Remote ischaemic conditioning—an unlikely treatment for acute ischaemic stroke

*JAMA* reports a promising new treatment for acute ischaemic stroke that falls in the category of “I would never have thought that might work.” Remote ischaemic conditioning (RIC) involves “brief, reversible episodes of ischaemia and reperfusion in one vascular bed to activate ischaemia tolerance in remote tissues and organs.” In practice, this means inflating a blood pressure cuff on both arms to 200 mmHg for five minutes, deflating for five minutes, and repeating this cycle four more times, twice a day for two weeks.

The largest randomised trial of RIC to date recruited adults with acute moderate ischaemic stroke who had not received thrombolysis or endovascular therapy. The primary endpoint—excellent neurological function after 90 days—was seen slightly more in those receiving RIC (67.4% versus 62% of controls, odds ratio 1.27, P=0.02), but the findings from this open label study need to be replicated before RIC can be said to be an effective treatment.


Will LAAO ever be more than an appendage to atrial fibrillation guidelines?

Using minimally invasive surgical techniques to occlude the clot-prone left atrial appendage in people with atrial fibrillation makes sense. However, left atrial appendage occlusion (LAAO) is included in NICE’s list of “do not dos”; do not offer it as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated.

A new virtual trial, which runs data from published studies through a mathematical model, explored the role of LAAO in people with high bleeding risk from anticoagulation. Unfortunately, the data used did not include patients on direct oral anticoagulants, which have largely replaced warfarin in the treatment of AF, meaning the conclusion that LAAO may be of most benefit to those with a high bleeding risk and low stroke risk is very much up for debate.


Letters to clinicians about cause of death

If GPs get a letter for every single outpatient follow-up appointment, why is there typically so little communication between clinicians after someone dies? In the US a randomised control trial in 2018 saw medical examiners send letters (including a safe prescribing injunction) to clinicians informing them when one of their patients had a fatal overdose of a controlled drug. They found reductions in overall, high dose, and new opioid prescriptions associated with the intervention compared with a control group.

A new secondary analysis found the letter led to a modest (3.7%) reduction in dispensing of 2 mg benzodiazepine pills one to four months after the letters were sent compared with the three months before. This doesn’t seem like a big effect, but I’m struggling to think of a reason why clinicians shouldn’t be informed when a patient dies in these circumstances.


More drugs to cross off the covid list

What endpoints should be used to determine the efficacy of treatments for covid-19? In a new US based study, looking at whether metformin, ivermectin, or fluvoxamine might be effective as treatment for people at high risk of complications, 2% of a cohort of 1323 people testing positive for covid with obesity or overweight were admitted to hospital within two weeks and two people (0.2%) died.

Given the small sample size, the researchers chose a composite primary endpoint of death, hospitalisation, emergency department visit, or hypoxaemia (home oxygen saturation reading of 93% or under). No difference was seen in this primary endpoint compared with controls for either of the three repurposed drugs, adding to the existing evidence that they shouldn’t be prescribed as treatments for covid-19.

But what about that composite endpoint? What is the sensitivity and clinical value of a low home oxygen saturation reading when over 20% of participants in all study arms reported hypoxaemia, yet so few required admission?


Did adenovirus cause the spike in acute hepatitis in children?

Remember the reports last year about a mysterious rise in the number of children with acute hepatitis, linked by the press to both covid and social distancing? *NEJM* publishes two case series that aim to shed light on the true cause, one from Birmingham, England, and one from Birmingham, Alabama.

At first glance, human adenovirus type 41 seems a likely culprit, being found in 27 of the 30 children who had molecular testing in the UK study and all nine in the US. But a linked editorial calls for more caution: no evidence has been seen of hepatocellular adenoviral infection on histological examinations in these cases: might the virus activity be an immunological response leading to acute hepatitis, or could adenovirus even be an “innocent bystander?”


