## STANDARD TREATMENT WORKFLOW (STW)

# Cutaneous Adverse Drug Reactions – Part A

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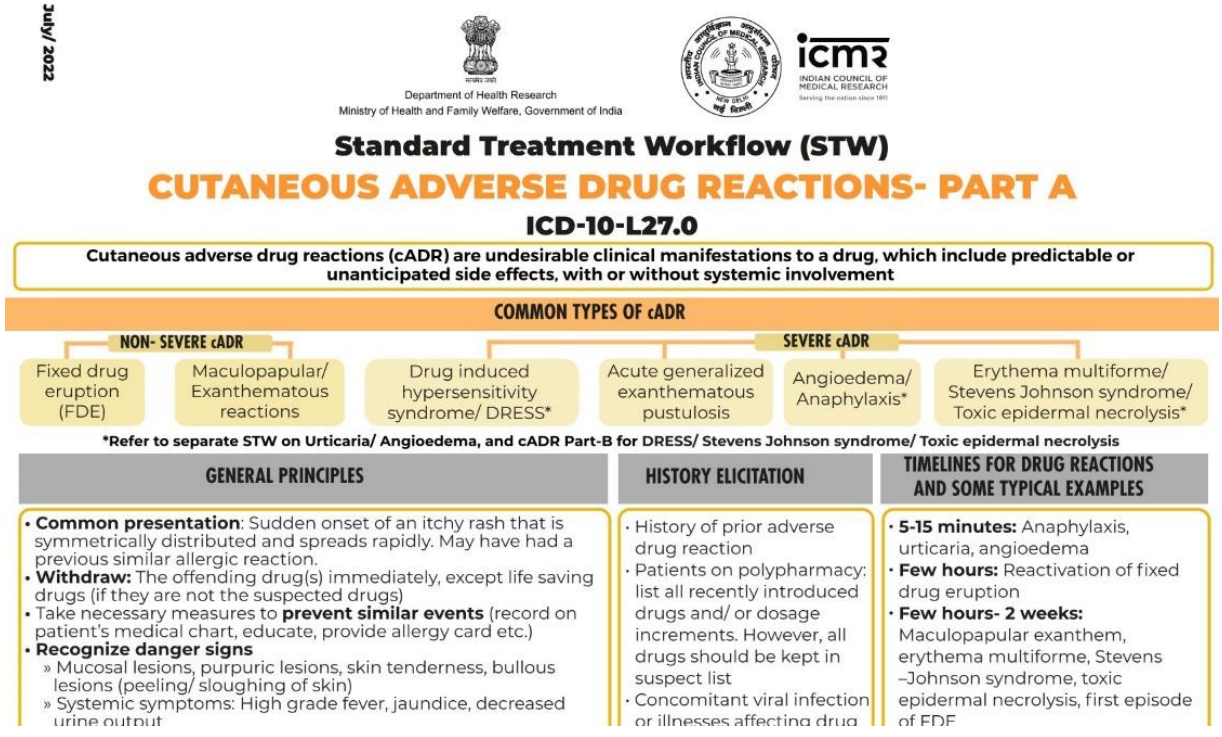

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# Standard Treatment Workflow (STW)

# CUTANEOUS ADVERSE DRUG REACTIONS- PART A

## 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-B for DRESS/ Stevens Johnson syndrome/ Toxic epidermal necrolysis

### GENERAL PRINCIPLES

- **Common presentation**: Sudden onset of an itchy rash that is symmetrically distributed and spreads rapidly. May have had a previous similar allergic reaction.
- **Withdraw:** The offending drug(s) immediately, except life saving drugs (if they are not the suspected drugs)
- Take necessary measures to **prevent similar events** (record on patient's medical chart, educate, provide allergy card etc.)
- **Recognize danger signs**
  - » Mucosal lesions, purpuric lesions, skin tenderness, bullous lesions (peeling/ sloughing of skin)
  - » Systemic symptoms: High grade fever, jaundice, decreased urine output
- **Action required:** Prompt and urgent care at a specialised centre. Apart from maintenance of vitals, withdrawal of all drugs, initiation of oral or intravenous corticosteroids, care of the eye, evaluation of secondary infection/ sepsis are important

### HISTORY ELICITATION

- History of prior adverse drug reaction
- Patients on polypharmacy: list all recently introduced drugs and/ or dosage increments. However, all drugs should be kept in suspect list
- Concomitant viral infection or illnesses affecting drug metabolism or excretion (eg. chronic kidney disease)

### TIMELINES FOR DRUG REACTIONS AND SOME TYPICAL EXAMPLES

- **5-15 minutes:** Anaphylaxis, urticaria, angioedema
- **Few hours:** Reactivation of fixed drug eruption
- **Few hours- 2 weeks:** Maculopapular exanthem, erythema multiforme, Stevens –Johnson syndrome, toxic epidermal necrolysis, first episode of FDE
- **4- 12 weeks:** DRESS syndrome, Dapsone syndrome, anticonvulsant induced hypersensitivity syndrome

