education

CLINICAL UPDATES

Updated guidelines on neonatal jaundice

Babies with gestational age <38 weeks, a sibling who had neonatal jaundice, jaundice in the first 24 hours, and those who are exclusively breast fed are at risk of developing hyperbilirubinaemia say updated NICE guidelines. Assess all babies for risk factors and examine regularly for jaundice in the first 72 hours. In all babies with suspected or obvious jaundice in the first 24 hours, measure and record bilirubin within two hours. Check bilirubin only in babies who are visibly jaundiced. Tell parents about the importance of picking up jaundice in the first 24 hours and provide information on how to do this. Reassure parents that neonatal jaundice is common and usually transient.

http://bit.ly/1Oi9umv

Guidance on new diagnostic test for pre-eclampsia

Placental growth factor (PlGF) is a protein involved in placental development of new blood vessels. In normal pregnancy, PlGF concentrations rise and peak at 26-30 weeks, but in pre-eclampsia they can be low, indicating possible placental dysfunction. PlGF based tests, used in conjunction with clinical judgment and clinical follow-up, can help rule out suspected pre-eclampsia in women between 20 and 34+6 days' gestation says new NICE guidance.

http://bit.ly/1XmEQdJ

Prescribing in Alzheimer's disease

Acetylcholinesterase inhibitors donepezil, galantamine, and rivastigmine are recommended for managing mild to moderate Alzheimer's disease says NICE guidance. If these are contraindicated or not tolerated, memantine may be used. Memantine is also recommended in severe Alzheimer's disease. GPs, nurse consultants, advanced nurse practitioners with specialist expertise in diagnosing and treating Alzheimer's disease, and other healthcare professionals with the relevant knowledge and skills are now able to initiate acetylcholineseterase inhibitors.

http://bit.ly/21ZGYZq

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ART OF MEDICINE

The family factor

Hayim was 22 years old. Like his brother, he had been totally incapacitated, bedridden, contracted, mute, and unresponsive from birth. Both children were cared for at home, primarily by their father.

Hayim was admitted with bilateral pneumonia. Days went by with no improvement. His father was almost always there. We got to know him and came to respect him: strong, wide shouldered, often smiling, he performed small tasks for his son, silently watching the changing shifts of doctors and nurses.

He once yelled at a nurse for not being gentle enough performing suction, causing his son discomfort. The nurses claimed that the father insisted on doing the suction himself without using proper sterile technique. "Let him do it," I said, "It's his way of showing his love for his son."

Gradually our attitude to Hayim changed. Instead of doing just what was necessary, we exerted ourselves, wanting to grant the father his only wish—to take his son home and be "as before."

We stopped thinking that it didn't matter much whether Hayim lived or died. We performed medical tasks that we would not have done if his father had not been there. We discussed the "family factor" effect in our departmental meeting.

Hayim's exceptional father taught us that the importance of patients to their family can have a major effect on doctors' attitudes and decisions.

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We welcome contributions to this column via our online editorial office: https://mc.manuscriptcentral.com/bmj.

Patient consent: Consent supplied by guardian.

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FAST FACT—DIAGNOSING HEART FAILURE

There are no pathognomonic features for heart failure, so it is important to consider this diagnosis in all patients with suspected symptoms and signs. A normal natriuretic peptide concentration (in the absence of drugs known to lower natriuretic peptides) virtually excludes the diagnosis. If the natriuretic peptide concentration is raised, the next step is to refer the patient for echocardiography and a specialist assessment.

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Treatments for paracetamol poisoning

Nicholas A Buckley,[1 2 3] Andrew H Dawson,[1 2 3] Geoffrey K Isbister[1 4]

WHAT YOU NEED TO KNOW

- Acetylcysteine or methionine is associated with reduced mortality if given within eight hours and perhaps even up to four days later
- Slower infusions of intravenous acetylcysteine reduce the risk of anaphylactoid reactions
- Consider activated charcoal for patients who present within two hours of a large overdose (>10 g) if risk of aspiration is low

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We based our tips for patients on the most common questions patients ask (Why do I have to take this? Do I have to take this? Will I have any long term problems after this?) and the MHRA model patient discharge card.[3] We asked some lay people who had not taken an overdose to advise on the wording of the tips for patients.

A 24 year old woman is brought to the emergency department semi-conscious after a suspected overdose; empty packs of paracetamol (acetaminophen) and diazepam are found with her. She is also taking carbamazepine for seizures. Her paracetamol concentration at the time of admission is 100 mg/L (660 µmol/L); she probably ingested the pills four to eight hours earlier.

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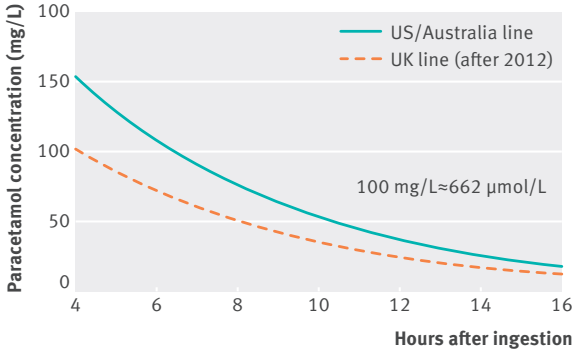
This is one of a series of occasional articles on therapeutics for common or serious conditions, covering new drugs and old drugs with important new indications or concerns. The series advisers are Robin Ferner, honorary professor of clinical pharmacology, University of Birmingham and Birmingham City Hospital, and Albert Ferro, professor of cardiovascular clinical pharmacology, King's College London. To suggest a topic, please email us at practice@bmj.com.

Effects of paracetamol poisoning

Paracetamol poisoning can cause severe hepatotoxicity owing to a minor but highly reactive metabolite produced by cytochrome P450 enzymes. At therapeutic doses, the metabolite (*N*-acetyl-p-benzoquinoneimine; NAPQI) is detoxified by glutathione. However, in paracetamol overdose, glutathione stores are depleted and hepatotoxicity ensues, starting about eight hours after the overdose and potentially leading to fulminant liver failure within a few days.

