education

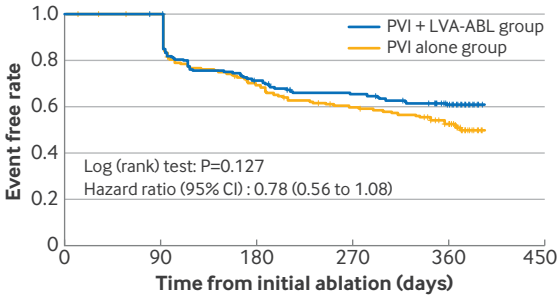
RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Metformin for knee osteoarthritis

Metformin was tested in the 1940s as a treatment for malaria, well before it became a mainstay of type 2 diabetes management. It's since been investigated for its effect on weight, fertility, various cancers, and more recently to prevent long covid. A new randomised controlled trial suggests it could be useful as a treatment to reduce pain in people with knee osteoarthritis.

The study recruited 107 people with non-severe but chronic pain caused by knee osteoarthritis and allocated them to receive metformin or placebo. In patients with knee osteoarthritis and overweight or obesity, metformin, 2000 mg/d, for 6 months had a moderate and statistically significant effect on knee pain reduction compared with placebo. The study has various limitations, including high rates of loss to follow-up and uncertainty over adherence, but further studies seem to be warranted: pain scores in the metformin group more than halved at six months (from 60.2 mm to 28.8 mm on a visual analogue scale, compared with a fall from 58.5 mm to 39.6 mm in the placebo group).

JAMA doi:10.1001/jama.2025.3471



Kaplan–Meier graph showing the primary endpoint of atrial fibrillation or atrial tachycardia recurrence-free rates after the initial ablation without antiarrhythmic drug use

MASUDA M, ET AL. NAT MED 2025 DOI:10.1038/S41591-025-03674-Y

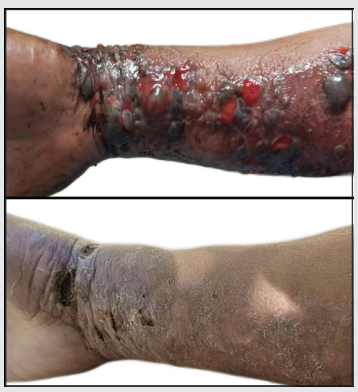
Current resistance to low voltage areas

The search for improved success rates from ablation for atrial fibrillation continues. Outcomes from studies where low voltage areas (LVAs) of myocardium are identified and ablated in addition to pulmonary vein isolation (PVI) have been mixed. A new trial randomised only people with atrial fibrillation and LVAs. Although those who had PVI and LVA ablation had higher rates of freedom from atrial fibrillation or atrial tachycardia recurrence without antiarrhythmic drug use after a year (figure), the difference was not statistically significant.

Nat Med doi:10.1038/s41591-025-03674-y

Lorundrostat for uncontrolled hypertension

There's certainly a gap in the market for an effective third or fourth line antihypertensive. A trial of lorundrostat, an aldosterone synthase inhibitor, found a placebo adjusted reduction in systolic blood pressure of 7.9 mm Hg (97.5% confidence interval −13.3 to −2.6) in people with a blood pressure above target despite being prescribed two to five antihypertensives. A complicated run-in period, however, makes it difficult to know how well these findings would apply to practice. Of the 926 participants initially enrolled, 641 people were excluded before randomisation: for 337 of them, their blood pressure fell below target after being switched to a standardised anti-hypertensive regimen, 112 were unwilling to comply with the trial



CLINICAL PICTURE

Rapidly progressive ulcerated and pruritic rash on the upper limb

This man in his early 40s from rural China presented to the emergency department with a six day history of an oedematous, ulcerated, and pruritic rash on his right upper limb, extending progressively from his wrist towards his elbow (figure, top). He had no medical history but, three days before the onset of his symptoms, he had assisted a neighbour in carrying a dead cow. He had no fever, shortness of breath, or evidence of systemic disease. Laboratory results showed neutrophilic leucocytosis. Polymerase chain reaction testing of vesicular fluid confirmed cutaneous anthrax.

