GUIDELINES

Diagnosis and management of drug allergy in adults, children and young people: summary of NICE guidance

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This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

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Previous articles in this series

- Early identification and management of chronic kidney disease in adults: summary of updated NICE guidance (*BMJ* 2014;349:g4507)
- Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance (*BMJ* 2014;349:g4356)
- The management of atrial fibrillation: summary of updated NICE guidance (*BMJ* 2014;348:g3655)
- Prevention and management of pressure ulcers: summary of NICE guidance (*BMJ* 2014;348:g2592)
- Management of psychosis and schizophrenia in adults (*BMJ* 2014;348:g1173)

All drugs have the potential to cause side effects or "adverse drug reactions," but not all of these are allergic in nature. The diagnosis of drug allergy can be challenging, and there is considerable variation both in how drug allergy is managed and in geographical access to specialist drug allergy services.[1] On the basis of a National Institute for Health and Care Excellence (NICE) analysis of hospital episode statistics, about half a million people admitted to NHS hospitals each year in England and Wales have a diagnostic label of "drug allergy," with the most common being penicillin allergy.[2] Fewer than 10% of people who think they are allergic to penicillin are truly allergic.[3] Inadequate clinical documentation of allergic drug reactions and a lack of patient information (provided to and by patients) may lead to an inappropriate label of allergy to penicillin or other drugs remaining on a medical record. This can prevent future prescription even when clinically indicated. This article summarises the most recent recommendations from NICE on drug allergy.[4]

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Assessment

When a course of treatment with a drug is started a patient may experience adverse symptoms for a variety of reasons. Not all reactions are caused by the drug itself and careful assessment is needed to establish the correct cause.

- When assessing a person who presents with possible drug allergy, take a history and undertake a clinical examination. The figure details the signs and allergic patterns of suspected drug allergy along with the timing of onset and should be used as a guide when deciding whether to suspect drug allergy. Although the figure describes common and important presenting features of drug allergy, other presentations are also recognised.
  [*Based on moderate quality evidence from observational studies and the experience and opinion of the Guideline Development Group (GDG)*]
- Be aware that the reaction is more likely to be caused by drug allergy if it occurred during or after use of the drug and:
  - The drug is known to cause that type of reaction or
  - The person has previously had a similar reaction to that drug or drug class
- Be aware that the reaction is less likely to be caused by drug allergy if:
  - There is a possible non-drug cause for the person's symptoms (for example, he or she has had similar symptoms when not taking the drug) or
  - The person has gastrointestinal symptoms only.
  [*Based on the experience and opinion of the GDG*]

Non-specialist management

General

If drug allergy is suspected:

- Consider stopping the drug suspected to have caused the allergic reaction and advise the person to avoid that drug in future
- Treat the symptoms arising from the acute reaction if necessary; send people with severe reactions to hospital.

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Do not offer a selective cyclo-oxygenase 2 (COX-2) inhibitor to people in a non-specialist setting if they have had a severe reaction, such as anaphylaxis, severe angio-oedema, or an asthmatic reaction, to a non-selective NSAID.
- For people who have had a mild allergic reaction to a non-selective NSAID but need an anti-inflammatory drug:
  - Discuss the benefits and risks of selective COX-2 inhibitors (including the low risk of drug allergy)
  - Consider introducing a selective COX-2 inhibitor at the lowest starting dose with only a single dose on the first day.
  [*Based on very low quality evidence from observational studies and the experience and opinion of the GDG*]

Measuring serum tryptase after suspected anaphylaxis

- After a suspected drug related anaphylactic reaction, take two blood samples for mast cell tryptase in line with recommendations on anaphylaxis.[5]
- Record the exact timing of both blood samples taken for mast cell tryptase:
  - In the person's medical records and
  - In the pathology request form.
  [*Based on very low quality evidence from observational studies*]

Measuring serum specific IgE

- Do not use blood testing for serum specific IgE to diagnose drug allergy in a non-specialist setting.
  [*Based on very low quality evidence from observational studies*]