Tom Nolan, clinical editor, *The BMJ*, London; sessional GP, Surrey

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Acute vertigo: getting the diagnosis right

Kiran Agarwal, James Harnett, Nishchay Mehta, Fiona Humphries, Diego Kaski

PRACTICE POINTER

What not to miss

The most common cause of acute vertigo is benign paroxysmal positional vertigo (BPPV), but in younger individuals vestibular migraine may be more common. However, 3% of patients presenting with vertigo will have had a stroke, and 35% of these strokes are missed. Patients discharged from emergency departments with “benign” dizziness are at a 50-fold increased risk of being hospitalised for stroke in the seven days following discharge compared with controls. Patients presenting with vertigo may be misdiagnosed with benign inner ear disorders such as labyrinthitis or Ménière’s disease over far more common conditions such as BPPV and vestibular migraine. Good history and examination are crucial to reach the correct diagnosis and ensure that stroke or other sinister pathology is not missed (see infographic on bmj.com).

Central (brain) causes of acute vertigo are more likely than peripheral (inner ear) aetiologies to require urgent triage and management. Most patients with acute vertigo will have a non-life-threatening cause, but patients with “red flags” (box 2), including vascular risk factors or associated neurological symptoms and signs, should be prioritised for triage.

Acute vertigo is the most common symptom of posterior circulation stroke (67%), and isolated vertigo, nausea, and unsteadiness can be the sole presenting symptoms, making it hard to differentiate from a benign inner ear disorder: one of the reasons that these strokes are often missed. In many posterior circulation strokes there will be associated neurological signs, such as an occipital headache (28%), dysarthria (31%), or unilateral limb weakness (41%).

Patients may not always volunteer these symptoms, so good history taking is paramount.

Other disorders not to miss that may present acutely with vertigo include infective causes (such as cerebral abscess, where the patient is typically systemically unwell) and inflammatory neurological disorders (such as multiple sclerosis, where the vertigo is usually accompanied by other central neurological signs). Brain tumours, whether primary or metastatic, are part of the differential diagnosis, although these are less likely to present with acute vertigo, and more commonly present with focal signs (such as limb weakness) or progressive unsteadiness, headache, or vomiting (as signs of raised intracranial pressure).
3 Associated symptoms
– Ask about new onset headache, new onset unilateral hearing loss (acute vertigo and hearing loss in a young adult (<40 years) without vascular risk factors may be more suggestive of viral labyrinthitis), loss of sensation over the face or limbs, marked gait unsteadiness, speech disturbance, diplopia, or dysphagia,20 all of which point to a central (brain or brainstem) cause.
– Ask about chest pain, palpitations, and breathlessness, which may indicate a cardiac cause such as arrhythmia (see box 3 for differential diagnoses of dizziness). Associated facial pallor, visual blurring, and muffling of sound can occur with orthostatic hypotension, and confusion can occur with hypoglycaemia.
– Ask about vascular risk factors (age >65 years, existing ischaemic heart disease, diabetes, hypertension, previous stroke or transient ischaemic attack14) as their presence will increase the suspicion of stroke in a patient with acute vertigo.

4 Triggers
– Were there any triggers to the event? Dizziness triggered by turning over in bed or looking up are suggestive of BPPV; dizziness (particularly “light-headedness”) on standing from sitting or lying is suggestive of orthostatic hypotension; trauma to the neck before onset of vertigo should raise suspicion for vertebral artery dissection. Ask about changes to medications or recent introduction of new ones (especially potentially vestibulo-toxic ones such as gentamicin).

Vomiting is not a useful discriminating symptom for peripheral versus central causes, as it can occur in both

What specific questions should you ask patients presenting with “dizziness”?

Most patients with acute vertigo will describe “dizziness”.17 Ask the patient what they mean by “dizziness” to identify whether this is vertigo or an alternative symptom such as light-headedness or non-vestibular symptoms (such as headache). Identifying whether the patient is describing spinning vertigo (where they see the world move around them) or an internal sensation of movement (spinning or swaying “inside the head”) does not help differentiate between the different causes of acute vertigo. Equally, vomiting is not a useful discriminating symptom for peripheral versus central causes, as it can occur in both.

Box 3 details the differential diagnoses for acute vertigo, following recent published diagnostic algorithms that focus on history and examination findings in patients with acute vertigo (such as TiTrATE18 and STANDING19).