The risk of hepatotoxicity is calculated from the blood concentration of paracetamol and hours since ingestion (figure). If the concentration is above the line on the nomogram, treatment should be considered. The risk of toxicity without treatment is low until concentrations are substantially higher than this line. The nomogram is inaccurate if presentation is very late or the overdose was taken over several hours. If a measurement cannot be obtained within eight hours, treatment decisions cannot wait for laboratory results. Risk is then based on reported ingested dose (≥200 mg/kg or 10 g in Australia, >75 mg/kg or 4 g in United Kingdom) or on evidence of hepatotoxicity if the overdose was taken >24 hours ago.



Nomograms for the treatment of paracetamol poisoning. Concentrations above the lines require treatment. Nomograms for clinical use usually show just one of the lines to avoid confusion. The US/Australia line is sometimes referred to as the Rumack-Matthew line and is commonly used in Canada, New Zealand, and parts of Europe and Asia

TIPS FOR PATIENTS

- Activated charcoal reduces the amount of paracetamol absorbed so may reduce the need for other treatments and time in hospital. It is safe but may temporarily reduce the effectiveness of other regular drugs
- Acetylcysteine is given to reduce liver damage, usually in a drip over 24 hours. Rashes, itch, nausea, and vomiting are common in the first hour or two
- In most countries life saving treatments can be given without patient consent in emergencies—for example, under a mental health act or as the treating doctor's "duty of care."[2 4] Acetylcysteine generally meets these criteria, but the evidence for charcoal is less clear
- No long term liver damage or adverse effects are expected after leaving hospital
- Return to hospital or seek medical help if symptoms such as nausea or abdominal pain emerge in the next few days

What are paracetamol poisoning antidotes?

Antidotes acetylcysteine and methionine provide a substrate for further glutathione synthesis,[1 2] thus detoxifying NAPQI and reducing hepatotoxicity. Intravenous acetylcysteine is the main antidote in many countries but is also available as an oral preparation. UK guidelines were updated in 2012, when the recommended treatment threshold was lowered, and they differ from other international ones.[3 4] This change benefits a small number of patients but results in side effects for a greater number of patients and increased costs.

Methionine, oral only, is used in some low income countries and is on the World Health Organization's essential medicines list.[5] Other treatments include early activated charcoal to reduce absorption of paracetamol and haemodialysis to increase elimination.

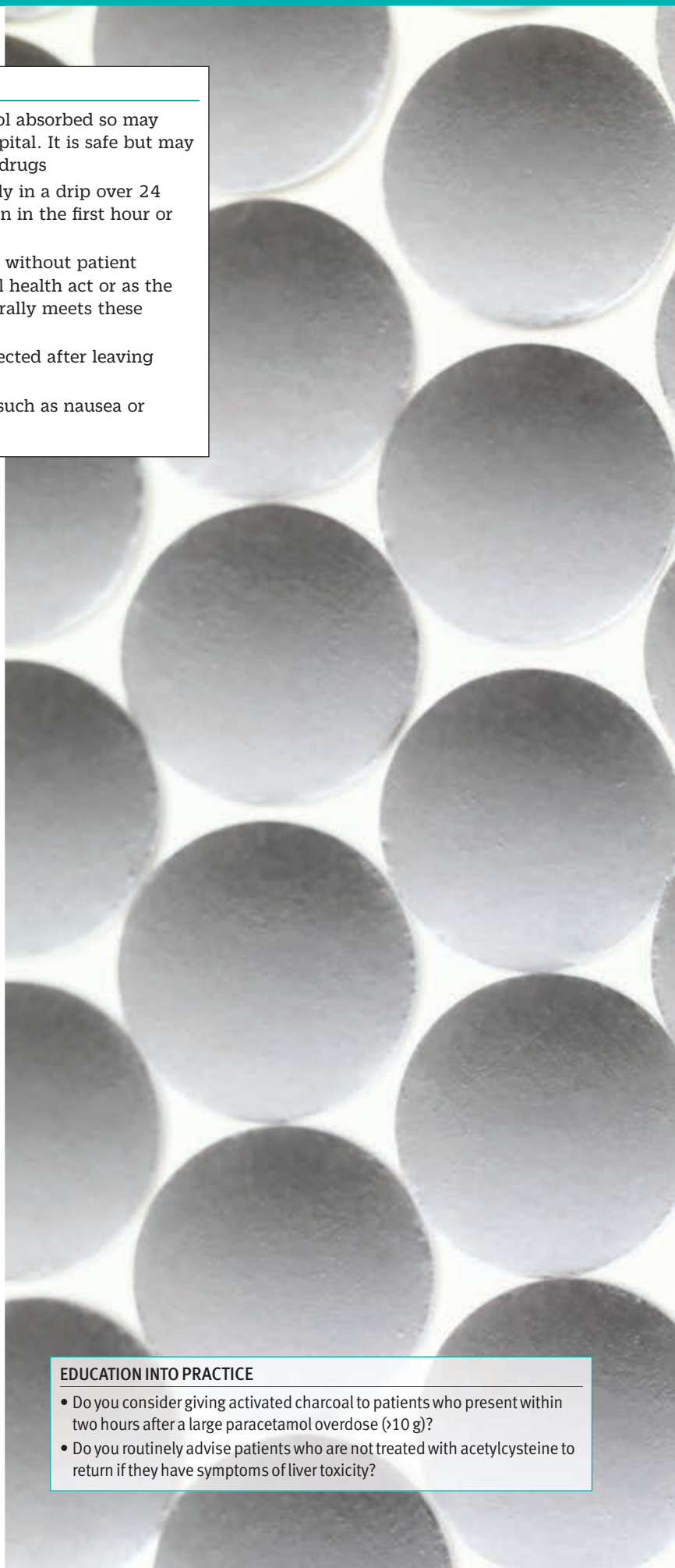
How well do they work?