Signs and allergic patterns of suspected drug allergy with timing of onset

Immediate rapidly evolving reactions

Anaphylaxis: a severe multisystem reaction characterised by:
- Erythema, urticaria, or angio-oedema and
- Hypotension or bronchospasm, or both

Urticaria or angio-oedema without systemic features

Exacerbation of asthma (for example, with non-steroidal anti-inflammatory drugs)

Onset is usually less than one hour after drug exposure (previous exposure not always confirmed)

Non-immediate reactions without systemic involvement

Widespread red macules or papules (exanthem-like)

Fixed drug eruption (localised inflamed skin)

Onset usually 6-10 days after first drug exposure or within three days of second exposure

Non-immediate reactions with systemic involvement

Drug reaction with eosinophilia and systemic symptoms or drug hypersensitivity syndrome characterised by:
- Widespread red macules, papules, or erythroderma
- Fever
- Lymphadenopathy
- Liver dysfunction
- Eosinophilia

Onset usually 2-6 weeks after first drug exposure or within three days of second exposure

Toxic epidermal necrolysis or Stevens-Johnson syndrome characterised by:
- Painful rash and fever (often early signs)
- Mucosal or cutaneous erosions, or both
- Vesicles, blistering, or epidermal detachment
- Red purpuric macules or erythema multiforme

Onset usually 7-14 days after first drug exposure or within three days of second exposure

Acute generalised exanthematous pustulosis characterised by:
- Widespread pustules
- Fever
- Neutrophilia

Onset usually 3-5 days after first drug exposure

Common disorders caused, rarely, by drug allergy:
- Eczema
- Hepatitis
- Nephritis
- Photosensitivity
- Vasculitis

Time of onset variable

Signs and allergic patterns of suspected drug allergy

Documenting and sharing information with other healthcare professionals

Computerised primary care record systems currently do not distinguish between drug allergy and non-allergic adverse drug reactions. This can lead to a false label of drug allergy, particularly if the person's reaction took place many years earlier and details about the drug and the reaction were never recorded or were misplaced.

- When people present with suspected drug allergy, document their reaction using a structured approach that includes:
  - The generic and proprietary name of the drug or drugs suspected to have caused the reaction, including the strength and formulation
  - A description of the reaction (see figure)
  - The indication for the drug being taken (if there is no clinical diagnosis, describe the illness)
  - The date and time of the reaction
  - The number of doses taken or number of days that the person had been taking the drug before onset of the reaction
  - The route of administration
  - Which drugs or drug classes should be avoided in future.
- Ensure that information about drug allergy status is updated and included in all:
  - GP referral letters
  - Hospital discharge letters.
- Prescriptions (paper or electronic) issued in any healthcare setting should be standardised and re-designed to record information on which drugs or drug classes to avoid to reduce the risk of drug allergy.

[*Recommendations in this section were based on very low quality evidence from observational studies and the experience and opinion of the GDG*]

Providing information and support to patients

Patients are often left bewildered after a suspected allergic reaction to a drug. Their fear of experiencing a further reaction can be heightened by a lack of information, especially if the original reaction was severe.

- Discuss the suspected drug allergy with the person (and family members or carers as appropriate) and provide structured written information (see documenting and sharing above). Record who provided the information and when.

[*Based on moderate quality evidence from qualitative studies and the experience and opinion of the GDG*]
- Ensure that the person (and family members or carers as appropriate) is aware of the drugs or drug classes that need to be avoided, and advise the person to check with a pharmacist before taking any over-the-counter preparations.

[*Based on moderate quality evidence from qualitative studies and the experience and opinion of the GDG*]

After specialist drug allergy investigations

- Allergy specialists should give the following written information to people who have undergone specialist drug allergy investigation:
  - The diagnosis—whether the reaction was allergic or non-allergic
  - The drug name and a description of the reaction (see figure)
  - The investigations used to confirm or exclude the diagnosis
  - Drugs or drug classes to avoid in the future
  - Any safe alternative drugs that may be used.

