

Drug Allergy – the facts

As a risk to life, drugs are the most significant causes of allergic reactions, being responsible for more deaths than food and insect stings combined. People who have experienced drug-related allergic reactions can be assured that the risk of a potentially fatal reaction can be minimised. They need to be educated about their allergy and wear a medical alert emblem at all times.

Anaphylactic reactions, as well as milder forms of allergy, are a response of the immune system.

Who is at risk?

The number of people across the UK who are allergic to drugs is unknown. Part of the problem is that cases are under-reported and there is the added difficulty of diagnosis: many patients, for example, have been labelled 'allergic to penicillin' from childhood, when in fact this is not the case.

Drug allergy can be experienced by anyone. It is not confined to those with an allergic tendency. People with other allergic conditions such as hay fever or food allergy can be reassured that they are no more at risk from drug allergy than the general population.

Anyone who is allergic to a drug and also has asthma faces a higher than average risk of experiencing severe reactions.

Signs to look for

Many people with drug allergy experience only mild or moderate symptoms. Mild allergic reactions include skin rash, itching and hives.

Severe symptoms include swelling in the mouth or throat, trouble breathing (e.g. asthma), feeling faint and collapse.

Not all allergic reactions to drugs are anaphylactic. Anyone who has reacted to a drug should be made aware that future reactions may be more severe.

If you have had any worrying symptoms after taking a drug, report them to your GP so they can be investigated.

The route of administration

Drugs are administered in a variety of ways, depending on their type and purpose. The route of administration is a significant factor in the risk of a reaction, its severity and the time it takes to develop. Anaphylactic drug reactions can occur after the administration of drugs in the following ways:

Injection: The most immediate and severe reactions are likely to follow injections, especially by the intravenous route, in which the drug is introduced straight into the bloodstream and is rapidly distributed throughout the body.

In patients allergic to the paralysing drugs given as part of a general anaesthetic, the onset of signs such as flushing, airway obstruction or drop in blood pressure may be apparent within seconds, and rarely take more than three minutes to start developing.

In the case of injections beneath the skin (subcutaneous) or into a muscle (intramuscular), a local reaction in the form of reddening, swelling or weals, and itching may be apparent at the injection site at an early stage. Fortunately, its swift appearance, combined with the presence of medical or nursing staff (who give these injections) means that there should be prompt recognition and treatment before the reaction has time to progress.

By mouth: Reactions to drugs taken by mouth may start within minutes, but may be delayed for up to two hours if the absorption of the drug is slow. In fact, some delayed-release drugs may cause reactions beginning many hours after administration.

Application to the skin: antibiotics applied to burns may on rare occasions cause reactions.

Vaccines

Drugs given by injection, such as vaccines, are those most likely to trigger anaphylactic reactions. These include vaccines used for the prevention and treatment of infectious disease, or those for desensitising patients allergic to insect venom, pollen, cats, etc.

An observation period of one hour is advisable for anyone having an injection who has suffered anaphylaxis in the past – whatever the cause. Signs of a severe reaction are likely to show themselves quickly.

It is advised that anyone having an anti-allergy vaccination should also be observed for one hour, extended if any signs of a generalised reaction become apparent.

People who have had a severe reaction to egg should discuss the suitability of the seasonal flu or yellow fever vaccine with their treating doctor or allergy specialist. Other vaccines whose components may have been prepared on egg medium, such as MMR, have been demonstrated to be safe, even in very egg-sensitive children.

If there is any concern whatsoever, that a patient may react to a vaccine, the vaccination can be given in hospital.

Insulin

Thousands of patients inject themselves two or more times a day safely with insulin. Being a protein, insulin has the potential to produce allergic reactions. The fact that anaphylaxis to insulin injections is rare may be due to the fact that such injections, once started, are usually continued for life, and a degree of tolerance is

thus induced. Insulin-induced anaphylaxis may be more common in patients whose treatment is interrupted or intermittent; this may apply more generally to other drugs too.

Antibiotics

These drugs, which include penicillin, are commonly used for treating infection. Allergy is sometimes blamed for symptoms they are thought to cause, but this is not always the case.

Infrequently, people allergic to one antibiotic may react to another within the same 'family' of antibiotics (this is known as cross-reactivity). For this reason, a doctor should be consulted to discuss whether drugs in the same family should be avoided.