The focus of the history should be on associated symptoms, timing of symptoms (whether episodic, acute, or chronic), and triggering events18:

1 Timing: onset and duration
– How quickly did the symptoms start? Acute onset of persistent vertigo (within seconds) is most common with stroke, whereas in vestibular neuritis or vestibular migraine onset is over several seconds or minutes. In BPPV the onset will be acute (over seconds) but will not be persistent (typically lasting only a few seconds).

2 Has this happened before?
– Recurrent episodic vertigo is seen in BPPV, vestibular migraine, Ménière’s disease, and vestibular paroxysmia (<1 in 2000 people).
What are the key clinical signs that will help with diagnosis?

Clinical examination of a patient presenting with acute vertigo can help in differentiating central from peripheral disorders. All patients should have a neurological examination, including assessment of cranial nerves and hearing. They should also have their gait examined.

Assess gait by asking the patient to walk a few steps (if they are able to) and to tandem walk (heel to toe). Most patients with dizziness (of any cause) will report unsteadiness, but in the context of a posterior circulation stroke this is typically severe: defined as an inability to maintain upright in a sitting or standing posture even with the feet apart. Patients with central causes of acute vertigo are often unable to walk without falling, whereas patients with a peripheral vestibular lesion will be uncomfortable and reluctant to move but are still able to walk with minimal assistance. A “bedside” assessment of hearing is of particular importance because patients with vertigo may not notice a loss of hearing (given the severity of the vertigo sensation). This can be done simply by rubbing your thumb and index finger over one ear, and then the other and asking about symmetry. Patients with anterior inferior cerebellar artery infarction may have isolated recurrent vertigo, fluctuating hearing loss, and/or tinnitus (similar to Ménière’s disease) as the initial symptoms for one to 10 days before the permanent infarction.

All patients presenting with brief episodic acute vertigo or unsteadiness should undergo a Dix-Hallpike manoeuvre (see video at www.bmj.com/content/366/bmj.l5215 24 ), particularly when the standard neurological examination is otherwise normal. This is because benign paroxysmal positional vertigo—the commonest cause of episodic vertigo worldwide—can only be diagnosed with a positional manoeuvre. In BPPV there will be torsional (and up-beating) positional nystagmus on the affected side only during a Dix-Hallpike manoeuvre. The presence of vertical positional nystagmus (such as downbeat nystagmus) or prominent vomiting suggests a central cause (such as stroke or space occupying lesion).

In patients with acute and persistent vertigo (for >24 hours) and nystagmus (of any kind), a normal head impulse test (a measure of peripheral vestibular function), presence of direction-changing nystagmus (suggestive of a cerebellar pathology), skew deviation (vertical misalignment of the eyes), and abnormal bedside test of hearing (so called HINTS plus assessment), has a sensitivity of 99% and specificity of 97% for stroke.

All patients presenting with brief episodic acute vertigo or unsteadiness should undergo a Dix-Hallpike manoeuvre

Imaging and further investigations (if appropriate before referral)

Routine serological investigations are rarely of diagnostic yield in patients with acute vertigo. However, finger prick glucose levels can help to rule out hypoglycaemia, calcium levels for hypocalcaemia or hypercalcemia, and inflammatory markers (C reactive protein and erythrocyte sedimentation rate); urine dipstick may help identify infectious causes; and lying/standing blood pressure should be measured to explore the possibility of postural hypotension.

Urgent brain imaging is always indicated where acute vertigo is accompanied by other central neurological signs, such as cranial nerve signs, limb weakness, or severe acute occipital headache. Computed tomography (CT) is highly sensitive for haemorrhage but has little value in detecting the small posterior circulation infarctions that present with isolated acute vestibular syndrome (sudden onset of vertigo/dizziness or unsteadiness lasting for ≥24 hours). Where magnetic resonance imaging is less readily accessible, it should be prioritised for patients with acute vertigo and vascular risk factors.

Patients without cranial nerve or neurological limb (weakness or sensory loss) signs, normal ocular alignment (no skew deviation), normal hearing, and healthy-looking eardrums can be safely discharged. However, they should be advised to seek urgent medical advice if new neurological symptoms develop within the next 24 hours, and if vertigo symptoms persist beyond three days they should be referred to neurology for a further opinion (box 4).