[*Based on moderate quality evidence from qualitative studies and the experience and opinion of the GDG*]

Referral to specialist services

This should enable either confirmation or exclusion of the drug allergy. Exclusion will allow the patient to have the same and related drugs in the future. It is not appropriate to refer all patients with a label of drug allergy because this would be costly and would overwhelm specialist drug allergy services. Therefore the GDG made the following recommendations relating to the causes of suspected allergy to drugs that most commonly lead to a referral to specialist drug allergy services.

General

- Refer people to a specialist drug allergy service if they have had:

– A suspected anaphylactic reaction (also see NICE guideline on anaphylaxis[5]) or
– A severe non-immediate cutaneous reaction (such as drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome, or toxic epidermal necrolysis).

[*Based on previous NICE guidance and the experience and opinion of the GDG*]

FURTHER INFORMATION ON THE GUIDANCE

The guideline made further recommendations on information held by the person with a drug allergy after specialist investigation.

After specialist drug allergy investigation

Advise people (and their family members or carers as appropriate) to carry information that they have been given about their drug allergy at all times and to share this whenever they visit a healthcare professional or are prescribed, dispensed, or about to be given a drug.

Methods

The guideline was developed according to National Institute for Health and Care Excellence (NICE) guideline methodology (www.nice.org.uk/guidelinesmanual). The Guideline Development Group (GDG) consisted of two consultant allergists, a consultant dermatologist, two general practitioners, a specialist nurse, a consultant paediatrician, two patient or carer members, two pharmacists, and a specialist respiratory consultant. The scope and full guideline were posted on the NICE website as part of a stakeholder consultation. A new cost effectiveness analysis was not undertaken owing to a lack of suitable data, but the cost implications of referral in some circumstances were calculated. NICE has produced four different versions of the guideline: a full version; a pathway; a version known as the "NICE guideline" that summarises the recommendations; and a version for patients and the public. All these versions are available from the NICE website (www.nice.org.uk/Guidance/CG183). Future updates of the guideline will be published according to the NICE guideline development programme.

Future research and remaining uncertainties

The GDG highlighted some important research questions:

What is the most effective documentation strategy to prevent people from being re-exposed to drugs to which they have a suspected or confirmed allergy (particularly electronic health records and different formats for patient held documentation)?

Which information strategies could be used to make people more likely to disclose their drug allergy in clinical practice?

Should all patients who have experienced a severe allergic reaction to a non-selective non-steroidal anti-inflammatory drug (NSAID) be assessed by specialist drug allergy services or should they be advised to take a selective cyclo-oxygenase 2 (COX-2) inhibitor without further investigations?

In children who have a suspected allergy to an antibiotic, is it clinically and cost effective to proceed directly (without skin or intradermal tests) to challenge with a diagnostic oral antibiotic rather than to refer them to specialist drug allergy services?

β lactam antibiotics

- Refer people with a suspected allergy to β lactam antibiotics to a specialist drug allergy service if they:
  – Need treatment for a disease or condition that can be treated only by a β lactam antibiotic or
  – Are likely to need β lactam antibiotics often in the future (for example, people with recurrent bacterial infections or immune deficiency).

  [*Based on cost effectiveness scenarios calculating the potential costs of referral to specialist services or non-specialist management, and the experience and opinion of the GDG*]

Non-steroidal anti-inflammatory drugs

- Refer people who need treatment with an NSAID to a specialist drug allergy service if they have had a suspected allergic reaction to an NSAID with symptoms such as anaphylaxis, severe angio-oedema, or an asthmatic reaction.
  [*Based on cost effectiveness scenarios calculating the potential costs of either referral to specialist services or non-specialist management, and the experience and opinion of the GDG*]

Local anaesthesia

- Refer people to a specialist drug allergy service if they need a procedure involving a local anaesthetic that they are unable to have because of suspected allergy to local anaesthetics.
  [*Based on the experience and opinion of the GDG*]

General anaesthesia

- Refer people who have had anaphylaxis or another suspected allergic reaction during or immediately after general anaesthesia to a specialist drug allergy service.
  [*Based on the experience and opinion of the GDG*]