Diagnosis of penicillin allergy

Penicillin allergy is a genuine problem, but the disease for which the penicillin has been administered may also cause allergy-like symptoms. This frequently leads to false diagnoses of penicillin allergy.

For example, a delayed rash following ampicillin or amoxycillin in the context of a childhood illness is common and almost always does not suggest an underlying penicillin allergy. But if the rash is immediate, or if there is nettle rash, or if there are other symptoms such as facial swelling, itching or even anaphylaxis, the doctor may decide testing is necessary. The person can be referred to an NHS allergy clinic, where skin prick testing (and occasionally intradermal skin testing) can be carried out, if appropriate; this is generally more helpful than blood tests.

The label 'allergic to penicillin' should not be applied lightly. Many people, wrongly deemed 'allergic to penicillin' in childhood, are unnecessarily denied a safe and useful treatment, as doctors are reluctant to administer penicillin and related antibiotics to those who say they are allergic.

The best advice is to discuss any symptoms with your doctor. And if you are one of those people labelled 'allergic to penicillin' since childhood, it is useful to try to find out why this label was applied. Medical records may hold the answer. It would be helpful to know which penicillin is thought to have caused the reaction.

The other aspect to this problem is that the concept of penicillin allergy becomes devalued by its inappropriate use, so that patients genuinely in danger of a severe reaction may be given this antibiotic.

Rashes after administration of antibiotics

Rashes occur occasionally during the course of antibiotic treatment, but these are not always signs of allergy to the antibiotic. The illness being treated (e.g. scarlatina) may be the cause of the rash. In others, the disease in conjunction with the antibiotic, as with ampicillin and glandular fever, may cause the problem, the antibiotic being well tolerated if taken again for some other reason.

In assessing whether the symptoms are the result of genuine allergy, the nature and timing of the rash are important. The typical symptoms present during a genuine anaphylactic reaction to an antibiotic might be an urticarial rash (hives or nettle rash, with itchy weals), starting within a couple of hours of the first dose of a

course. If symptoms begin quickly, this may also be a sign of a severe reaction. If the person has asthma, the risk of severe symptoms is higher than for a non-asthmatic person.

How likely am I to react to antibiotics?

In the case of penicillin, the incidence of severe allergic reactions is less now than in the years immediately after the introduction of these antibiotics. This may be because of improved methods of production and storage, since impurities or breakdown products caused some of the symptoms that patients experienced. Some people who reacted to penicillin in the past may be able to take it now.

Analgesics

This is a large group of drugs with pain-killing, fever-reducing and anti-inflammatory properties, known as the 'aspirin-like drugs' or as 'non-steroid anti-inflammatory drugs' (NSAIDs).

Analgesics and anaphylactoid reactions

Analgesics frequently induce reactions with features similar to those of anaphylaxis, such as breathing problems, urticaria (nettle rash) and angioedema (facial swelling), but the mechanism of these reactions does not involve an immunological response. It is caused by a pharmacological side-effect of this group of drugs and strictly speaking, this is not allergy. Such reactions are known as 'anaphylactoid' or 'pseudo-allergic', to differentiate them from the true anaphylactic reactions seen, for example, with vaccines or penicillins. Genuine allergic reactions to analgesics are rare.

Testing for sensitivity to analgesics

Anaphylactoid reactions are rarely life-threatening, and are more dose-related than true allergic reactions, in which minute doses of the drug can precipitate severe reactions. Because of this, challenge testing for sensitivity to analgesics (in which the patient ingests the drug under medical supervision) is a safer procedure than for antibiotic allergies. The substance is not likely to have a severe effect when administered in small quantities.

Sensitivity to drugs in the same group

Anyone who has had an anaphylactoid reaction to aspirin or ibuprofen should be considered sensitive to the other drugs in this group until it is proved otherwise. Paracetamol is the least likely drug in this group to cause reactions and the vast majority of aspirin-sensitive patients (about 95 per cent) will tolerate paracetamol.

If a patient who has not had paracetamol for some time starts reacting to aspirin or ibuprofen, a supervised paracetamol challenge under medical supervision may be useful, to avoid their finding out that they are in the 5 per cent, when they are not under medical supervision.

Since reactions are generally mild and dose-related, such challenges with paracetamol can safely be carried out in a primary care or outpatient department, unless the NSAID reaction has been particularly severe. Doses of 250, 500 and 1000 mg at two-hourly intervals would be appropriate for most such patients.