Acetylcysteine and methionine

Original data supporting the use of these antidotes in paracetamol poisoning come from cohort studies. Paracetamol poisoning treated within eight hours with intravenous or oral acetylcysteine is consistently associated with avoidance of serious hepatotoxicity and death in cohort studies.[2-8] Data from the 1970s, before such antidotes were available, show that 3-5% of patients died.[9] Smaller cohort studies suggest similar favourable outcomes with early methionine (table 1).[1]

A randomised controlled trial (RCT; n=50) found that treatment with acetylcysteine up to four days later reduces risk of death, even in those with established liver failure (number needed to treat (NNT) to prevent death 4, compared with no use of acetylcysteine).[10]

Despite treatment, hepatotoxicity (eg alanine aminotransferase >1000 U/L) still occurs, particularly with very large overdoses (>50 g) even if people receive early treatment, and in those treated >8-10 hours after the overdose and those with increased susceptibility (eg people with chronic alcohol use or malnutrition and those taking enzyme inducing drugs).



EDUCATION INTO PRACTICE

- Do you consider giving activated charcoal to patients who present within two hours after a large paracetamol overdose (>10 g)?
- Do you routinely advise patients who are not treated with acetylcysteine to return if they have symptoms of liver toxicity?

Reported rates of hepatotoxicity and death when antidotes used in high risk paracetamol poisonings (concentration more than double the nomogram line)*[1-8]				
	Hepatotoxicity		Death	
Antidote	<10 h	10-24 h	<10 h	10-24 h
Methionine[1]	6/43 (14%)	14/31 (45%)	0	2 (6%)
Oral NAC[8]	17/206 (8%)	199/578 (34%)	1 (0.5%)	9 (0.4%)
IV NAC[2]	1/33 (3%)	18/27 (67%)	0	2 (7%)

*IV=intravenous; NAC=acetylcysteine.

No clinical trials have compared intravenous versus oral acetylcysteine[6] or acetylcysteine with methionine.[6]

Activated charcoal

No RCTs have looked at activated charcoal specifically for paracetamol poisoning.[11] RCTs of its routine use in all poisoning in both developed and developing countries show no overall improvement in outcomes such as mortality or hospital stay.[12 13]

A cohort study of patients who ingested >10 g of paracetamol found that early (<2 h) use of charcoal was associated with reduced need for acetylcysteine.[14] If we assume that the link was causal, the NNT to obviate the need for further treatment was 7. This is biologically plausible as the duration of paracetamol absorption is prolonged with larger overdoses.

Haemodialysis

This removes a small proportion of ingested paracetamol but also removes acetylcysteine. It is not generally recommended and will not be discussed further.[15]

How safe are they?

Intravenous acetylcysteine is associated with anaphylactoid reactions such as rash, pruritis, vomiting, flushing, wheeze, and hypotension in RCTs, with numbers needed to harm (NNH) of 2-10, depending on the rate of infusion.[7 16] Anaphylactoid reactions do not reflect an allergy but seem to be related to peak acetylcysteine concentration in rapid loading doses; slower initial infusions may reduce the risk.[7 17] Other serious adverse effects arise from excessive dosing owing to errors in dose calculation[18] (eg lethal anaphylactoid reactions from 10-fold dosing errors[19]). Less serious adverse effects such as nausea and vomiting are also common.[7 16]

Oral methionine is commonly associated with vomiting, but data on its adverse effect profile are limited.[11]

Two large RCTs show that activated charcoal is very safe.[12 13]

What are the precautions?

Deliver intravenous acetylcysteine in a closely monitored area such as the emergency department, with capacity to treat anaphylactoid reactions. Ensure correct dose calculation and use an infusion pump to ensure intended infusion rates are not exceeded.

Consider avoiding activated charcoal if oral acetylcysteine or methionine is likely to be given because it impairs their absorption (although outcomes are no worse when it is given before oral acetylcysteine[20]). It also enhances elimination of anticonvulsants and oral contraceptives—advise patients of the short term increased risk of treatment failure (seizures, pregnancy) and that they should take appropriate precautions.

How are they given and monitored?

Acetylcysteine is often given as a three bag intravenous infusion regimen diluted in 5% dextrose—150 mg/kg over one hour, then 50 mg/kg over four hours, and finally 100 mg/kg over 16 hours. Monitor the patient for infusion reactions over the first few hours. If necessary, slow the infusion or temporarily stop it. Consider using inhaled salbutamol (for wheeze) and histamine blockers (for skin reactions). Two bag infusions with the same total dose but slower initial infusion rates are being used to reduce the rate of infusion reactions (eg 200 mg/kg over four hours then 100 mg/kg over 16 hours). Such regimens are unlicensed but have shown similar efficacy in cohort studies.[23]

Towards the end of the infusion, check liver function tests and paracetamol concentrations in patients with signs of liver damage (such as nausea and right upper quadrant abdominal tenderness) and those who took large overdoses (more than double the standard nomogram line). If alanine aminotransferase is raised or paracetamol is >10 mg/L, consider longer treatment with a continuous infusion of 150 mg/kg/day.

Oral acetylcysteine is usually given as 140 mg/kg initially and then 70 mg/kg four hourly for up to 72 hours and oral methionine as four doses of 2.5 g four hourly. The durations suggested are a legacy from the first studies. Shorter (for acetylcysteine) or longer (for methionine) courses would make sense in many patients to cover the time that paracetamol concentrations remain high. Nausea and vomiting are the commonly reported adverse effects and monitoring is used to check adherence.

Oral activated charcoal is given orally as 50 g in suspension. The patient should be cooperative and alert, or intubated, to avoid the risk of aspiration. Routine blood test monitoring is not needed.

Case outcome

The patient was not fully conscious but did not require intubation so she could not safely receive activated charcoal (which might also have interfered with her carbamazepine, which was confirmed as being in the normal range). She received intravenous acetylcysteine as soon as the paracetamol result was obtained. Risk assessment with the nomogram had to use a "worst case" scenario, which assumed up to eight hours had elapsed, putting the concentration above the treatment line. She was also potentially at higher risk because she was taking carbamazepine (CYP450 enzyme inducer) and this also caused some baseline changes in her liver function tests.