### 1) FDE

- **Distinctive drug eruption:** usually recur at the same site on drug re-exposure
- **Acute FDE:** dusky red-violaceous plaques with or without vesiculation or bullae
- **Common sites:** lip, genitalia, proximal extremities, low back, sacrum
- **Local symptoms:** pruritus, burning, and pain; solitary or numerous (latter is difficult to differentiate from toxic epidermal necrolysis). Resolve with persistent hyperpigmentation
- **Clinical variants:** bullous, generalised, pure mucosal
- **Common drugs that cause FDE:** Sulfonamides, tetracyclines, quinolones, NSAIDS, dapsone, antimalarials, barbiturates, nitroimidazoles

**REFER TO HIGHER CENTER IF**
- There are atypical symptoms
- Uncertain diagnosis
- Severe reaction (multiple lesions, bullae, severe mucosal lesions, systemic symptoms)

### MANAGEMENT

**PRIMARY HEALTH CENTRE**
- Withdraw the drug
- General management: Bullous/ moist/ oozy lesions- normal saline compresses
- Topical steroid: Betamethasone valerate cream BD for cutaneous lesions
- Antihistamines –Tab Pheniramine maleate 25 mg BD/TID for itching
- Review patient in 1 week

**SECONDARY LEVEL CARE**
- Continue treatment as described at primary care level
- If severe: add short course of oral steroids: Prednisolone 0.5 mg-1 mg/kg for 3-5 days

**TERTIARY LEVEL**
- Admit the patient if the episode is generalized and severe
- Histopathology in doubtful cases
- If the oral mucositis is severe, consider parenteral steroids
- Provocation tests may be done after resolution of symptoms (usually after 1-6 months) by an oral challenge with each suspected individual drug consecutively

### 2) MACULOPAPULAR/EXANTHEMATOUS REACTIONS

- Abrupt onset, erythematous maculopapular eruption
- Typically starts on the trunk, spreads symmetrically to extremities. Dependent areas may have purpuric lesions
- Usually accompanied by mild systemic symptoms- pruritus, low grade fever, mild eosinophilia
- All drugs taken in the last 4 weeks are suspects. May manifest within 48 hours if the patient has taken the drug previously
- Commonly observed with co-trimoxazole, cephalosporins, anti-tubercular drugs, aminopenicillins, quinolones, dapsone, NSAIDS, anticonvulsants, nevirapine, abacavir, allopurinol, leflunomide
- Differential diagnosis: Viral exanthem, Rickettsial rash, HIV, Kawasaki disease (in children)
- Fever and prodromal symptoms (coryza, malaise) occur before the development of rash in most viral exanthems and the drug history is usually negative prior to it

**RED FLAG SIGNS**
- Mucosal involvement
- Purpuric lesions
- Bullous lesions
- Skin tenderness
- Facial/ acral edema
- Erythroderma
- Systemic symptoms - High grade fever, hepatitis, renal involvement, significant eosinophilia

### MANAGEMENT

**PRIMARY CARE**
- Withdraw the suspect drug(s)
- Pheniramine maleate 25 mg TID
- Calamine lotion
- Refer to higher center if symptoms persist or red flag signs present

**SECONDARY CARE**
- Confirm the diagnosis by history and clinical findings
- Admit if red flag signs are present
- Laboratory tests: CBC (Eosinophilia supports the diagnosis), LFT, serum creatinine, urine M/E
- Treatment: in severe cases, prednisolone 0.5-1 mg/ kg/ day x 5-7 days (after ruling out infection)

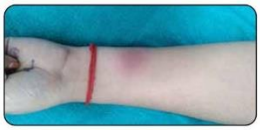
**TERTIARY CARE**
- Admit if red flag signs are present
- Confirm diagnosis of drug rash
- Additional lab tests if required: ANA, HIV, skin biopsy
- Consider DRESS if rash is progressing or significant organ involvement is evident

### DRUG PROVOCATION TEST

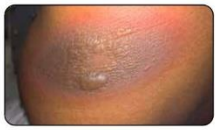
**In the absence of any reliable *in vitro* test in clinical setting, oral drug challenge is the only way to detect the responsible drug**

Usually undertaken when drug avoidance is impractical, especially in case of polypharmacy or life saving medicines (e.g. antituberculous therapy)

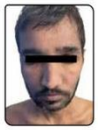
- Take a written consent prior to challenge
- Contraindicated in active illness or pregnancy
- Assess the risk benefit ratio
- Caution: patients on antihistamines, oral steroids and tricyclic antidepressants may have a modified response to the challenge
- A negative test only indicates that the patient is not allergic to the drug at the time of challenge
- The dose of drug for challenge depends on the severity of the previous reaction and the pharmacokinetic profile
- Drug provocation should always be done
  - After admission/ under observation except in cases with FDE
  - Usually in the daytime so that the faintest erythema is appreciated
  - It should be treated immediately and aggressively with an appropriate dose of systemic corticosteroid which may be required for only 1-2 days
  - Drug provocation in cases with DRESS has to be avoided or if provoked, a prolonged retreatment is required
  - In case of SJS-TEN drug provocation should be done only if the drug cannot be avoided. Provocation is preferred with a chemically unrelated molecule
- Intradermal tests can be done in IgE mediated reactions
- Patch test has a low sensitivty and should not be relied upon in severe cADR

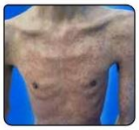


FDE



BULLOUS FDE





MACULOPAPULAR RASH