Box 4 | When and why to refer

The key features of a patient’s history and examination that warrant acute referral for neurology review include:

- Presence of any central nervous system signs—Gaze-evoked direction changing nystagmus (for example, nystagmus beats to the left when patient looks left and beats to the right when patient looks right); nystagmus on upwards or downwards gaze; marked gait ataxia; broken smooth pursuit; new onset unilateral hearing loss; loss of sensation over the face or limbs; speech disturbance
- Prolonged continuous and severe vertigo for ≥24 hours with no improvement and at least one vascular risk factor (age ≥60 years, hypertension, diabetes, smoking, obesity)
- Severe nausea and vomiting accompanied by acute vertigo, unable to tolerate oral fluids
- First attack or newly suspected diagnosis of vestibular migraine

EDUCATION INTO PRACTICE

- Do you carry out a Dix-Hallpike manoeuvre in patients with brief episodes of acute vertigo or imbalance?
- Do you check hearing (finger rub) in patients with acute vertigo?

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We discussed this article with a patient who had recently experienced acute vertigo and had been assessed in both general practice and an emergency department. He highlighted the need for correct diagnosis and prompt treatment to avoid prolonged complications.
How should aerosol generating procedures be defined?

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In a healthcare setting, aerosol generating procedures (AGPs) include any medical practice or technique that enables aerosols to be transmitted from one person to another. AGPs have been described as increasing the risk of transmitting viruses that cause severe acute respiratory syndrome (SARS) and covid-19,1 2 and precautionary measures are recommended for clinicians who undertake AGPs, to minimise nosocomial infection.

Uncertainty exists over how to define an AGP, and around the levels of risk associated with various procedures.3 Practices that are frequently defined as AGPs include tracheal intubation and extubation, open airway suctioning, sputum induction, bronchoscopy, non-invasive ventilation (NIV), and manual ventilation. Those generally not considered AGPs include ventilator circuit disconnection, oral suctioning and hygiene, transoesophageal echocardiography, and chest tube insertion or removal. Nebuliser treatment, high flow nasal cannula (HFNC), and high frequency jet ventilation are sometimes listed as AGPs.

For the examples that are listed consistently as AGPs, the risk of aerosolisation may be overestimated, and focusing on risk reduction for these procedures underappreciates the risks of aerosolisation in many unlisted patient care activities. Classifying a procedure as an AGP also generates stigma, which may result in unnecessary withholding of treatment and negative impacts on patient care.

Current recommendations on personal protective equipment for healthcare workers is based on the risk of airborne transmission of a particular procedure, but this approach does not fully account for the high variability of aerosolisation in clinical settings.

What is the evidence of uncertainty?

Classification of AGPs is based largely on the reported risks of nosocomial infections during the SARS outbreak of 2003. A systematic review of five case-control studies and five retrospective cohort studies reported an increased risk of superspreading events with tracheal intubation, tracheostomy, non-invasive ventilation, and mask ventilation before tracheal intubation.4 However, tracheal suctioning, bronchoscopy, and nebuliser treatment were not found to increase nosocomial infection. The included studies have several limitations that may affect the extent to which they can be used to define and classify AGPs. First, the included studies were retrospective in nature with limited sample size, and were categorised as “very low” certainty of evidence according to the GRADE (Grading of recommendations, assessment, development, and evaluations) framework. Second, awareness of, and compliance with, appropriate infection control measures— which varied considerably between studies—might have significantly mitigated nosocomial infection. Third, no data were provided in the included studies on how aerosols were generated and dispersed, suggesting that aerosol transmission was not fully considered at the time. Recent data indicate that, during the covid-19 pandemic, the death rate of healthcare workers in general practice and psychiatry has been higher than in workers in intensive care units who routinely perform the above named high risk AGPs.5 The current approach of defining and classifying AGPs for covid-19 may have overlooked the biological plausibility of aerosol generation and dispersion of SARS-CoV-2.

