DRUG ERUPTIONS

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GUIDELINES FOR ASSESSMENT OF POSSIBLE ADVERSE DRUG REACTION

- Exclude alternative causes, especially infections (viral especially, clinically difficult to distinguish from the adverse effects of drugs used to treat infections).
- Examine interval between drug introduction and onset of reaction.
- Note any improvement after drug withdrawal.
- Determine whether similar reactions have been associated with same compound (BNF and contact Drug Information, Whiston ext 1565).
- Note any reaction on readministration of the drug if this is felt to be safe.

CLINICAL FINDINGS:

▪Cutaneous: Confluent erythema, Facial oedema, central facial involvement, Skin pain, Palpable purpura, Skin necrosis, Blisters with epidermal detachment, Epidermis separating readily from dermis with lateral pressure (Nicolsky's sign), Mucous membrane erosions,
Urticaria, swelling of tongue.

▪General: High fever (temperature >40_0C), Enlarged lymph nodes, Arthralgias or arthritis, Shortness of breath, wheezing, hypotension.

LABORATORY RESULTS:

- Eosinophil count >1000/µl,
- lymphocytosis with atypical lymphocytes
- abnormal liver functions.

DRUG INDUCED ACUTE URTICARIA, ANGIOEDEMA, AND ANAPHYLAXIS

Urticaria

▪ Transient erythematous, oedematous papules and wheals, with pruritus. Anywhere including palms, soles, scalp.
▪ Duration of individual lesions < 24 hours. ▪ "Acute" with episode lasting for less than 6 weeks, "chronic" lasting Longer.
▪ Drugs more often associated with acute urticarial: antibiotics, (penicillins, cephalosporins, sulfonamides, tetracyclines), NSAIDS, contrast media. Latex allergy (especially with direct contact with mucosal surfaces) can induce local or generalized urticaria.
▪ Treatment: -NB Withdraw causative agent, avoid in future
-Primarily treated with H1 antihistamines

Angioedema
▪ Reflect transient oedema in the deep dermal/subcutaneous tissues.
▪ Acute pale/pink swelling, usually the face (eyelids, lips, ears, nose), less often extremities, genitalia, frequently unilateral or asymmetric.
Larynx/epiglottis involved: may impair swallowing/upper-airway, obstruction/stridor. ▪ Oropharynx oedema (buccal mucosa/tongue) can occur (impaired swallowing).
▪ May be complicated by life-threatening anaphylaxis.
▪ Associated with urticaria in 50% of cases.
▪ ACE inhibitor induced angioedema (1-2 per 1000 new users) (onset: few minutes to years), penicillins, NSAIDS, contrast media, monoclonal antibody therapy.
▪ Treatment: -Withdraw offending drug and avoid in future
-H1 antihistamines. -If severe or breathing/swallowing difficulties, systemic corticosteroids, subcutaneous adrenalin/epinephrine

Anaphylaxis
▪ Acute life-threatening reaction. ▪ Combines skin (urticaria and/or angioedema) with systemic manifestations (hypotension and tachycardia).
▪ Treatment: - As per A+E protocol. Withdraw drug and avoid in future.
-Antihistamines, systemic corticosteroids, subcutaneous/iv adrenalin.

EXANTHEMATOUS DRUG ERUPTION

▪ Synonyms: Morbilliform eruption or maculopapular drug eruption.
▪ Most common drug reactions affecting skin,usually starts within 7-14 days of starting new drug. ▪ Mimics a measles-like viral Exanthem, systemic involvement minimal. ▪ Symmetric, erythematous macules, start on trunk/upper extremities, progressively confluent, polymorphic features, no mucosal involvement, pruritus, low grade fever.
▪ Drugs involved : Many!- including Penicillins, Carbamazepine, Allopurinol, Gold Salts, Sulfonamides.
Viral infections may increase incidence of morbilliform drug reactions (frequency of Penicillin-induced exanthematous eruption in mononucleosis: close to 100%).
▪ Diff diagnosis: viral exanthems (EBV, CMV,entero-, adeno-, HHV-6, early HIV). [polymorphic features and blood eosinophilia favour a drug reaction]
▪ Treatment: Discontinue offending agent, largely supportive, topical steroids/ antihistamines may alleviate pruritus.