For people who react to paracetamol, codeine-based painkillers are often well tolerated. Caution in reading labels and asking advice from a pharmacist are both essential. Bear in mind that aspirin is sometimes named only as acetylsalicylic acid.

Anti-hypertensives

Many different types of drug are used nowadays in the treatment of high blood pressure, some of which can cause anaphylactoid reactions, but true allergic sensitivity to such drugs is rare. In those with a predisposition to asthma, the beta-blockers are likely to precipitate bronchoconstriction, and should be avoided.

ACE inhibitors, whose names generally end in '-pril', can produce an anaphylactoid response such as a dry cough or angio-oedema, particularly if the swelling affects the lips, tongue and lower half of the face. Since the patient may tolerate the drug for months or even years before this problem arises and because it can be episodic, in spite of continuing treatment, it may not occur to the patient or their doctor that it is the ACE inhibitor that is to blame.

As ACE inhibitors can cause severe life-threatening airway obstruction, an urgent review of the anti-hypertensive treatment regimen is required in any person who has experienced angio-oedema. ACE inhibitors should not be taken, for any cause, by anyone who has experienced angio-oedema, even if the angio-oedema was triggered by something other than an ACE inhibitor.

General anaesthesia

Drugs used in general anaesthesia pose a particularly difficult problem, since the patient is generally asleep when the reactions start and recognition depends on the anaesthetist observing such symptoms as falling blood pressure, airway obstruction, etc., rather than symptoms reported by the patient. Fortunately, sensitivity to drugs used in general anaesthesia is rare, but because such drugs are injected directly into the bloodstream, symptoms may be severe and rapid in onset and progression.

Identifying the cause

It is common for several drugs to be given together, or in quick succession, at the induction of general anaesthesia; these include induction agents (to render the patient unconscious), neuromuscular blockers (to paralyse the patient temporarily, to facilitate airway intubation and the surgical procedure), antibiotics, painkillers and blood or plasma substitute infusions. Any one of these drugs may be implicated in anaphylactic or anaphylactoid reactions during anaesthesia. It is important to identify which agent was responsible and which alternatives are likely to be safe to use in future.

Referral to a centre with experience of anaesthetic-related reactions is important and this should be the responsibility of the anaesthetist who was present. Skin prick testing is a useful part of the investigative

procedure. Provision of accurate details of the drugs administered, the timing and nature of the reaction observed, and any blood test results relevant to the case, are essential.

In some cases the anaesthetic may not be responsible for the symptoms; for example the person may be having a reaction to the latex used in gloves or medical equipment.

Local anaesthetics

These are rare as causes of anaphylactic or anaphylactoid reactions. Sudden episodes of loss of consciousness, blood pressure drop or heart irregularity can occur during the induction of local anaesthesia for dental procedures and these may point to an anaphylactic or anaphylactoid reaction. Subsequent investigation with skin testing followed by a challenge is usually negative, pointing to some other cause, such as a fainting reaction. It is important for patients not to be inappropriately labelled as 'allergic' to useful and safe drugs.

In Summary

With all drug allergies, but especially with those associated with the risk of an anaphylactic reaction, it is vital for the patient to be aware of exactly which drug was responsible and, if possible, which alternatives have been identified as safe. Information relating to drug allergies needs to be prominently recorded in primary care and hospital patient notes, but this is not a substitute for the patient themselves being responsible for bringing such information to the attention of doctors, pharmacists or nurses, who may subsequently treat the patient.

It is important that anyone with drug allergy wears a medical alert bracelet or pendant, or carries a letter from a doctor explaining their allergy.

The content of this Fact Sheet has been **Peer Reviewed by Dr Lawrence Youlten, Medical Director, London Allergy Clinic and Visiting Consultant in Allergy, Addenbrooke's Hospital, Cambridge.**

Disclaimer – The information provided in this leaflet is given in good faith. Every effort has been taken to ensure accuracy. All patients are different, and specific cases need specific advice. There is no substitute for good medical advice provided by a medical professional.

About the Anaphylaxis Campaign – *'supporting people with severe allergies'*

The Anaphylaxis Campaign is the only UK wide charity to exclusively meet the needs of the growing numbers of people at risk from severe allergic reactions (anaphylaxis) by providing information and support relating to foods and other triggers such as latex, drugs and insect stings. Our focus is on medical facts, food labelling, risk reduction and allergen management. The Campaign offers tailored services for individual, clinical professional and corporate members. Visit our website www.anaphylaxis.org.uk.