Aerosol generation depends on the flow rate of air in the airway. A high flow rate initiates shear stress on the air-mucus interface in the airway and produces aerosols. By contrast, coughing and sneezing produce flow rates at least 10 times greater,4 and are therefore major sources of aerosolisation. Two studies of healthy volunteers6 7 found that coughing and shouting generated 10 to 300 times more aerosols than NIV and HFNC. In a recent observational study,8 tracheal intubation and extubation produced fewer aerosols than coughing. Overall, these investigations contradict the findings of previous epidemiological studies. As a result, classifications of AGPs vary between professional guidelines, especially in the context of covid-199 (appendix 1, see bmj.com).
In healthcare settings, aerosol generating procedures such as ventilation enable airborne pathogens to be transmitted from one person to another. To help prevent transmission, it can be helpful to understand the principles of aerosol generation and dispersion. Clinicians should assess the risks of aerosolisation from aerosol generating procedures, and adopt appropriate precautionary measures.

**Aerosol generation**

Normal tidal breathing produces a range of respiratory particles. Airflow in the airways imposes shear stress on the mucus-air interface that leads to the formation of aerosols and droplets.

Aerosols are predominantly formed in small airways such as terminal bronchioles. Coughing and sneezing generate higher flow rates, producing an average of 3000–40 000 smaller respiratory particles.

**Environmental factors that affect dispersion**

The activities of healthcare workers upstream can reduce downstream exposure to aerosols and airborne droplets.

**Dispersion distances**

<table>
<thead>
<tr>
<th>Oxygen flow (L/min)</th>
<th>Maximum exhaled air distance (cm)</th>
<th>Maximum distance travelled by exhaled air in simulation studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-rebreathing oxygen mask</td>
<td>4-12</td>
<td>&lt;10</td>
</tr>
<tr>
<td>High flow nasal oxygen therapy</td>
<td>30-60</td>
<td>13-17</td>
</tr>
<tr>
<td>Simple oxygen mask</td>
<td>4-10</td>
<td>20-40</td>
</tr>
<tr>
<td>Venturi oxygen mask</td>
<td>24-40% oxygen</td>
<td>33-40</td>
</tr>
<tr>
<td>Nasal cannula</td>
<td>3-5</td>
<td>36-60</td>
</tr>
<tr>
<td>Jet nebuliser Normal lung</td>
<td>Driven by air at 6 L/min</td>
<td>45</td>
</tr>
<tr>
<td>Jet nebuliser Severe lung injury</td>
<td>Driven by air at 6 L/min</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Non-invasive ventilation</td>
<td>Inspiratory pressure 10-18 cmH₂O, Expiratory pressure 4 cmH₂O</td>
<td>40-95</td>
</tr>
</tbody>
</table>
Is ongoing research likely to provide relevant evidence?

We searched the clinicaltrials.gov and ISRCTN registries in March 2022 and identified 18 ongoing studies related to aerosolisation or AGPs. AERosolisation And Transmission of SARS-CoV-2 in Healthcare Settings (AERATOR) is a prospective cohort study that aims to quantify aerosol generation during and after routine dental, orthopaedic, respiratory, critical care, and ophthalmology surgeries. Three other clinical studies are evaluating the distribution of aerosolisation during nasogastric tube insertion, use of metered dose inhaler or nebuliser, and procedures related to routine oral care.

Other ongoing clinical trials are investigating the use of barrier methods such as aerosol boxes or aerosol reducing mouth guards to minimise dispersion of aerosols in various medical procedures. Additional research questions are shown in the box (right). Field studies in hospital isolation rooms and detection of viral particles in air samples by polymerase chain reaction and viral culture during respiratory treatments are of particular interest.

What should we do in the light of the uncertainty?

Given the uncertainty, and the high variability of aerosolisation in clinical settings, healthcare workers should understand the principles of aerosol generation and dispersion (infographic). They should assess the risks of aerosolisation whenever they encounter patients, and adopt appropriate precautionary measures. Frontline healthcare workers may need to undertake substantial training to achieve this. Alternatively, applying universal airborne precaution level of personal protective equipment in all patient encounters may eliminate the uncertainty, but this approach is likely to be constrained by resources.

