Beaumont Hospital

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Departments of Immunology & Clinical Microbiology

Guideline on Evaluation of a Patient with Suspected Antimicrobial Allergy

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TABLE OF CONTENTS

1.0 Drug hypersensitivity reactions (DHR)

1.1 Introduction to DHR

Drug hypersensitivity reactions (DHRs) are adverse effects of drugs that clinically resemble allergic reactions.

The term **drug allergy** should be confined to DHRs for which a definite immunological mechanism is demonstrated (either antibody or T cells). DHRs may be **allergic** or **non-allergic**.

DHRs may be **immediate** (typically <1hr and always <6hrs post administration of first dose) or **non-immediate** (usually >24hours and always >1 hour post administration of first dose) of the implicated drug.

Types of DHRs relevant to antimicrobial allergy		
Type of DHR	**Immediate**	**Non-immediate**
Time of onset	<1hour usually; Always <6 hours	>24hours usually; Always >1hour
Mechanisms	IgE mediated	IgG, IgM, T cells
Manifestations	Urticaria* Angioedema** Rhinitis Conjunctivitis Bronchospasm GI symptoms Anaphylaxis	Delayed urticaria* Maculopapular eruptions Fixed drug eruptions Vasculitis Toxic epidermal necrolysis (TEN) Stevens Johnson syndrome (SJS) Acute generalised exanthematous pustulosis (AGEP) DRESS Hepatitis Tubulointerstitial nephritis Cytopenias Drug fevers

***Urticaria** consists of red patches and wheals (hives) on the skin. The lesions can vary from a few millimetres to several centimetres in diameter, are often surrounded by a red flare and are usually itchy. They may be round or form rings, a map-like pattern or giant patches. While the rash may last several days, individual lesions may last a few minutes or several hours and may change shape or migrate. **Atypical urticaria** is characterised by individual lesions which last >24 hours, and/or lesions which result in bruising. Atypical urticaria is not typical of an IgE mediated reaction and is suggestive of an atypical vasculitis, which may be mediated by IgG or IgM and may be a form of non-immediate DHR.

****Angioedema** is deeper swelling of subcutaneous, or submucosal tissue. The swelling may affect any part of body, with eyes, lips and tongue most commonly involved, including respiratory and gastrointestinal mucosa. Angioedema may be itchy, or painful. Laryngeal swelling can be life-threatening.

1.2 Assessing a patient with a DHR

A full history and clinical examination must be undertaken, with documentation of all relevant information. It should be possible to classify the DHR as either:

- **Immediate,** or within 6 hours of administration, with features of an IgE mediated reaction
- **Non-immediate, with no systemic features**
- **Non-immediate with systemic features,** including DRESS, SJS/TEN and variants, AGEP, cytopenias, hepatitis or tubulointerstitial nephritis

	Reaction more likely due to drug allergy	**Reaction less likely due to drug allergy**
Timing of reaction	Symptoms during or after use of drug	Symptoms reported when not on the drug
Drug	Similar prior reaction to the same drug or similar drug class	
Reaction type		Gastrointestinal symptoms only reported

1.3 Documenting a DHR

The following information must be documented by the healthcare professional (HCP) reviewing a patient with a DHR:

- Source of history- patient, relative, HCP
- Medication (generic and brand) – dose & route
- Indication for treatment – if no diagnosis, describe the illness
- Signs and symptoms experienced – if rash, nature of the rash **MUST** be recorded (ask patient to photograph on their phone)
- Number of doses taken prior to the onset of the reaction
- Timing of onset in relation to initiation of medication & evolution
- Treatment given/severity/need for ED or inpatient treatment
- Has the suspect drug been taken since? If yes, what if anything happened? (check with pharmacist if patient uncertain)
- Concurrent medications at the time of the event, and relationship of the event to initiation of any of these drugs?
- Has the patient experienced similar symptoms in the absence of drug exposure? (e.g., chronic spontaneous urticaria)
- Any other known drug allergies

In some clinical situations, it is difficult to make an immediate accurate judgement about whether the patient is truly allergic to the drug, and a pragmatic decision to use an alternative is often taken. However accurate documentation as above is essential to allow future assessment of the DHR, which is often important in facilitating optimal therapy into the future.