Overcoming barriers

Major problems identified by this guideline include: poor clinical documentation of drug allergy; the lack of provision of patient information; lack of a specific section to record drug allergy on prescriptions issued in general practice; and inability of current clinical information systems to differentiate between adverse drug reaction and drug allergy. Measures that would help overcome these barriers to implementation include improved clinical systems that provide the relevant codes or options to differentiate and record specific drug allergies separately from adverse drug reactions, with outputs that are sensitive but do not lead to unnecessary alerts (which can induce clinicians to habitually override the system). A re-design of standard prescription forms and hospital drug charts to enable the inclusion of structured drug allergy information would also improve patient safety. Implementation of this guideline would be further enhanced if the *BNF* included a section on the recognition of symptoms and signs of drug allergy. In addition, clinician training, including e-learning modules and auditing, would facilitate the documentation of drug allergies.

The members of the Guideline Development Group were: Michael Ardern-Jones, Lee Yee Chong, Margaret Constanti, David Cousins, Kathleen deMott, Tamara Diaz, Matthew Doyle, George Du Toit, Katharina Dworzynski, Mandy East, Pam Ewan, Martin Harker, Kate Kelley, James Larcombe, Grace Marsden, Nicola Mundy, Shuaib Nasser (chair), Alice Osborne, Su Park, Vicki Pollit, Gill Ritchie (guideline lead), Carlos Sharpin, Paul Whittaker, and Andrew Williams.

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RATIONAL IMAGING

Non-invasive imaging in pancreatitis

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This series provides an update on the best use of different imaging methods for common or important clinical presentations. To suggest a topic, please email us at practice@bmj.com

An active 73 year old patient with a history of cholecystectomy, hypothyroidism, and hypertension presented to the emergency department with a five hour history of severe epigastric pain. Her admission blood tests showed an amylase of 782 U/L and a white cell count of 21.2×10^3/μL, with a neutrophil count of 17.5×10^3/μL. The patient's initial modified Glasgow score for predicting the severity of pancreatitis on admission was two, scoring on both age and white cell count. A repeat Glasgow score the following day was three, also scoring on lactate dehydrogenase (883 IU/L). The modified Glasgow score assesses the patient over a range of criteria (age, arterial oxygenation, white cell count, serum calcium, urea, lactate dehydrogenase and aspartate aminotransferase/alanine aminotransferase, albumin, and blood glucose). A score of three or higher within the first 48 hours in cases of pancreatitis suggests acute severe pancreatitis. Her respiratory function then deteriorated, with an oxygen partial pressure of 11.5 kPa on 15 L oxygen via a non-rebreathe mask, and she was admitted to the intensive care unit.

LEARNING POINTS

Early pancreatitis

Ultrasound is indicated in the first 24 hours, mainly to identify gallstones as the cause of pancreatitis rather than to contribute to the diagnosis

Early endoscopic retrograde cholangiopancreatography (ERCP) should be considered in patients with gallstone induced acute pancreatitis if cholangitis and biliary obstruction are suspected

Deteriorating pancreatitis

To stage, and identify complications in, patients with persisting organ failure, signs of sepsis, or deterioration in clinical status 3-7 days after admission, a contrast enhanced computed tomography (CE-CT) scan should be considered

Early CE-CT (<72 hours after presentation) may underestimate the extent of necrosis as there is often a lag effect between disease extent and radiological appearances, therefore giving false assurance and less reliable surgical information on the extent of pancreatic necrosis

Obstructive pancreatitis

Despite the high spatial resolution of CE-CT, detection of gallstones within the common bile duct can be limited by their isodensity to the bile fluid; however, sensitivity to stones is very good and similar to that of magnetic resonance imaging

ERCP and endoscopic ultrasound are yet more sensitive but are invasive

Severe pancreatitis

CE-CT remains the preferred imaging modality for severe pancreatitis; its ready availability and use in subsequent interventional procedures, with excellent depiction of any complications, makes it the front runner

Magnetic resonance imaging has a growing evidence base, but it is not used widely yet

Diagnosis of pancreatitis

Abdominal pain together with raised plasma concentrations of pancreatic enzymes (amylase and lipase) are the cornerstones of diagnosis of pancreatitis. However, positive imaging in the presence of one of these can secure a diagnosis (particularly in the case of a late diagnosis with amylase and lipase less than three times greater than the normal limit).[1]

What is the first imaging investigation within 72 hours of presentation?

