pustules and targetoid lesions may be seen

MANAGEMENT

PRIMARY CARE

- Withdraw drugs
- Assess vitals, stabilise the patient and refer to higher center
- Symptomatic relief: Antihistamines, emollients
- Do not add any unnecessary new medications

SECONDARY CARE

- Same as primary care
- CBC, absolute eosinophil count (optional), LFT, renal function- monitored at least weekly
- CXR, ECG and ECHO to rule out myocarditis
- **Treatment**
- If no evidence of major organ involvement
- First line- Systemic steroids- Prednisolone 0.5-2 mg/kg, slow taper after symptoms and signs resolve (over months if needed)
- Antihistamines-Pheniramine 25 mg TID, bland emollients like liquid paraffin
- If there is severe organ involvement- liver, renal or cardiac refer to tertiary center for multidisciplinary intensive care

TERTIARY CARE

- Same as primary/ secondary care
- Second line - Cyclosporine (if the renal function is normal)
- Management will require a multidisciplinary team approach, depending on the organ(s) involved
- In the presence of severe liver failure, hemophagocytic syndrome, gastrointestinal bleeding, multiorgan failure, the patient may require intensive care treatment

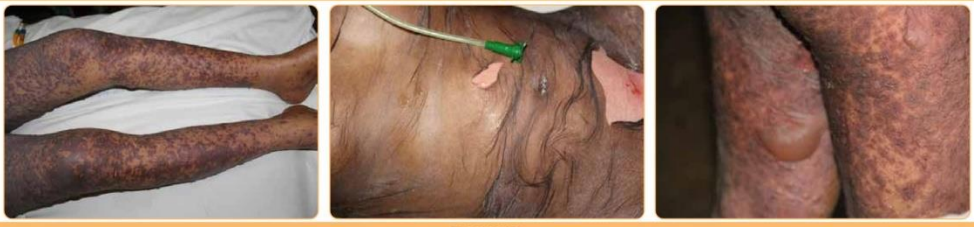
STEVENS JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN)

- Acute, severe mucocutaneous reactions associated with epidermal detachment and/ or tenderness, and widespread erythematous lesions with central dusky erythema or vesiculation often associated with high grade fever
- Usually observed with aromatic anticonvulsants, allopurinol, nevirapine, abacavir, NSAIDs, co-trimoxazole
- The classification of SJS, TEN is based on the extent of detachment
- D/d-Staphylococcal scalded skin syndrome, pemphigus

TYPE	DETACHMENT (% BSA)	WIDESPREAD ATYPICAL TARGETS *OR ERYTHEMATOUS MACULES
SJS	<10%	Present
SJS-TEN	10-30%	Present
TEN	≥30%	Present
TEN without SPOTS	≥10%	Absent

*Atypical targets (Red macules with purpuric vesiculations/ crusted centers)

TOXIC EPIDERMAL NECROLYSIS



PROGNOSIS

SCORTEN PROGNOSTIC FACTORS	POINTS
Age > 40 years	1
Tachycardia > 120 bpm	1
Neoplasia	1
Initial detachment > 10%	1
Serum urea > 60 mg/dL	1
Serum bicarbonate < 20mmol/L	1
Blood glucose > 252mg/ dL	1

Assess prognosis with a SCORTEN score done within 24 hours of presentation and repeated 3 days later

SCORTEN SCORE	ESTIMATED MORTALITY %
0-1	3
2	12
3	35
4	58
≥ 5	> 90

INVESTIGATIONS

- Chest X- ray
- ECG
- **Laboratory tests-** CBC, LFT, KFT, electrolytes, magnesium, phosphate, lactate
- Blood gas analysis
- **Microbiology-** Pus culture from infected areas and blood culture
- **Skin biopsy-** Not usually required unless the diagnosis is in doubt
- **Optional-** In TEN, biopsy and direct immunofluorescence is useful to rule out SLE and pemphigus

MANAGEMENT

PRIMARY CARE

- See primary care for drug rash with eosinophilia and systemic symptoms (DRESS)

SECONDARY CARE

- Assess vitals, stabilise the patient, nutrition and fluid replacement as appropriate
- Local care for skin and mucosae
- Skin care- dilute potassium permanganate baths/ saline compresses/ Chlorhexidine baths
  - Detached epidermis can be left in situ and covered with non-adherent dressing (sterile vaseline gauze)
  - Topical antibiotics (Mupirocin or Fucidin) on sloughed off areas
  - Oral care- Rinse mouth with Chlorhexidine 2-3 times, soft paraffin on lips as needed, steroid mouth washes
  - Eye care- refer to ophthalmologist
- Antibiotics-broad spectrum antibiotics (in case of sepsis or secondary infection) to cover staph, strep and pseudomonas. Change according to culture results and avoid suspected drug class
- Adjuvant systemic therapy (ideally within the first 24-72 hours of onset)
  - The role of systemic steroids is limited to early phase of SJS/TEN. High doses for longer periods can increase the risk of sepsis and metabolic complications. However judicious use of Prednisolone 1-2 mg/kg or equivalent dose of intravenous Dexamethasone for 3-7 days may be of benefit
  - Cyclosporine in a dose of 3-5 mg/kg for a period of 10-14 days (with monitoring)
- If skin detachment >10% refer to a center with an ICU familiar with management of skin failure
- If < 10% follow the treatment as described

TERTIARY CARE

- Admit in specialized units within dermatology wards if vitals are stable and follow secondary care treatment
- Barrier nursing
- If patient has SIRS/ sepsis or in shock, admit to ICU
- Long term follow up will be required to address complications: ophthalmic, skin and respiratory tract involvement

ANY DRUG BELONGING TO ANY MEDICINAL SYSTEM CAN CAUSE cADR

This STW has been prepared by national experts of India with feasibility considerations for various levels of healthcare system in the country. These broad guidelines are advisory, and are based on expert opinions and available scientific evidence. There may be variations in the management of an individual patient based on his/her specific condition, as decided by the treating physician. There will be no indemnity for direct or indirect consequences. Kindly visit the website of DHR for more information: (**stw.icmr.org.in**) for more information.
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