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CLINICAL REVIEW

Metastatic spinal cord compression: diagnosis and management

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This is a shortened version; the full version is on thebmj.com

CPD/CME
0.5 CREDITS

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE
No patients were asked for input in the creation of this article.

Between five and 10 in every 200 patients with terminal cancer will have metastatic spinal cord compression (MSCC) within their last two years of life. It is an oncological emergency.[1 2] MSCC is caused by compression of the dural sac and its contents (spinal cord or cauda equina) by an extradural or intradural mass,[3] and it leads to irreversible neurological damage such as paraplegia or tetraplegia depending on the level of the lesion. Extradural masses are the more common, and their causes and presentation are the focus of this review.

Who gets MSCC?

Vertebral metastases occurs in 3–5% of all patients with cancer. As well as MSCC, they can cause pain and vertebral collapse. Most adult series highlight that cancers of the prostate, breast, and lung account for 15-20% of cases each.[6] However, virtually any systemic cancer can metastasise to the spine.

Evidence from a Scottish audit carried out in the late 1990s and from a Canadian population based study suggests that the incidence may be up to 80 cases per million people per year.[8 9] UK NICE guidance has approximated this to 4000 cases each year in England and Wales.[6]

How does it present?

MSCC may be the presenting symptom of cancer. A recent UK retrospective cohort study reported that 21% (27/127) of the MSCC patients presenting to a London cancer centre over a year had no pre-existing cancer diagnosis.[7] MSCC can be particularly hard to diagnose in those with poor functional status, advanced age, or comorbidities.

Figure 1 shows the most common sites for MSCC. However, 30-50% of patients show multi-level involvement, so whole spine imaging is imperative when MSCC is suspected.

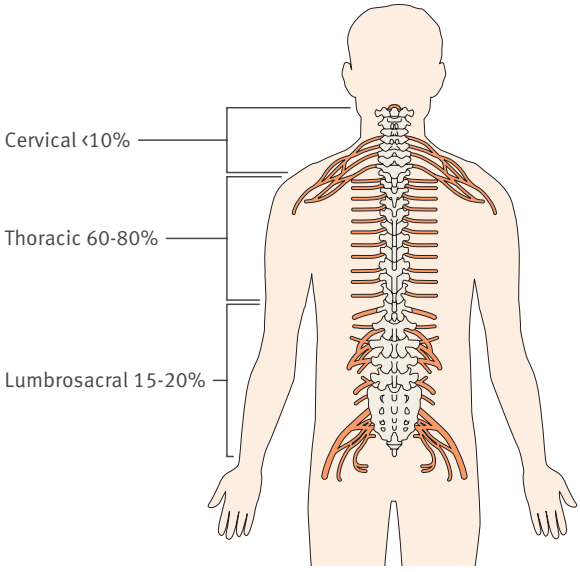


Fig 1 | Distribution of sites for metastatic spinal cord compression[1]

Pain

Back pain is the most common first symptom, occurring in 95% of patients for up to two months before signs related to MSCC appear.[5] The pain can be either localised (in and around the spinal column) or radicular (nerve root pain affecting one or both sides of the body). In the Scottish audit of 319 patients with MSCC, 37% of patients had radicular pain, 15% had localised spinal pain, and 47% had both.[8] Patients may report lower thoracic and upper lumbar radicular pain as abdominal pain.

Pain often increases in severity over time and may be worse on straining or coughing or on lying down due to epidural plexus distension. UK NICE guidance recommends having a higher index of suspicion in those with a known cancer diagnosis or severe unremitting pain, especially if it is localised to the upper or middle spine or the pain is aggravated by increased intra-abdominal pressure.[6]

It can also be difficult to distinguish pain in those with spinal metastases from pain that has progressed to cord compression. UK NICE guidance provides a checklist (see box 1) for distinguishing between the two and recommends magnetic resonance imaging (MRI) of the whole spine within seven days for those with pain alone (in whom the

WHAT YOU NEED TO KNOW

- Metastatic spinal cord compression is an oncological emergency and may be the first presentation of a cancer
- Magnetic resonance imaging of the whole spine is the investigation of choice
- Offer corticosteroids and analgesia and consider spinal stability while the patient is assessed
- Timely referral for neurosurgery or radiotherapy, or both, provides better outcomes longer term, but palliative care is the treatment of choice for some patients

suspected diagnosis is spinal metastases) compared with an MRI whole spine within 24 hours for those with pain and neurological signs, indicating possible MSCC.[6]

Motor deficit

Limb weakness is the second most common symptom, affecting 60-85% of patients at the time of diagnosis of MSCC.[1 5] Patients may complain of an unsteady gait or a rapid onset of difficulty in walking, standing, or transferring from bed to chair that has progressed over days or a few weeks. Frail patients with advanced disease may not report the weakness, but carers may note a sudden deterioration in functional ability. Most published guidance focuses on the importance of minimising delays before starting treatment in a bid to prevent paraplegia.[2-9] The strongest predictor of neurologic outcome with treatment is the neurologic status when treatment is initiated.[10] A large, well designed German retrospective cohort study found an association between slower development of motor deficits before the start of radiotherapy and a better functional outcome after treatment.[11]

Sensory deficit

Sensory symptoms are less common and may predate objective sensory signs. Patients may complain of paraesthesia, decreased sensation and numbness of toes and fingers, which may extend 1-5 dermatomes below the true level of cord compression. Radicular sensory loss and loss of tendon reflex on clinical examination map to the anatomical level of compression more accurately than subjective symptoms. A combination of rapid onset sensory and motor symptoms should raise a high degree of suspicion of MSCC.