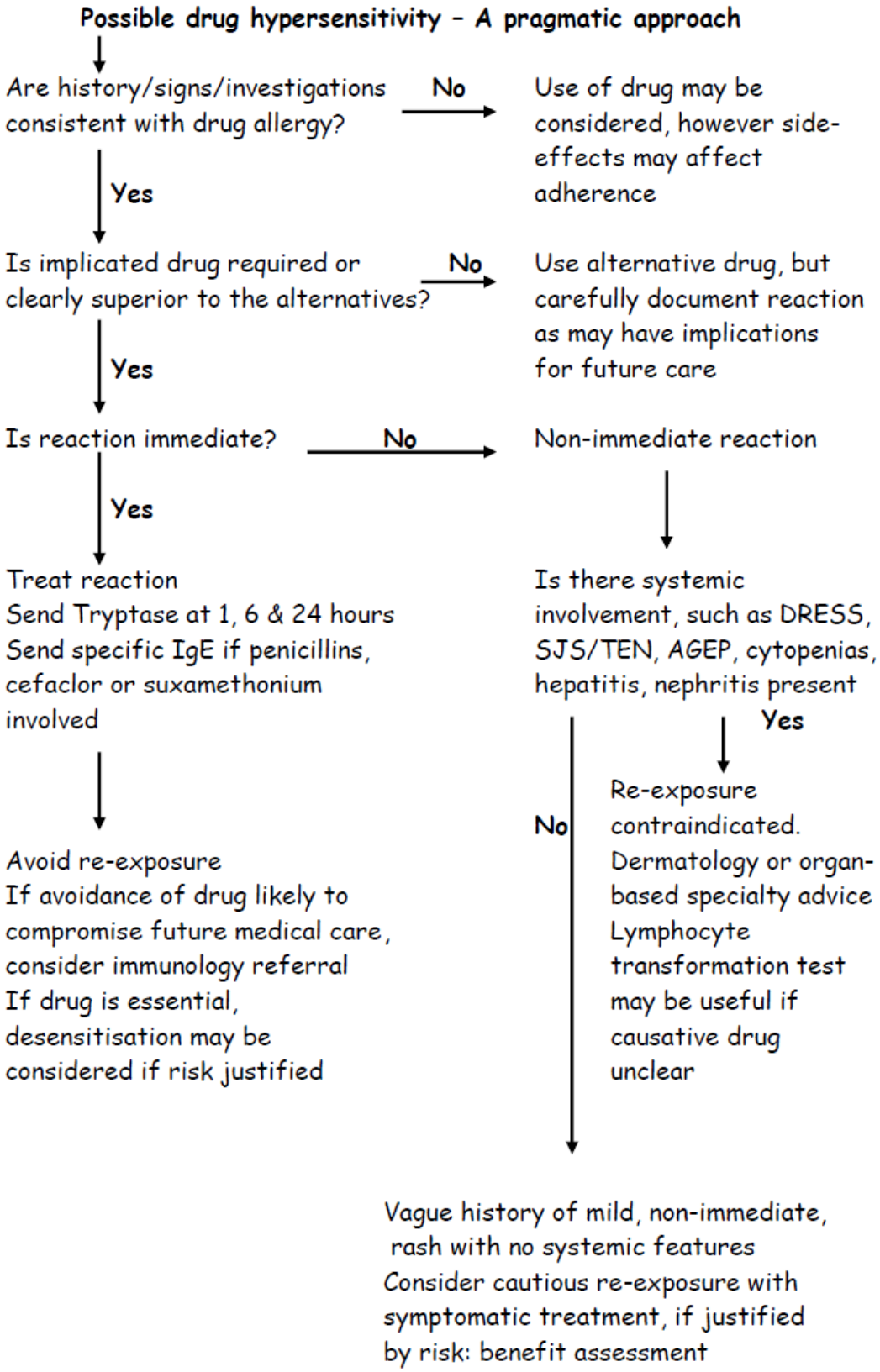
2.0 Evaluating a drug allergy history

Many patients give a history of drug allergy, which fails to distinguish true allergy from adverse events. The risk of drug allergy is similar to the general population when:

- Symptomatology is not compatible with allergy
- Chronology of events is not compatible with allergy
- Drug taken since the putative DHR with no reaction (check with pharmacy if patient uncertain or discrepancies in the record)
- Alternative diagnosis subsequently made for what was initially thought to be a DHR
- Family history of drug allergy (atopic tendency is heritable, not the specific allergy). However, some guidelines for DRESS suggest that family members should avoid a medication which caused this reaction in a relative
- Same symptoms recurred in the absence of medication. When similar symptoms recur in the absence of medication this does not exclude an allergy, but offers a potential alternative explanation. Referral to immunology may be appropriate if the medication is important for a patient's care. This scenario is common in patients with chronic spontaneous urticaria +/- angioedema (CSUA), which is often triggered by infection. Specialist input may be necessary to differentiate infection-induced exacerbation of CSUA from co-existing antimicrobial allergy

When a rash occurs after a course of antimicrobials has finished, in the absence of mucosal involvement or systemic features, drug allergy is unlikely. Rarely, this may be due to a non-immediate reaction. However, the drug can be considered for use, with the patient given appropriate instructions on what to do if the rash recurs.

2.1 A pragmatic approach to a possible DHR



2.2 What to do when your patient has a DHR?

- Document the reaction as detailed above, together with your diagnosis
- Inform the patient/carer
- Advise the use of medical identification jewellery
- Provide the patient with a written record of the reaction and what drugs/drug classes they should avoid
- Advise patients of the need to inform pharmacists of their drug allergies
- Ensure that the GP is informed
- Ensure DHR/allergy is documented in the appropriate portion of the patient's healthcare record

2.3 Penicillin allergy – additional information

Avoid all β lactams in patients with significant penicillin allergy = immediate reaction to penicillin and has not tolerated cephalosporins since **OR** non-immediate, but severe reaction to penicillin and has not tolerated cephalosporins since.

Cephalosporins are suitable for use in a patient with known penicillin allergy, who tolerates cephalosporins **OR** patient with a non-immediate / non-severe reaction to penicillin

β lactam antimicrobials include; penicillin, amoxicillin, flucloxacillin, co-amoxiclav, piperacillin-tazobactam, **cephalosporins*** and **carbapenems****.

*** Cross-reactivity with cephalosporins is less frequent than originally thought. Penicillin allergic patients who have negative skin testing/challenge to cephalosporins can receive a third generation cephalosporin.**

**** Cross-reactivity with carbapenems is rare. However, the choice of a carbapenem for a penicillin allergic patient requires careful consideration. Carbapenems are restricted agents in Beaumont Hospital & their use should ALWAYS be discussed with clinical microbiology or infectious diseases.**

2.4 When to refer to immunology?

- Any patient with suspected anaphylaxis
- Patients with symptoms suggestive of an immediate DHR, when there is doubt about the causative agent
- Patients requiring a treatment for disease, to which the patient has had an immediate DHR

- Patients who have a high likelihood of future need of the medication to which they have had an immediate DHR

- Consider referral in patients with a history of immediate allergy to β-lactams (e.g., penicillins, cephalosporins) and at least one other class of antimicrobials; those with immediate DHR and conditions associated with increased need for antimicrobials (e.g. cystic fibrosis, immunodeficiency) or with frequent infections requiring frequent antimicrobial treatment.

Please note, the service provided by the immunology department is for the assessment of immediate hypersensitivity.
When a patient has had a non-immediate, severe cutaneous adverse reaction, further assessment should be completed by the dermatologist involved in their acute care. The immunology service does not have the capacity, or the expertise to advise about these conditions.

3.0 References

- Demoly P, Adkinson NF, Brockow K *et al*. International Consensus on drug allergy. *Allergy* 2014 (69) 420-437.

4.0 Summary of changes from previous guideline version

V1.1 Oct 2019 – Reviewed with some minor editing changes only
Not applicable – This is the first version of this guideline