Coughing and other forms of forced expiration can generate large quantities of aerosols, and these may be further dispersed over long distance if medical devices with a high oxygen flowrate, such as HFNC or jet nebuliser, are used concomitantly. Simulation studies estimate that exhaled air travels up to 1 metre from a patient using an oxygen mask, nasal cannula, HFNC, venturi mask, jet nebuliser, or non-rebreathing masks (infographic). High flow rate, coughing, and NIV increase dispersion in an exponential fashion, whereas a tight-fitting mask, exhalation filter, suction, or expired gas scavenging minimise dispersion. Thus, understanding dispersion characteristics may reduce exposure to respiratory particles. Simulation studies also suggest use of barriers or enclosures to block aerosol dispersion (eg, using an aerosol box during tracheal intubation). Environmental studies have suggested an association between inefficient ventilation and airborne transmission in SARS and covid-19. Negative pressure isolation rooms can dilute and remove aerosols within the room and should be considered if available.

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Recommendation for further research

- What is the relative importance of aerosol, droplet, contact, and indirect transmission modes in healthcare settings?
- What is the role and extent of airborne transmission in patient care activities or medical procedures?
- What factors determine the risk of aerosolisation during patient care activities or medical procedures?
- What is the relative importance of aerosolisation during AGPs?
- How does aerosol dispersion relate to risk of infection and how does the healthcare setting affect the risk?
- What are the settings and risk factors for superspreading events?
- How can healthcare policy address the risk of airborne transmission from activities related to patient care and medical procedures that carry risks of aerosolisation?

How Patients and Healthcare Workers Were Involved in the Creation of This Article

We sought feedback from physicians, residents, nurses, and respiratory therapists when compiling and modifying this manuscript. They made suggestions and edits to improve the clarity and illustration of the article and infographic.

How This Article Was Created

We performed a systematic search of the literature in Medline, Embase, the Cochrane CENTRAL register of controlled trials and the Cochrane Database of systematic reviews from January 2000 to April 2021. For search terms, see bmj.com
The study looked at how different durations and doses affected bacterial resistance to penicillin. It included 814 children who developed pneumonia in the community and were admitted to hospital. The children were treated at 29 hospitals in the UK and Ireland. All were older than 6 months (average age was 2.5 years) and were due to receive only amoxicillin (oral syrup) after they went home.

When children were discharged from hospital, they were randomly put into groups which received different courses of amoxicillin to take at home. They took either a low dose (35-50 mg/kg/day) or a high dose (79-90 mg/kg/day) of amoxicillin. They took the syrup for seven days (long course) or for three days (short course) with a placebo for the remaining four days. These doses and durations of treatment are commonly given to children in the UK who have been hospitalised with pneumonia.

To assess the effectiveness of each of the treatment strategies, researchers looked at whether a second antibiotic was prescribed within 28 days. Duration of symptoms and frequency of side effects/adverse events were secondary outcomes.

What did this study do?

Since 2010, most children in the UK have been vaccinated against Streptococcus pneumoniae. This has reduced the number of cases of pneumonia, but has not reduced the number of children admitted to hospital with the condition. Many are, however, discharged quickly.

The ideal dose and duration of antibiotics to treat pneumonia in children is supported by limited data. The National Institute for Health and Care Excellence recommends a five day course in children aged 1-4. The World Health Organization recommends a three day course; guidelines across Europe vary between five and 10 days.

In this study, researchers set out to explore the effectiveness and safety of three and seven day courses of amoxicillin at high and low doses in children with pneumonia.

What was this study needed?

To check for signs of penicillin resistance, the researchers collected nose and throat swabs from just over half the children. They compared swabs taken before treatment with those at day 28 and did not find signs of antibiotic resistance related to duration or dose of antibiotic.

What did it find?

The researchers found that, regardless of antibiotic dose and duration:

- Around one in eight children in each group was prescribed a second antibiotic; no difference was seen between the groups
- Most symptoms (including fever and wheeze) lasted the same length of time in all groups; the only slight difference was in cough (12 days with the short course, and 10 days with the long course)
- Adverse events (including rash, thrush, and diarrhoea) were the same in each group.
- To check for signs of penicillin resistance, the researchers collected nose and throat swabs from just over half the children. They compared swabs taken before treatment with those at day 28 and did not find signs of antibiotic resistance related to duration or dose of antibiotic.

Why is this important?

A three day course of amoxicillin was as effective as a seven day course for treating children with pneumonia. Children on the short course had a mild cough for longer than those on the long course, but the cough did not interfere with the child’s normal activities.

This finding may prompt more widespread use of short courses of antibiotics for children with pneumonia. This will reduce antibiotic usage, which is needed to help prevent antibiotic resistance.