Autonomic dysfunction

This is often a late consequence of MSCC and may present as bladder and bowel dysfunction such as urinary retention, urinary or faecal incontinence, or constipation.[4]

Direct questioning to exclude this is recommended (for example, "Are you able to open your bowels and pass urine normally?" "Have you had any accidents where your bowels have opened or you have passed urine without warning?"). Constipation was the commonest bowel symptom in a prospective audit and occurred in 67% of all patients with MSCC.[5]

Cauda equina syndrome

Patients with cauda equina syndrome present differently. They often report decreased awareness at presentation on passing urine or opening bowels, without a motor deficit and sometimes in the absence of pain. The main clinical signs are decreased sensation over the buttocks, posterior-superior thighs, and perineal region in a saddle distribution, with most patients exhibiting decreased anal sphincter tone on examination. Urinary retention with overflow incontinence is an important predictor, with a sensitivity of 90% and a specificity of 95%.[12]

How to confirm the diagnosis

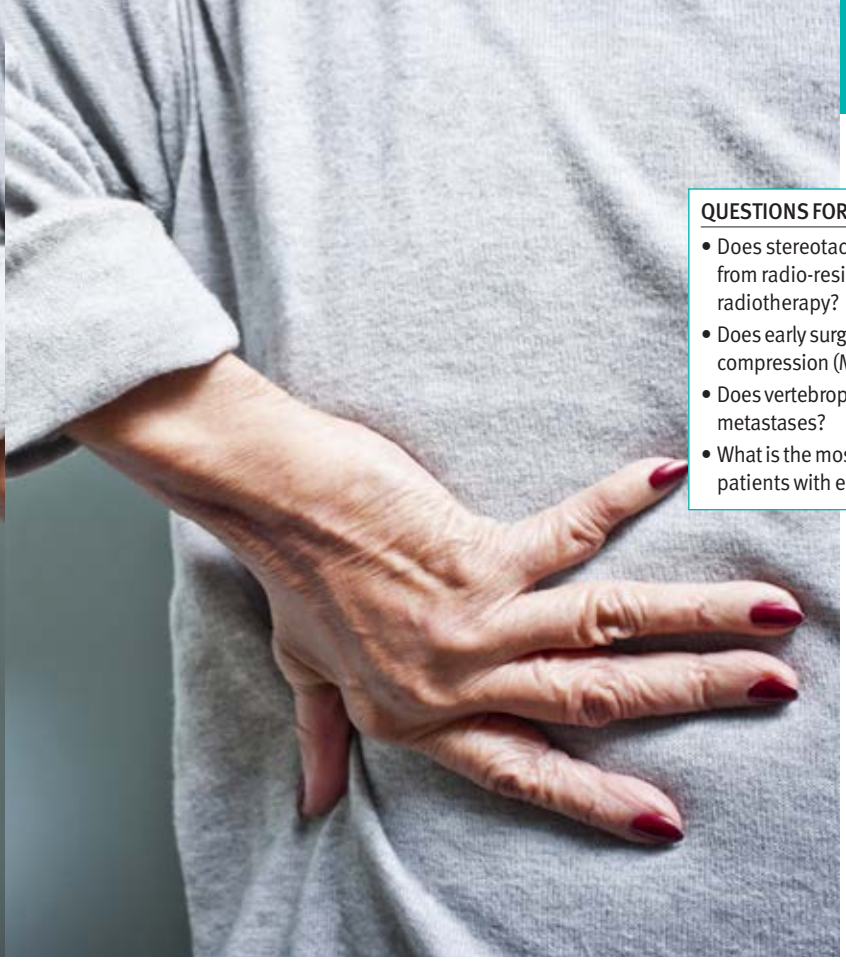
Magnetic resonance imaging (fig 2) of the whole spine is the imaging method of choice and has a sensitivity of 93% and specificity of 97%.[2-14] The implication is therefore that a few

Box 1 | NICE recommendations for diagnosis and management of patients at risk of or with metastatic spinal cord compression (MSCC)[6]

- Contact the relevant team (ideally via a designated MSCC coordinator) urgently (within 24 hours) to discuss the care of patients with cancer and pain with any of the following characteristics suggestive of spinal metastases:
  - Pain in the middle (thoracic) or upper (cervical) spine
  - Progressive lower (lumbar) spinal pain
  - Severe unremitting lower spinal pain
  - Spinal pain aggravated by straining (for example, at stool) or when coughing or sneezing
  - Localised spinal tenderness

Nocturnal spinal pain preventing sleep.

- Contact the MSCC coordinator (or equivalent) immediately to discuss the care of patients with cancer and symptoms suggestive of spinal metastases, who have any of the following neurological symptoms or signs suggestive of MSCC and view them as an oncological emergency:
  - Neurological symptoms (including radicular pain, any limb weakness, difficulty in walking, sensory loss, and bladder or bowel dysfunction)
  - Neurological signs of spinal cord or cauda equina compression
- Perform frequent clinical reviews (such as daily, depending on setting) of patients with cancer who develop lower spinal pain that is clinically thought to be of non-specific origin (that is, not progressive, severe, or aggravated by straining and has no accompanying neurological symptoms). In particular, look for:
  - Development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours)
  - Development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately)
- Perform frequent clinical reviews of patients without a prior diagnosis of cancer who develop suspicious spinal pain (with the characteristics outlined above) with or without neurological symptoms. Treat or refer patients with stable and mild symptoms by normal non-specific spinal pathways, or refer by cancer pathway if concerned. In particular, look for:
  - Development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours)
  - Development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately)



QUESTIONS FOR THE FUTURE

- Does stereotactic radiotherapy improve mobility in patients with spinal metastasis from radio-resistant tumours or patients who have received prior standard radiotherapy?
- Does early surgical intervention reduce the incidence of metastatic spinal cord compression (MSCC) in those with spinal metastases?
- Does vertebroplasty or kyphoplasty reduce the incidence of MSCC in those with spinal metastases?
- What is the most clinically effective and cost effective regimen of radiotherapy to treat patients with established MSCC?

patients (7%) will have the diagnosis missed on MRI and a smaller number (3%) will have a false positive result. In the UK, NICE guidance recommends MRI is carried out within 24 hours of clinical suspicion.[6]

Computed tomography (CT) is often used to aid surgical or radiotherapy treatment planning, but it is not recommended for definitive diagnosis of MSCC. CT myelography is now rarely used except in those with contraindications to MRI. Bone scintography and plain radiography have no role in the diagnosis.