Ultrasound is recommended within 24 hours of a diagnosis of pancreatitis.[2] Although its proponents support its value in the diagnosis and assessment of pancreatitis itself, bowel gas can prevent effective assessment in some patients. Therefore, ultrasound is usually used to identify obstructing gallstones as the cause of pancreatitis rather than contributing to the diagnosis. Ultrasound is relatively cheap and quick and causes no harm to the patient. However, it is user dependent and is of reduced usefulness in obese patients. A positive ultrasound scan can be very useful, as urgent therapeutic endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy should be performed in patients with acute pancreatitis and suspected or proved gallstones who satisfy the criteria for predicted or actual severe pancreatitis (see next section) or when cholangitis, jaundice, or a dilated common bile duct is present.[2] However, ultrasound has a poor negative predictive value with many false negatives.[3]

Which patients need further imaging?

Once diagnosed, a patient's progress can be monitored with scoring systems to assess the severity of disease,

such as the modified Marshall system, Apache II, the modified Glasgow pancreatic score, and the sequential organ failure assessment (SOFA) score. The modified Marshall scoring system, which assesses organ failure in the cardiovascular, respiratory, and renal systems, has the benefit of simplicity, universal applicability across international centres, and the ability to stratify severity of disease easily and objectively.[1] Patients with no organ failure are considered to have mild disease, which generally resolves without imaging. Patients with transient organ failure that resolves within 48 hours of onset are said to have "moderately severe pancreatitis" and have been shown to have a good prognosis.[4] However, if they have local or persistent systemic features (such as raised white cell count), a contrast enhanced computed tomography (CE-CT) scan may be needed to exclude a complication. It is advised that patients with persisting organ failure, signs of sepsis, or deterioration in clinical status three to seven days after admission should have a CE-CT scan.[1 5] In patients with "acute severe pancreatitis," which is defined as organ dysfunction that continues for longer than 48 hours, CE-CT should be considered.

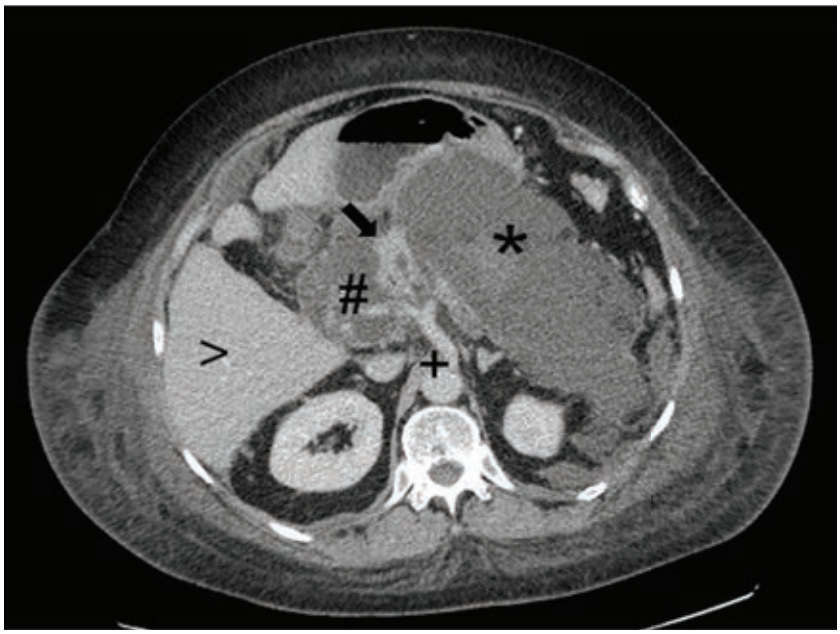

Fig 1 | Axial computed tomography slice of 73 year old patient (day 9) showing severe acute pancreatitis. At the level of the coeliac axis (+) and liver (›), there is a pancreas with very little residual enhancing pancreatic tissue (arrow) and a large acute necrotic collection (*). There is also a collection in the lesser sac (#)