The low dose was as effective as the high dose. But the researchers caution that the effective dose depends on whether bacteria are resistant to antibiotics. This finding might be more difficult to implement in practice, especially in countries which have higher levels of antibiotic resistance than in the UK.

What's next?

The researchers hope their findings will guide prescribing advice in the UK and lead to routine use of the short course. Many children do not like taking antibiotics; both parents and children may welcome the short course.

This study did not find an increase in pneumococci resistant to penicillins in the nose and throat. The researchers caution that resistant bacteria may have been developing elsewhere in the body. Other bacteria (not examined in this study) could have developed resistance. The researchers are carrying out laboratory studies to explore the impact of amoxicillin dose and duration on the development of resistance in other bacteria.
A 31-year-old man presented to his family doctor with a one-year history of painful swelling of his left second toe. The swelling was persistent, did not improve with rest or leg elevation, and was exacerbated by prolonged walking and working. The pain was worse at night. He thought the symptoms were related to tight footwear. There was no history of preceding trauma or fever.

On clinical examination, the patient was afebrile. The proximal aspect of his second toe was swollen and tender (fig 1). No definite mass was palpated, and the passive motion of the proximal interphalangeal joint was similar to that of the contralateral toe, with pain at the end range of flexion and extension of the joint. The patient’s erythrocyte sedimentation rate, C-reactive protein (CRP), and white cell count were all within the normal ranges. Radiography showed a radiolucent lesion in the plantar cortex of the neck of the proximal phalanx (fig 2).

1 What are the differential diagnoses for a painful swollen toe with a lytic lesion at the phalangeal cortex?
2 What further investigations are required?
3 What is the diagnosis?

Submitted by Tun Hing Lui, Wing Nin Raphael Lo, Hi Shan Sally Cheng, and Xiaohua Pan
Patient consent obtained.

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CASE REVIEW
A painful swollen toe

1 What are the differential diagnoses for a painful swollen toe with a lytic lesion at the phalangeal cortex?
Common differentials include osteoid osteoma, Brodie abscess (an intraosseous abscess as a form of subacute osteomyelitis with predilection for metaphysis of tubular bone), enchondroma, and simple bone cysts. Other differentials include Langerhans cell histiocytosis, eosinophilic granuloma, tuberculosis, chondrosarcoma or intraosseous glomus tumour.

2 What further investigations are required?
Osteoid osteoma can mimic subacute osteomyelitis in clinical presentation and radiographic appearances. The absence of osteosclerosis surrounding the lytic lesion cannot exclude osteoid osteoma. Osteoid osteoma does not cause any significant rise in CRP value. However, the lack of systemic symptoms and normal serum inflammatory markers also cannot exclude Brodie abscess.

Magnetic resonance imaging may be useful for differentiating Brodie abscess from other lesions, especially if the “penumbra sign” (a T1-weighted hyperintense rim lining of the lytic lesion) is present. In this case, a subperiosteal lesion with adjacent bone marrow oedema and adjacent soft tissue oedema was observed. However, osteoid osteoma of the toe cannot be excluded because of local soft tissue inflammation and hypertrophy induced by high prostaglandin levels.

3 What is the diagnosis?
Osteoid osteoma of the toe. This is a benign painful osteoblastic tumour in the cortex with a lucent nidus with surrounding osteosclerosis. The nidus contains blood vessels, osteoid cells and other bone cells. In osteoid osteoma of the toe, the nidus is typically found in the subperiosteal or marrow region, and the bone sclerosis is usually not significant and may be less obvious on close comparison to the lesion. The typical clinical presentation includes worsening pain at night and improvement with non-steroidal medication.

LEARNING POINTS
• In young adults with painful swollen toes and no history of trauma, chronic infection should be considered.
• Delayed diagnosis is common for osteoid osteoma of the toe because of local soft tissue inflammation and hypertrophy induced by high prostaglandin levels.