When not to investigate or treat

In some situations where MSCC is suspected, it might be more appropriate not to investigate or treat if there is little or no prospect of a favourable outcome and the benefits and burdens have been discussed fully with the patient. Such situations include well established paralysis of more than a week's duration, poor baseline performance status, and predicted lifespan of only days to weeks from underlying disease. In these cases, palliative care with consideration of empirical corticosteroids (oral or subcutaneous dexamethasone 8 mg twice daily) may be the preferred treatment.

What should you do while awaiting diagnosis?

Current advice is to give steroids and analgesia and to protect vulnerable spinal alignment from further damage through rest and appropriate immobilisation.

What is the role of steroids?

Evidence from randomised controlled trials suggests corticosteroids provide a beneficial adjunctive therapy in patients with myelopathy from epidural compression.[15 16] One randomised study detected higher ambulation rates in patients with MSCC who received dexamethasone before radiotherapy compared with those who did not (81% *v* 63% at 3 months, P=0.046).[17]

UK guidelines recommend that, unless contraindicated, all patients with MSCC are offered an immediate loading dose of 16 mg of dexamethasone (given intravenously or orally) followed by a short course of 16 mg dexamethasone daily (given in divided doses, such as 8 mg twice daily orally).[6] Steroids are contraindicated if lymphoma is the suspected cause of the MSCC as the oncolytic effect of the steroids may impair tissue diagnosis. A Norwegian prospective study that reported a high incidence of serious side effects and no change in ambulation with higher dose (96 mg) dexamethasone in MSCC patients.[18] Anecdotal evidence suggests that patients who respond neurologically to the initiation of steroid therapy tend to respond better to radiotherapy.

Weaning steroids

Corticosteroids may provide analgesic benefit and initial improvement of neurological function.[19] Long term benefit is limited with no evidence of improved survival and unacceptable side effects that can be debilitating and occasionally fatal.[20]

After radiotherapy or surgery, UK guidelines recommend weaning steroid dose gradually and completely over 4-6 weeks, or to the lowest dose that maintains stability of symptoms. For those patients who do not proceed to surgery or radiotherapy,

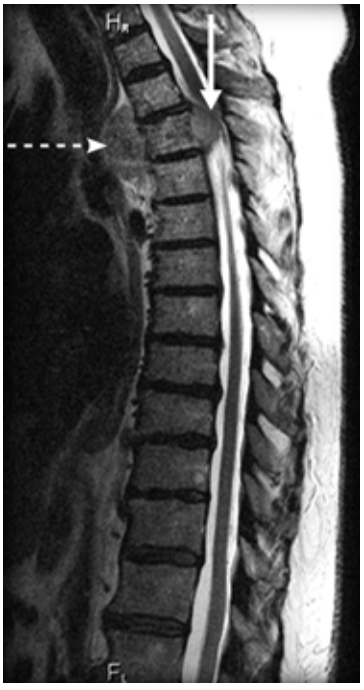


Fig 2 | Sagittal T2 weighted magnetic resonance image of the thoracic spine showing a tumour mass in the upper thoracic spinal canal (broad arrow) and in the prevertebral region just in front of the spine (thin arrow). The spinal canal component is causing compression of the underlying spinal cord

discussions should be undertaken about reduction in dexamethasone with a view to stopping it. In this case, a Norwegian study advises a quicker dose reduction from 16 mg to zero in 14 days.[21]

What analgesia to prescribe?

Pain associated with MSCC has both bony and neuropathic elements. The mechanism of bony pain is partially through inflammatory mediators and therefore responds well to treatment with steroids. The WHO pain ladder should be used to guide analgesia, with appropriate use of neuropathic adjuvant analgesics. Seek specialist advice from the pain or palliative care team where necessary and remember to prescribe both regular analgesia plus "as needed" analgesia.

Alignment

Regardless of setting, patients with severe pain on movement suggestive of spinal instability, or any neurological symptoms or signs suggestive of MSCC, should ideally be nursed flat with neutral spine alignment (including "log rolling" with use of a slipper bed pan for toileting) until bony and neurological stability are ensured (ideally after MRI and neurosurgical review) and cautious remobilisation with physiotherapy input may begin.[6]

Treatment

Definitive treatment may include any combination of radiotherapy, surgery, and chemotherapy. If therapy is appropriate and the patient wants this, it should be started before any further neurological deterioration occurs and ideally within 24 hours of the confirmed diagnosis of MSCC.[6]

To guide treatment plans, it is important for patients to have a histological or cytological diagnosis of malignancy. If this was not established earlier in the patient's course, needle biopsy or open biopsy should be undertaken as soon as possible and ideally before radiotherapy or surgery.[1 22]

When deciding on definitive treatment with the patient, consider the patient's performance status, extent of metastatic disease, spinal stability, underlying tumour radiosensitivity, and degree of spinal cord compression.[22]

Radiotherapy

Historically, radiotherapy has been viewed as first line treatment because it has been shown to be as effective as a decompressive laminectomy with a lower incidence of complications.[15] It also improves outcomes (including reducing local recurrence rates) after surgery and in patients who are not surgical candidates.[10]

There are three goals of treatment with radiotherapy:

- Prevention of neurological deterioration
- Improvement of neurological function
- Pain relief.

For patients with a good prognosis (ambulant or with immobility for <24 hours), urgent treatment is indicated within 24 hours of diagnosis.

Patients with a poor prognosis include those with less than six months' life expectancy, poor performance status, and established paraplegia for >24 hours. In these patients the median survival is of the order of 1-2 months with poor chance of neurological recovery. Radiotherapy is indicated only for pain relief, but in rare cases some patients may show neurological recovery.