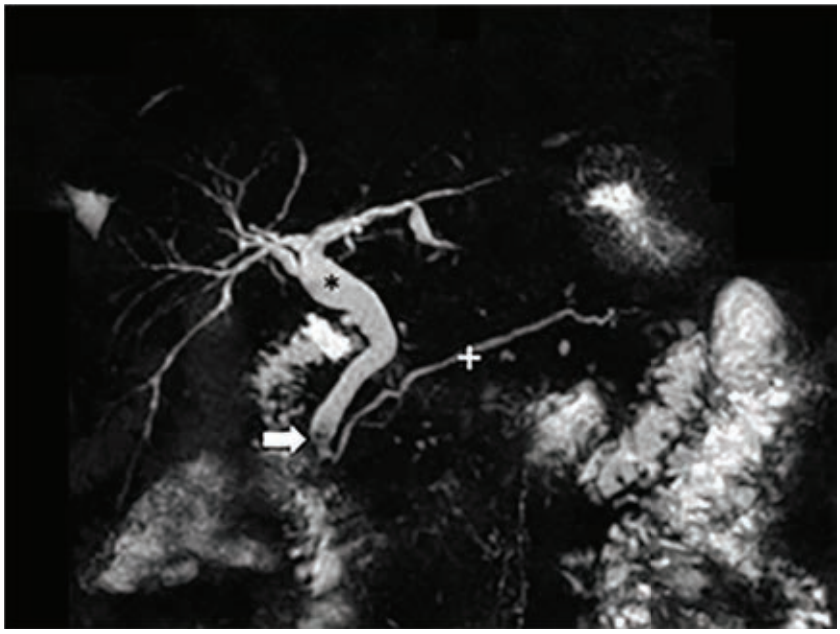

Fig 2 | Magnetic resonance cholangiopancreatography image: volume rendered through maximum intensity projection of a different patient who presented with right upper quadrant pain and raised liver/pancreatic enzymes. It shows a dilated common bile duct (*), a distal filling defect (arrow), and a normal calibre pancreatic duct (+)

Generally, early computed tomography within the first 72 hours of presentation is not used for detection or staging of pancreatitis or for detection of local complications.[1 5] This is largely because early CE-CT (within three days) does not necessarily change the patient's management, which is usually conservative. Complications do not generally develop in the early phase, particularly in cases of mild-moderate disease, which generally do not require a computed tomography scan at any stage. Additionally, early CE-CT can initially underestimate the extent of necrosis, as a lag effect often exists between disease extent and radiological appearances, therefore giving false assurance and little useful surgical information. Exceptionally, if the diagnosis in an acutely unwell patient is uncertain, CE-CT is used during the admission process.

Computed tomography imaging in severe pancreatitis

In our case, despite best supportive care the 73 year old patient's respiratory function deteriorated and she required intensive care for persistent organ failure and had a CE-CT scan (fig 1), which showed severe acute pancreatitis with extensive necrosis and associated nectrotic collections. CE-CT comes with a significant radiation dose, and patients with pancreatitis generally have serial CE-CTs, which compounds this. However, the advantages of this quick and accurate assessment generally outweigh the risks of future radiation induced cancer (although a clinical decision needs to be made). Clinical attempts to optimise renal function may reduce the risks of contrast induced nephropathy, especially in patients with established renal failure. CE-CT primarily allows two things. Firstly, it permits a radiographical assessment of the severity of pancreatitis. Secondly, it helps to determine whether surgical or radiological intervention is indicated, through accurate detection of complications. It aids identification of interstitial oedematous pancreatitis, nectrotising pancreatitis, acute peripancreatic fluid collection, acute necrotic collection, and, later on, walled-off necrosis or pancreatic pseudocyst formation, all of which have been well described recently.[1] Other complications, including portal vein thrombus, pancreatic abscess, splenic or gastroduodenal artery aneurysm, and duodenal or biliary obstruction secondary to extrinsic compression or stricturing, are also best seen using CE-CT.