LEARNING MODULE
You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

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MINERVA

A corn-like lesion
This is a primary nodular melanoma on the heel of a Chinese man in his 50s. The patient presented with a six month history of a cutaneous lesion on his heel that had continued to enlarge despite treatment with antibiotic ointment and two rounds of cryotherapy. On examination a hard nodule with central ulceration was observed. Although the presumed diagnosis was verruca vulgaris (a “corn”), lack of response to treatment prompted excisional biopsy, which indicated malignant melanoma. Acral lentiginous melanoma is the most common type of melanoma in the Asian population, but further extensive surgical excision and immunohistochemical staining confirmed that the tumour was primary nodular melanoma, with no involvement of lymph nodes and no evidence of metastasis. Among the four major histological subtypes of cutaneous melanoma, nodular melanoma is characterised by rapid growth rate. Although it accounts for 14% of all melanomas, nodular melanoma is responsible for more than 40% of melanoma related deaths. Nodular melanoma should be considered in patients with a history of symmetrical, firm and rapidly enlarging pink or variegated nodules for more than one month. Clinical features of this rare but important invasive malignancy can appear similar to verruca vulgaris, but lesions will continue to increase in size despite treatment with destructive methods such as laser therapy and liquid nitrogen.

If you would like to write a Minerva picture case, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

Kidney stones
In a case series of more than 40,000 people with primary hyperparathyroidism, the cumulative incidence of recurrent kidney stones was over 30% among people treated surgically. For comparison, the incidence was only 18% in those managed medically. However, it’s hard to draw useful conclusions about the value of parathyroidectomy from these data because people treated surgically had higher rates of stone formation before treatment and higher serum calcium concentrations (J Clin Endocrinol Metab doi:10.1210/clinem/dgac193).

Nightingale diagrams
When time series data are plotted with the time variable along the x axis, seasonal variation can be hard to spot. Florence Nightingale invented a radial plot to get around this problem and to draw attention to the fact that, during the winters of the Crimean war, deaths from disease among British soldiers far outnumbered deaths inflicted by the enemy (www.sciencemag.org/article/how-florence-nightingale-changed-data-visualization-forever/). A similar chart of weekly deaths in England and Wales shows the impact of Covid-19 on deaths in April and May 2020 and in the winter of 2021 compared with deaths in the same periods in previous years (www.cebm.net/covid-19/covid-19-florence-nightingales-daigrams-for-deaths/).

Art improves life
Virtual visits to an art gallery improve the quality of life for older people, according to a trial from Canada. Among 100 participants, all over 65, those randomised to weekly online guided tours of the Montreal Museum of Fine Arts showed improved scores for social isolation, wellbeing, quality of life, and frailty when compared with controls who didn’t participate in cultural activities (Front Med doi:10.3389/fmed.2022.969122/full).

Dealing with difficult patients
All doctors have had to deal with patients who behave in challenging ways. Minerva enjoyed a thoughtful essay pointing out that the real challenge is to respond in a way that will remedy the situation rather than making it worse. Demanding behaviour is often a result of previous medical encounters that haven’t gone well. When doctors recognise that patients have legitimate reasons for their behaviour, progress is possible (Postgrad Med J doi:10.1136/postgradmedj-2022-141976).

Depressive symptoms before and after stroke
Data from 11,000 participants in the English Longitudinal Study of Ageing show, perhaps not surprisingly, that depressive symptoms are common in survivors of stroke and that they persist for several years. More surprisingly, and less easily explained, depressive symptoms were also increased before the acute event (Neurology doi:10.1212/WNL.00000000000200756).

Cardiorespiratory fitness
Regardless of age, sex, and race, people with better cardiorespiratory fitness are less likely to die. Among 750,000 US veterans whose fitness was measured with an exercise treadmill test, all cause mortality was inversely related to fitness during 10 years of follow-up. The effect was large. Those in the bottom 20% of fitness were four times more likely to die than those in the top 2% (J Am Coll Cardiol doi:10.1016/j.jacc.2022.05.031).

What’s in a name?
Calling a dog a cat won’t stop it barking. Surely the World Health Organization has more useful things to do than rename monkeypox? Admittedly, monkeypox is not a good name. The virus’s natural host is small mammals, not monkeys. On the other hand, chickenpox, which has nothing to do with chickens and isn’t caused by a pox virus, isn’t a good name either and nobody feels the need to change that label (www.theatlantic.com/health/archive/2022/08/who-monkeypox-name-change/671162/).