One randomised trial reported similar functional outcome with the three different radiotherapy schedules, but single radiation dose was associated with higher in-field recurrence.[22 23]

Surgery

A growing body of evidence indicates that surgery is superior to radiotherapy in retaining or regaining neurological function and relieving pain. A US randomised controlled trial reported 42/50 (84%) of patients randomised to neurosurgery plus postoperative radiotherapy achieved the primary endpoint of the ability to walk on completion of treatment, compared with 29/51 (57%) of those randomised to radiotherapy alone.[24]

The choice of surgery versus other treatments can be hard to determine. Discussions with patients should take into account their overall fitness, prognosis, and preferences.[6]

Patients with spinal instability, good life expectancy, or radio-resistant tumours are likely to have a much better neurological outcome with tumour resection and spinal stabilisation before radiation.[10] The Spinal Instability Neoplastic Score (SINS) is a validated tool to determine clinical instability.[26]

A Canadian systematic review found no direct evidence to support the type of surgery best undertaken nor whether surgical salvage should be attempted if a patient is progressing on or shortly after radiotherapy. The reviewers advised consideration of pretreatment ambulatory status, comorbidities, technical surgical factors, the presence of bony compression and spinal instability, potential surgical or radiotherapy complications, and patient preferences.[14]

Rehabilitation

Discharge planning and ongoing care, including rehabilitation, starts at admission and is ideally led by a named individual within the clinical team. Successful planning involves the patient and his or her carers, oncology team, rehabilitation team, and community support, including primary care and specialist palliative care, as required. The aim is to focus on patient centred goals of care, maximising physical function in the context of overall quality of life. Rehabilitation should be provided in the patient's preferred place of care, usually started in the acute setting and then continued in the community, hospice, or specialised inpatient rehabilitation unit.

Quality of life

Little is known about the psychological impact of MSCC.[14] A recent literature review using thematic analysis concluded that patients with MSCC report good quality of life and low levels of distress in over 50% of cases, with only a minority reporting severe distress. Greater awareness of and further research into the psychological impact are required to determine those at risk and the most effective strategies for support.[28]

Competing interests: None declared.

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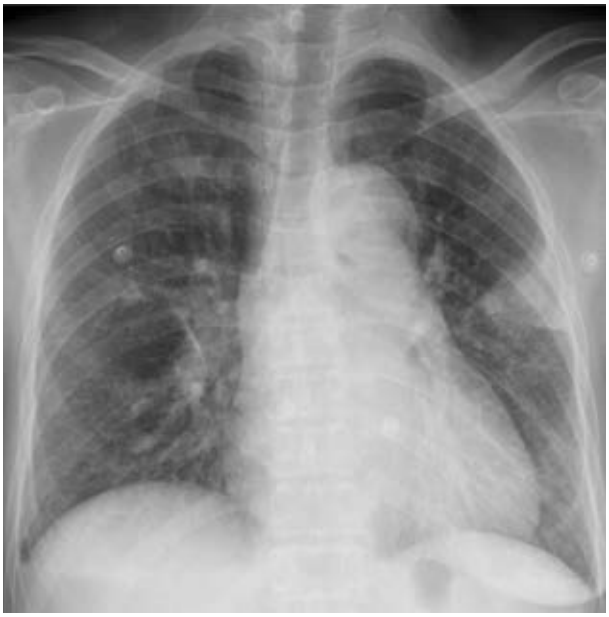
CASE REVIEW **Patent ductus arteriosus illuminating an old eponym**

A 60 year old woman was sent from primary care for assessment of acute left sided pleuritic chest pain and dyspnoea without sputum production. She had been experiencing malaise, intermittent fever, and rigors for four weeks. A patent ductus arteriosus (PDA) had been identified in late adulthood 10 years earlier, after a murmur was detected on routine medical examination. This was confirmed by transthoracic echocardiography; there were no other signs of haemodynamic importance.

At presentation she had a fever (39.0°C) with left sided pleural rub. Precordial examination identified a continuous "machinery" murmur. Electrocardiographic findings were within normal limits and laboratory investigations confirmed normocytic anaemia, leucocytosis, and preserved renal function. Group B streptococcus was isolated from all three separate blood cultures. Her pleural rub corresponded to an abnormality on chest radiography (figure).

1 What abnormality on chest radiography corresponds to the pleural rub?
2 Given the clinical presentation and history of PDA, what is the likely cause of this abnormality?
2 What investigation would confirm the cause of this abnormality?
4 What is the initial cardiac imaging technique of choice?



Submitted by Tom Ford and David Rees Patient consent obtained.

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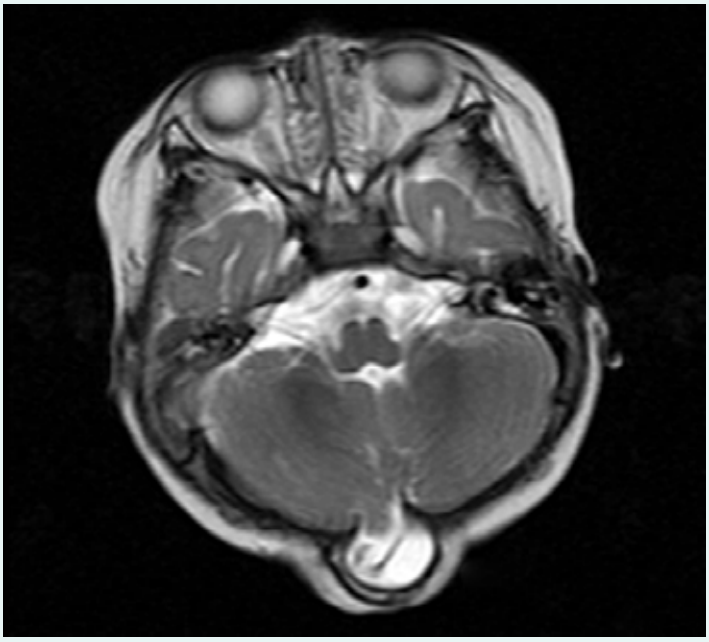

SPOT DIAGNOSIS

A boy with a sac-like protrusion at the occipital region

A 1 year old boy presented to the neurosurgery clinic with a sac-like protrusion at the occipital region that had been present since birth. He was born at full term by caesarean section. He had no neurological symptoms and the swelling had not enlarged since birth. On examination, his head circumference was normal for age. The protrusion was 2.5×2.5 cm and his cry impulse was positive. A systemic examination found no associated anomalies. Magnetic resonance imaging of the head was performed (figure). What is the diagnosis?