Bacillus anthracis is a zoonotic pathogen endemic in livestock-raising regions across Eurasia, Africa, and North America. Cutaneous anthrax is the most common presentation in humans and should be suspected in patients with a black, depressed eschar, surrounding

procedures and visits, 58 were excluded because of "physician decision," and 134 for unspecified "other" reasons.

N Engl J Med doi:10.1056/NEJMoa2501440

The MASH report

Hepatologists have been trying for decades to get the rest of us to be interested in steatohepatitis. In case you missed it (I did), NAFLD and NASH were rebranded as MASLD and MASH in 2023. MASH—metabolic dysfunction–associated steatohepatitis—may be about to cut through into the mainstream thanks to a positive study for the effect of SGLT-2 inhibitor semaglutide. The multicentre trial recruited 1197 people with MASH and fibrosis stage 2 or 3 on liver biopsy and found resolution of steatohepatitis without worsening of fibrosis occurred in 62.9% of participants randomised to semaglutide after 72 weeks compared with 34.3% in the placebo group.

N Engl J Med doi:10.1056/NEJMoa2413258

Treatment for hand eczema

DELTA FORCE has landed—a study ofdelgocitinib cream in people with severe chronic hand eczema. It found that the JAK (janus kinase) inhibitor was slightly more effective than the oral retinoid alitretinoin and was associated with fewer side effects (headache, nasopharyngitis, and nausea).

Over six months, 86% of participants in the study completed the course of delgocitinib (compared with 59% of the alitretinoin group).

Lancet doi:10.1016/S0140-6736(25)00001-7

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oedema, and a history of potential exposure such as contact with infected animals or contaminated animal products. Contact tracing should be undertaken and post-exposure prophylaxis offered. This patient was treated with intravenous ciprofloxacin and oral linezolid for 10 days, with a good clinical response (figure, bottom).

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Patient consent obtained.

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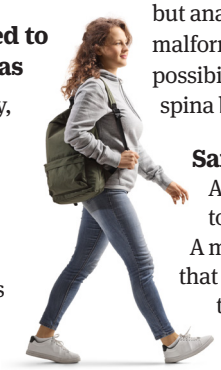
MINERVA From the wider world of research

Mitochondria movement

Mitochondria have their own genome and it's thought that they evolved from free-living bacteria engulfed by eukaryotic cells. Far from being static, these intracellular organelles have recently been observed to move between cells, possibly as an adaptation to rescue compromised tissue (*Nature* doi:10.1038/d41586-025-01064-5). Whether there are any implications for human health isn't yet clear.

Walking speed linked to cardiac arrdhythmias



People who walk briskly, whether by self report or as measured by accelerometry, are less likely to experience cardiac arrhythmias according to an analysis from UK Biobank. Among 400 000 participants followed over 14 years, arrhythmias, most commonly atrial fibrillation, were 30% less frequent in brisk walkers than in those who walked slowly (*Heart* doi:10.1136/heartjnl-2024-325004).

Food additives and type 2 diabetes

A large longitudinal study of nutrition in France grouped the myriad chemicals used as food additives into five categories (*Plos Med* doi:10.1371/journal.pmed.1004570). Over eight years of follow-up, two of these five categories showed weak associations with the incidence of type 2 diabetes. One category was dominated by emulsifiers such as pectin and guar gum. The other consisted of additives found in artificially sweetened beverages and sugary drinks.

First trimester exposure to macrolides

Pregnant women who need antibiotics are sometimes prescribed macrolides. Findings from a registry study, also from France, are fairly reassuring about the lack of risk to the fetus (*Plos Med* doi:10.1371/journal.pmed.1004576). Outcomes in 140 000 women exposed to macrolides during the first trimester were compared with those of 600 000 women exposed to amoxicillin. Overall, there were no differences in rates of major congenital malformations but analysis of individual malformations raised the possibility of a small increase in spina bifida and syndactyly.

