Drug allergy (suspected or confirmed)

Suspected drug allergy is any reaction caused by a drug with clinical features compatible with an immunological mechanism. All drugs have the potential to cause adverse drug reactions, but not all of these are allergic in nature. A reaction is more likely to be caused by drug allergy if:

- The reaction occurred while the patient was being treated with the drug, or
- The drug is known to cause this pattern of reaction, or
- The patient has had a similar reaction to the same drug or drug-class previously.

A suspected reaction is less likely to be caused by a drug allergy if there is a possible non-drug cause or if there are only gastro-intestinal symptoms present.

The following signs, allergic patterns and timing of onset can be used to help decide whether to suspect drug allergy:

Immediate, rapidly-evolving reactions (onset usually less than 1 hour after drug exposure)

- Anaphylaxis, with erythema, urticaria or angioedema, and hypotension and/or bronchospasm. See also Antihistamines, allergen immunotherapy and allergic emergencies p. 291
- Urticaria or angioedema without systemic features
- Exacerbation of asthma e.g. with non-steroidal anti-inflammatory drugs (NSAIDs)

*Non-immediate reactions, **without** systemic involvement* (onset usually 6–10 days after first drug exposure or 3 days after second exposure)

- Cutaneous reactions, e.g. widespread red macules and/or papules, or, fixed drug eruption (localised inflamed skin)

*Non-immediate reactions, **with** systemic involvement* (onset may be variable, usually 3 days to 6 weeks after first drug exposure, depending on features, or 3 days after second exposure)

- Cutaneous reactions with systemic features, e.g. drug reaction with eosinophilia and systemic signs (DRESS) or drug hypersensitivity syndrome (DHS), characterised by widespread red macules, papules or erythroderma, fever, lymphadenopathy, liver dysfunction or eosinophilia
- Toxic epidermal necrolysis or Stevens–Johnson syndrome
- Acute generalised exanthematous pustulosis (AGEP)

EvGr Suspected drug allergy information should be clearly and accurately documented in clinical notes and prescriptions, and shared among all healthcare professionals. Patients should be given information about which drugs and drug-classes to avoid and encouraged to share their drug allergy status.

If a drug allergy is suspected, consider stopping the suspected drug and advising the patient or carer to avoid this drug in future. Symptoms of the acute reaction should be treated, in hospital if severe. Patients presenting with a suspected anaphylactic reaction, or a severe or non-immediate cutaneous reaction, should be referred to a specialist drug allergy service. Patients presenting with a suspected drug allergic reaction or anaphylaxis to NSAIDs, and local and general anaesthetics may also need to be referred to a specialist drug allergy service, e.g. in cases of anaphylactoid reactions or to determine future treatment options. Patients presenting with a suspected drug allergic reaction or anaphylaxis associated with beta-lactam antibiotics should be referred to a specialist drug allergy service if their disease or condition can only be treated by a beta-lactam antibiotic or they are likely to need beta-lactam antibiotics frequently in the future (e.g. immunodeficient patients). A For further information see Drug allergy: diagnosis and management. NICE Clinical Guideline 183 (September 2014) www.nice.org.uk/guidance/cg183.

Oral side-effects of drugs

Drug-induced disorders of the mouth may be due to a local action on the mouth or to a systemic effect manifested by oral changes. In the latter case urgent referral to the patient's medical practitioner may be necessary.

Oral mucosa Medicaments left in contact with or applied directly to the oral mucosa can lead to inflammation or ulceration; the possibility of allergy should also be borne in mind.

Aspirin tablets p. 130 allowed to dissolve in the sulcus for the treatment of toothache can lead to a white patch followed by ulceration.

Flavouring agents, particularly **essential oils**, may sensitise the skin, but mucosal swelling is not usually prominent.

The oral mucosa is particularly vulnerable to ulceration in patients treated with cytotoxic drugs, e.g. methotrexate p. 963. Other drugs capable of causing oral ulceration include **ACE inhibitors, gold, nicorandil p. 225, NSAIDs, pancreatin p. 103, penicillamine p. 1158, proguanil hydrochloride p. 654,** and **protease inhibitors**.

Erythema multiforme or Stevens-Johnson syndrome may follow the use of a wide range of drugs including **antibacterials, antiretrovirals, sulfonamide derivatives,** and **anticonvulsants**; the oral mucosa may be extensively ulcerated, with characteristic target lesions on the skin. Oral lesions of toxic epidermal necrolysis have been reported with a similar range of drugs.

Lichenoid eruptions are associated with **ACE inhibitors, NSAIDs,** methyldopa p. 157, chloroquine p. 651, **oral antidiabetics, thiazide diuretics,** and **gold**.

Candidiasis can complicate treatment with **antibacterials** and **immunosuppressants** and is an occasional side-effect of **corticosteroid inhalers**.

Teeth and jaw *Brown staining* of the teeth frequently follows the use of chlorhexidine mouthwash, spray or gel p. 1275, but can readily be removed by polishing. **Iron** salts in liquid form can stain the enamel black. Superficial staining has been reported rarely with co-amoxiclav suspension p. 582.

Intrinsic staining of the teeth is most commonly caused by **tetracyclines**. They will affect the teeth if given at any time from about the fourth month *in utero* until the age of twelve years; they are contra-indicated during pregnancy, in breast-feeding women, and in children under 12 years. All tetracyclines can cause permanent, unsightly staining in children, the colour varying from yellow to grey.

Excessive ingestion of **fluoride** leads to *dental fluorosis* with mottling of the enamel and areas of hypoplasia or pitting; fluoride supplements occasionally cause mild mottling (white patches) if the dose is too large for the child's age (taking into account the fluoride content of the local drinking water and of toothpaste).

The risk of *osteonecrosis of the jaw* is substantially greater for patients receiving intravenous bisphosphonates in the treatment of cancer than for patients receiving oral bisphosphonates for osteoporosis or Paget's disease. All patients receiving bisphosphonates should have a dental check-up (and any necessary remedial work should be performed) before bisphosphonate treatment, or as soon as possible after starting treatment. Patients with cancer receiving bevacizumab p. 909 or sunitinib p. 1057 may also be at risk of osteonecrosis of the jaw.

Periodontium *Gingival overgrowth* (gingival hyperplasia) is a side-effect of phenytoin p. 339 and sometimes of ciclosporin p. 883 or of nifedipine p. 174 (and some other calcium-channel blockers).

Thrombocytopenia may be drug related and may cause bleeding at the gingival margins, which may be spontaneous or may follow mild trauma (such as toothbrushing).

Salivary glands The most common effect that drugs have on the salivary glands is to *reduce flow* (xerostomia). Patients with a persistently dry mouth may have poor oral hygiene;