Drug eruption handout

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>>> Steven Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)

- Dermatological emergency
- <10% body surface area (BSA) = SJS, 10-30% BSA = SJS/TEN overlap, >30% BSA = TEN
- Starts 7-21 days after initiation of culprit medication – however, occurs rapidly if culprit medication re-challenged
- **Clinical features**
  - Preceded by coryzal symptoms/eye pain/throat pain by 1-3 days
  - Then develop cutaneous lesions with cephalocaudal spread – dusky/dusky-red macules with epidermal detachment + erosions, macular atypical targets and bullous lesions
  - Nikolsky positive
  - Extremely painful
- Development of severe mucositis involving aerodigestive tract, ocular and genital mucosa
- **Common drug culprits**: sulfonamides, allopurinol, aromatic anticonvulsants (phenytoin, carbamazepine, lamotrigine, phenobarbital, oxcarbazepine), NSAIDs, aminopenicillins (amoxicillin, ampicillin), quinolones, antiretrovirals, sulfasalazine
  - Drugs with longer half-lives associated with increased mortality
  - Certain HLA allotypes increase risk of SJS/TEN in certain ethnic populations → CONSIDER HLA TESTING PRIOR TO INITIATION (via Red Cross Australia [Lifeblood] or DHM; cost ~$60-80)
    - HLA-B*1502 – Han Chinese and lamotrigine
    - HLA-B*15:02 –Han Chinese/Thai/ Malaysian/ East Indians and carbamazepine
    - HLA-B*15:02 – Han Chinese and phenytoin
    - HLA-A*31:01 – Europeans and carbamazepine
    - HLA-B*58:01 – Han Chinese and allopurinol
- Risk of mortality estimated by SCORTEN
- **Immediate management**: stop culprit drug, resuscitation, analgesia, call ambulance and send to nearest ED, liaise with local dermatology/ENT/gynaecology/urology services
  - Extremely helpful if thorough drug timeline is available
- Majority of patients with SJS/TEN will need retrieval to Royal North Shore Hospital for burns unit and multi-team management

>>>> Drug reaction with eosinophils and systemic symptoms (DRESS)

- **Dermatological emergency/severe cutaneous drug reaction**
  - 5-10% mortality rate
- Occurs 2-6 weeks after introduction of culprit drug; faster if rechallenged
- **Common culprit drugs**: aromatic anticonvulsants, sulfonamides, allopurinol, dapsone, minocycline, nevirapine, abacavir
- **Clinical features**
  - Often polymorphous rash
  - Fever
  - Facial and ear swelling are often present
  - Lymphadenopathy, hepatosplenomegaly
  - +/- mild mucosal involvement
  - Marked eosinophilia, atypical lymphocytes
  - Hepatic and renal involvement common
- Eosinophils can infiltrate any organ → broad
- **Immediate management**: stop culprit drug, resuscitation, send to nearest emergency department and liaise with local dermatology service
  - Extremely helpful if thorough drug timeline is available

>>>> Acute generalised exanthematous pustulosis

- Severe cutaneous drug reaction
- 1-2% mortality rate
- Occurs within days of exposure to culprit drug
- **Common culprit drugs**: β-Lactam antibiotics, macrolides, calcium channel blockers, tetracyclines, oral antifungals, sulfonamides, carbamazepine
- **Clinical features**
  - Fever
  - Sheets of small subcorneal non-follicular pustules on face and/or intertriginous areas which can become generalised
  - +/- mucosal involvement
  - Rarely has systemic involvement – but can develop hepatic, renal, pulmonary involvement
  - Resolves with desquamation of involved areas
- **Management principles** – stop culprit drug, topical corticosteroids until resolution, urgent referral to ED/dermatology service (depending on severity)

>>>> Erythema multiforme

- Usually viral-induced (90%), but rarely secondary to drugs
  - Most common – HSV, mycoplasma
- Occurs 5-28 days after drug exposure
- Divided into EM minor (little to no systemic features or mucosal involvement) and EM major (severe mucosal involvement and systemic features)
- **Culprit drugs**: NSAIDs, sulfonamides, anticonvulsants, beta-lactams, allopurinol
- **Clinical features**
  - Typical target lesions (three different zones)
  - Atypical lesions (two different zones and/or poorly defined border)
  - Lesions favour acrofacial areas
  - Mucosal erosions – lips most commonly involved
  - +/- bullae
  - Fever and arthralgias
- Does not progress to SJS/TEN
- **Principles of management (for drug-induced cases)** – stop culprit drug, antipyretics, topical corticosteroids, systemic corticosteroids, ED referral if severe mucositis, urgent ophthal input if ocular involvement

>>>> Mobilliform/exanthematous drug eruption

- Most common type of cutaneous drug eruption
- Mobilliform = measles-like (maculopapular)
- Occurs 1-2 weeks after starting a new medication (more rapidly if re-challenge)
- **Most common culprit drugs**: beta-lactam antibiotics, allopurinol, aromatic anticonvulsants, sulfonamides, NSAIDs, abacavir, nevirapine
- No mucosal membrane / end-organ involvement
- **Clinical features**
  - Mobilliform eruption – erythematous macules and papules which appear symmetrically on upper limbs and trunk initially, then can become widespread
  - Pruritic
  - Mucosa usually spared
  - Can develop purpuric-appearing change on lower limbs
  - Can be associated with mild eosinophilia
- Early severe drug reactions can present the same – hence the need for monitoring to ensure improving
- **Management principles** are based on discontinuation of the culprit drug, topical corticosteroids until resolving, general skin care measures, and monitoring

>>>> Fixed drug eruption

- Initial episode usually occurs within 1-2 weeks of initiation of culprit drug; re-challenges often occur within 1-2 days
- **Common drug culprits**: trimethoprim, NSAIDs, tetracyclines, pseudoephedrine, paracetamol
    - Often medications which are taken intermittently
- **Clinical features**
    - Erythematous to violacenous oval well-demarkated plaque – most commonly found on hands, feet, anogenital region – usually recurs at same site time after time
    - Can develop bullous component
    - Can become generalised – this is a dermatological emergency
- Management principles – discontinue culprit drug, topical steroids, if generalised patient should be sent to nearest emergency department as requires specialised care

>>>> Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)

- Occurs hours-days after exposure to culprit drug
- **Common drug culprits**: amoxicillin/other beta-lactam antibiotics; multiple other drug triggers described
- **Clinical features**
    - Sharply demarcated symmetrical erythema in anogenital region (hence its other name of Baboon syndrome) and at least one other flexural site
    - No mucosal involvement
    - Systemically well
- **Principles of management:** cease culprit drug, topical corticosteroids until resolved