Magnetic resonance imaging (MRI)

Magnetic resonance cholangiopancreatography (MRCP), a heavily weighted T2 MRI sequence, is particularly useful for delineating fluid filled structures and is therefore

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- Investigating urinary tract infections in children (*BMJ* 2013;346:e8654)

useful in the evaluation of common bile duct and filling defects, such as gallbladder stones (fig 2). Magnetic resonance cholangiography has a sensitivity of 89-100% and a specificity of 83-100% for gallstones.[6] MRI is as good as ultrasound in detecting gallstones in the gallbladder but better at detecting distal common bile duct stones,[7] which is the more pertinent finding in cases of pancreatitis. However, its sensitivity for bile duct stones is not as good as that of ERCP or endoscopic ultrasound, although MRI is not invasive and is therefore often preferred.[8] Although MRI can be logistically difficult, owing to practical concerns such as placing a potentially sick, intubated patient in a narrow tunnel that makes monitoring difficult, free breathing sequences can be used to obtain an MRCP in patients who cannot hold their breath. In the acute setting, MRI assessment of pancreatitis has the benefit of no radiation burden and can diagnose pancreatitis as well as CE-CT can.[9] MRI's excellent soft tissue resolution may help it to characterise the content of peripancreatic collections and therefore the potential for drainage.[10]

However, despite these advantages of MRI, CE-CT remains the preferred imaging modality for severe pancreatitis. Not only does CE-CT have good sensitivity for complications of pancreatitis, but CE-CT, and its interpretation, is more readily available in the acute setting in the United Kingdom,[11] and any image guided percutaneous intervention, such as fluid aspiration or drainage, will usually be done under computed tomography guidance. A recent computed tomography scan with intravenous contrast can provide a useful interventional "road map," without the need for further intravenous contrast during the procedure. Additionally, on MRI, the signal from the biliary tract can overlap with signals from other fluid filled structures such as the duodenum or stomach,[12] and although this is less of a problem on modern scanners, it could cause confusion with regard to potential artefactual collections.

Outcome

Despite repeated computed tomography guided drainages of the acute necrotic collections, this patient underwent a total necrosectomy, in which all necrotic tissue (often the majority of the organ) is debrided. She then had a perforation of the transverse colon, a rare complication of pancreatitis, resulting in a right hemi-colectomy and end ileostomy. The patient survived.

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ANSWERS TO ENDGAMES, p 36 For long answers go to the Education channel on thebmj.com

ANATOMY QUIZ

Scaphoid view radiograph of the left wrist

A: Metacarpophalangeal joint of the ring finger
B: Hook of the hamate bone
C: Ulnar styloid process
D: Carpometacarpal joint of the thumb
E: Distal pole of the scaphoid
F: Proximal pole of the scaphoid

STATISTICAL QUESTION

Pitfalls of statistical hypothesis testing: multiple testing

Statements *a* and *b* are true, whereas *c* is false.

CASE REPORT A 20 year old man with a high pressure steam burn

1 Scalds (including steam), flame burns, and contact burns are the three main causes of major burn injuries in adults. The annual incidence is 0.2-2.9 per 10 000 in Europe.
2 Signs of potential airway compromise are related to the external burn (for example, facial burn), direct thermal injury to the respiratory tract (for example, stridor), inhalation of noxious substances (for example, carbonaceous sputum), or reduced consciousness.
3 A systematic advanced trauma life support (ATLS) approach involving simultaneous assessment and resuscitation should be initiated immediately at the scene of injury, if it is safe to do so. The initial lifesaving measures are to establish control of the airway, stop the burning process, and gain intravenous access for fluid resuscitation.
4 Early complications associated with high mortality are burn shock and inhalational injury; the main late complication is sepsis. These complications lead to multiorgan failure, which is the main cause of death.
5 Successful rehabilitation requires the involvement of several key healthcare professionals. The physical aspects of rehabilitation will require physiotherapists, occupational therapists, and burns plastic surgeons, whereas psychologists and psychiatrists are involved in the psychosocial aspects.