Parental consent obtained.

Submitted by Yong-Hai Zhou and Ming-Hua Zheng

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answers

CASE REVIEW **Patent ductus arteriosus illuminating an old eponym**

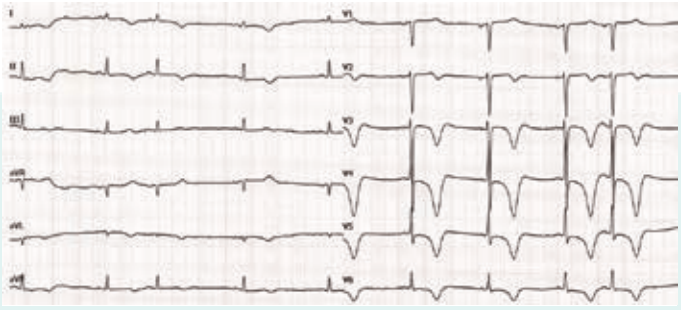
1 The wedge shaped peripherally based opacity in the left mid zone.
2 Pulmonary embolism and infarction owing to septic pulmonary emboli from the infected PDA.
3 Computed tomographic pulmonary angiography (CTPA) would confirm left sided pulmonary embolism leading to distal pulmonary infarction.
4 Echocardiography (initially with a transthoracic study) is the initial imaging technique of choice for investigating suspected endocarditis.

SPOT DIAGNOSIS **A boy with a sac-like protrusion at the occipital region**

The diagnosis is occipital encephalocele.

How the brain can influence ECGs

A man with focal epilepsy presenting with disorientation developed two simple partial seizures characterised by left sided faciobrachial clonic movements. An electrocardiogram (ECG) suggested myocardial ischaemia (inverted T waves in leads V2-V6, aVL, DI, DII, aVF). Serial highly sensitive troponins, brain computed tomography, chest radiography, and echocardiography were normal making an acute coronary syndrome unlikely. His ECG returned to baseline a few weeks after treatment with antiepileptic drugs. Similar ECG patterns have been described in central nervous system disorders in the absence of primary heart disease. This case is a reminder that the ECG can be modified by such disorders.



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The skills of uncertainty

Uncertainty is common in medicine, as in life, and sharing uncertainty is a skill that every doctor has to learn, often by trial and error. Done badly, it can increase anxiety and reduce trust. Done well, it can put the doctor alongside the patient, which is especially important at the end of life. A narrative review of this difficult topic (*Postgrad Med J* doi:10.1136/postgradmedj-2015-133371) suggests that skills and insights for sharing uncertainty are best found within palliative care, and that they should be more widely used and learnt from.

Psoriasis, obesity, and diabetes

It's long been known that psoriasis is associated with overweight and type 2 diabetes. To probe whether this has a genetic component, Danish investigators examined data from a cross sectional, population based study of 34 781 Danish twins, 20-71 years old (*JAMA Dermatol* doi:10.1001/jamadermatol.2015.6262). They found 449 psoriasis discordant twins and used variance component analysis to measure genetic and non-genetic effects on the associations. After adjusting for confounders, they conclude that psoriasis and obesity have a common genetic cause.

Don't take a kiloton of paracetamol

Britain gets through 6300 tons of paracetamol a year, but France tops us with 10 kilotons. A witty editorial in the *European Journal of Hospital Pharmacy* (doi:10.1136/ejhpharm-2016-000952) muses on what pain killing power results from these nuclear weapon levels of consumption. The answer is not a lot: fast acting formulations of non-steroidal anti-inflammatory drugs work better for acute pain, and there is no evidence that paracetamol works for chronic pain. Its potential harms, however, are very measurable.

Wheezy data gathering

There are dozens of journals of occupational medicine, and they all run articles on occupational asthma, triggered by anything from boiling broccoli to beryllium. But the systems for ascertaining and tracking work related asthma in the UK are poor, as shown by a telephone survey in *Occupational Medicine* (doi:10.1093/occmed/kqw028). The authors call for simpler, more practical, and evidence based approaches to health surveillance.

Robotic adoption

Physicians are advised to use new drugs early, while they still work. Surgeons need to use new techniques early, before they are debunked. Robots were favourites with teaching hospitals wanting to boast about being at the cutting edge of urology (*Med Care Res Rev* doi:10.1177/1077558716642690). Nearly half of US academic hospitals acquired them in the decade up to 2008 then failed to produce any properly designed comparative effectiveness research that might have justified them.

Ever more atypical mycobacterial infections

The uncommon mycobacteria that invade the human upper limb are an odd lot, and in Texas they are getting odder. In a series of 34 cases from a university hospital there (*Hand* doi:10.1177/1558944716642764), just 14 were caused by *Mycobacterium marinum*, the commonest culprit, while the others were caused by *M abscessus*, *M fortuitum*, and even rarer non-marinum species. These seem to occur sporadically in mostly healthy people.

Septal ablation: a new use for glue

Alcohol delivered through the septal coronary artery has been used for 20 years to reduce the bulk of the interventricular septum in people with hypertrophic cardiomyopathy. Turkish cardiologists pioneered the use of *N*-butyl cyanoacrylate instead because this glue ingredient doesn't spread or cause damage to local tissues as alcohol can. In an article in *Hand* (doi:10.1177/1558944716642764), they survey the literature on glue ablation and describe their own case series.

Naughty celebrity chefs

Some celebrity chefs waste expensive food, shout obscenities all the time, treat staff like trash, and provide ballast for television schedules. They can also be terrible role models for kitchen hygiene, according to a survey of 100 cookery shows (*J Public Health* doi:10.1093/pubmed/fdw026). Some don't wash their hands after handling raw meat, plonk stuff in dishes with said hands, lick their fingers, and don't use thermometers. TV chefs should wear a health warning on their aprons.

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