STANDARD TREATMENT WORKFLOW (STW)

Cutaneous Adverse Drug Reactions - B

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STANDARD TREATMENT WORKFLOW (STW)

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**

- Fixed drug eruption (FDE)*
- Maculopapular/Exanthematos reactions*
- Drug induced hypersensitivity syndrome/ DRESS
- Acute generalized exanthematos 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/ Exanthematos 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, hepatorenal 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 vital, stabilise the

**SECONDARY CARE**
- Same as primary care
- CBC, absolute eosinophil count (optional), LFT, renal function monitored at least weekly

**TERTIARY CARE**
- Same as primary/secondary care
- Second line - Cyclosporine (if the renal function is normal)
**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 unpredictable side effects, with or without systemic involvement.

### Drugs with Erythema and Symmetric Syndromes (DRESS)

<table>
<thead>
<tr>
<th>Non-Severe ADR</th>
<th>Severe ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed drug eruption (FDE)</td>
<td>Maculopapular/Exanthematous reactions*</td>
</tr>
<tr>
<td>Drug induced hypersensitivity syndrome (DRESS)</td>
<td>Acute generalized exanthematous pustulosis</td>
</tr>
<tr>
<td>Angioedema</td>
<td>Erythema multiforme/Stevens-Johnson syndrome/Toxic epidermal necrolysis</td>
</tr>
</tbody>
</table>

*Refer to separate STW on Urticarial Angioedema, and CADR Part A for FDE/ Maculopapular/Exanthematous reactions

When to suspect DRESS syndrome

- Exposure to a high risk drug
- Clinical presentation (fever, 38°C-40°C, rash, leukocytosis with eosinophilia, lymphadenopathy, hepatitis renal dysfunction
- Resurfacing of the rash involves >50% body surface area, facial edema, desquamation and/or erythrodermia
- Occasionally, pastes and target lesions may be seen

### MANAGEMENT

#### PRIMARY CARE

- Withdraw the drug
- Assess vital signs, stabilize 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

#### 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 vesication often associated with high grade fever
- Usually characterized by the pattern of rash distribution (target-like, bullae, eosinophilic dermatitis)
- The classification of SJS, TEN is based on the extent of detachment
- DSA (Staphylococcal scalded skin syndrome, pemphigus

#### TOXIC EPIDERMAL NECROLYSIS

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

<table>
<thead>
<tr>
<th>SORCEN PROGNOSTIC FACTORS</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;60 years</td>
<td>1</td>
</tr>
<tr>
<td>Tachycardia &gt;100 bpm</td>
<td>1</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1</td>
</tr>
<tr>
<td>Initial detachment &gt;10%</td>
<td>1</td>
</tr>
<tr>
<td>Serum urea &gt;40 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>Serum creatinine &gt;20 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>Blood glucose &gt;250 mg/dL</td>
<td>1</td>
</tr>
</tbody>
</table>

#### INVESTIGATIONS

- Chest X-ray
- Laboratory tests - CBC, LFT, KFT, electrolytes, magnesium, phosphates, lactate
- Blood gas analysis
- Microbiology: Plus 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)
- Assess vital signs, stabilize the patient, nutrition and fluid replacement as appropriate
- Local care for skin and mucosa
- Skin culture x4 potassium permanganate baths/saline compresses/Chlorhexidine baths
- Detached epidermis can be left in situ and covered with non-adherent dressing ( sterile, watertight dress)
- Topical antibiotics (Mupirocin or Fusidic) 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
- Antibiotic broad-spectrum antibiotics (in case of sepsis or secondary infection) to cover staph, strep and pseudomonas

#### SECONDARY CARE

- Adjunct 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
- Cyclophosphamide in a dose of 5-10 mg/kg for a period of 3-4 months (with monitoring)
- If skin detachment >10% refer to a center with ICU familiar with management of skin failure
- if >10% follow the treatment as described

#### TERTIARY CARE

- Admit in specialized units within dermatology wards if vials are stable and follow secondary care treatment
- Barrier nursing
- If patient has SIRS/ sepsis or in shock, admit to ICU

**ANY DRUG BELONGING TO ANY MEDICINAL SYSTEM CAN CAUSE ADR**

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