DRUG HYPERSENSITIVITY SYNDROME

▪ Synonym: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). ▪ Specific, severe, idiosyncratic skin reaction with systemic manifestations, within 2-6 weeks after starting drug.
▪ Characterized by rash (morbilliform, later oedematous, additionally

vesicles, bullae, pustules, erythroderma, purpuric lesions), to face (hallmark), upper trunk/extremities. ▪ Fever, hepatitis, lymphadenopathy, arthralgias/arthritis, myocarditis, interstitial pneumonitis, eosinophilia with often atypical lymphocytes.
▪ Drugs involved: anticonvulsants (Phenytoin, Carbamazepine, Phenobarbital) and Sulphonamides most frequently, also lamotrigine, Allopurinol, Gold, Dapsone, Minocycline.
▪ Treatment: Early withdrawal, hospitalization, bedrest,
-Systemic corticosteroids are first line treatment.

ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS (AGEP)

▪ >90% drug induced, (occasionally mercury sensitivity/enteroviral).
▪ Acute febrile drug eruption. Numerous small, non-follicular sterile pustules (starting on face, axillae, groin) on oedematous erythema base, within 2 days of starting drug. ▪ Association (50%) of oedema (hands/face), purpura, vesicles, bullae, erythema multiforme like lesions, mucous membrane involvement. ▪ Lasts 1-2 weeks, followed by desquamation. ▪ Diff Diagnosis: acute pustular psoriasis (additional skin lesions >frequent in AGEP). ▪ Drugs involved: antibiotics (β-Lactam, macrolides), also calcium channel blockers, antimalarials, Terbenafine, Nystatin, INH, Metronidazole, Vancomycin, Doxycycline
▪ Treatment: -Withdraw drug, topical steroids, antipyretics.

FIXED DRUG ERUPTION

▪ Solitary, sometimes multiple, sharply demarcated, plaque, bulla, or erosion reoccuring with rechallenge of offending drug, at identical skin site (i.e. fixed).
▪ Drugs involved: sulfonamides, NSAIDS, barbituates, tetracyclines, Carbamazepine, Phenolphthalein in laxatives.
▪ Treatment: -Withdraw drug.

DRUG-INDUCED PHOTOSENSITIVITY

Combination of light [Ultraviolet (UV) or visible] plus drug [injection, ingestion, topical application] lead to several forms of cutaneous inflammation. Divided into 2 major types: phototoxic and photoallergic

PHOTOTOXIC DRUG-INDUCED PHOTOSENSITIVITY

▪ Can occur in all individuals who receives a sufficient amount of phototoxic drug, together with sufficient UV exposure. Clinically an exaggerated sunburn, BUT with shorter than expected exposure time.
▪ Erythema, oedema, vesicles, bullae limited sun-exposed areas, later

Hyperpigmentation. ▪ Drugs involved: tetracyclines, NSAIDS, fluoroquinolones, amiodarone,psoralens, phenothiazines, sulfonamides. Offending drug may be continued by decreasing sun exposure, dose of drug or both.

PHOTOALLERGIC DRUG-INDUCED PHOTOSENSITIVITY

Clinically: pruritic, papular eruption, resembles dermatitis or lichen planus, primarily in sun-exposed sites, over time involving non-sunexposed areas. ▪ Drugs commonly involved: thiazide diuretics, sulfonamides, sulfonureas, phenothiazines (all containing sulfur moiety), additionally quinine, quinidine, tricyclic antidepressants, antimalarials, NSAIDS.
▪ Treatment: -Usually transient, resolve IF diagnosis is made promptly and offending drug discontinued.

For Erythema Multiforme, SJS, TEN, and vasculitis please see other chapters.