Sarcopenia

As people get older they tend to lose lean muscle mass. A multinational trial reports that it's difficult to influence this trend (*J Am Geriatr Soc* doi:10.1111/jgs.19266). Two thousand healthy, physically active older adults were randomised to daily supplemental vitamin D, omega 3 fatty acid supplements, and a thrice weekly home exercise programme, either alone or in combination. Measured by dual energy x ray absorptiometry after three years treatment, none of these interventions improved muscle mass or influenced the incidence of sarcopenia.

The replication crisis

The Brazilian Reproducibility Initiative tackled the replication crisis head on (*bioRxiv* https://www.biorxiv.org/content/10.1101/2025.04.02.645026v2). Fifty six laboratories collaborated in attempts to replicate the findings of more than 150 experiments reported in biomedical papers. Judged by the criterion of having statistically significant results in the same direction as the original paper, less than half could be replicated. Effect sizes were an average of 60% larger in the original papers than in the replication attempts.

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CHOOSING WISELY

Enteral tube feeding in people with advanced dementia

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This article is part of a series of Education articles based on recommendations from international Choosing Wisely campaigns. The BMJ thanks Wendy Levinson and Karen Born at Choosing Wisely for valuable advice and supporting the selection of topics. Choosing Wisely had no input into the peer review process or editorial decision.

0.5 HOURS

Dementia is a chronic, progressive, and irreversible disease affecting cognition, behaviour, and function. Alzheimer's disease, vascular dementia, and mixed dementia (Alzheimer's and vascular pathology) constitute most cases. Worldwide, more than 57 million people are living with dementia, and this number is expected to increase to more than 152 million in 2050.[1] The regions projected to have the highest percentage increases in dementia cases are north Africa, the Middle East, and eastern sub-Saharan Africa.[1] A recent meta-analysis found that mean survival time from onset of Alzheimer's disease was 7.6 years, and this was shorter for people with non-Alzheimer's dementia (6.5 years for vascular dementia and 6.8 years for dementia with Lewy bodies).[2] While there is heterogeneity in disease progression, people dying from dementia typically experience a prolonged advanced stage.[3 4] Many people with advanced dementia experience burdensome symptoms and poor quality of life, and many of their family caregivers experience substantial caregiver strain, including physical, psychological, emotional, behavioural, and financial stress.[4-6]

Difficulty eating is a common complication of advanced dementia and can manifest as dysphagia, the inability to feed oneself, and the refusal to eat.[4 7] Many professional society guidelines advise against recommending enteral feeding tubes in patients with advanced dementia and instead suggest oral feeding (see box).[8-19]

WHAT YOU NEED TO KNOW

- Difficulty eating is a common complication of advanced dementia. Choosing Wisely lists and professional society guidelines recommend against insertion of enteral feeding tubes
- Early discussions about prognosis, shared decision making, and advance care planning that anticipates feeding difficulties may improve care in advanced dementia
- Rates of enteral tube feeding in advanced dementia have declined in the UK, Europe, US, and Canada
- A palliative approach to feeding problems in advanced dementia can promote goal concordant care

Nasogastric tube feeding involves passing a flexible, fine-bore, radio-opaque tube into the stomach via the nose.[20] Nasogastric tubes are intended to provide temporary enteral nutrition for no more than 4-6 weeks.[21] Percutaneous endoscopic gastrostomy (PEG) tube feeding involves insertion of a feeding tube through the abdominal skin into the lumen of the stomach, and can be inserted by either an endoscopic or interventional radiology approach.[21 22] Assisted oral feeding involves offering regular reminders to swallow, prompting multiple swallows for each mouthful, encouraging soft coughs after each swallow, decreasing bolus size, and judicious use of thickeners (where appropriate).[23-25]

Here we discuss why enteral tube feeding is not recommended and consider some of the barriers to reducing it. Much of the existing evidence related to enteral tube feeding in advanced dementia mixes nasogastric and PEG tube feeding. As such, where evidence relates to both nasogastric and PEG tube feeding this is described as enteral tube feeding. If evidence is limited to either nasogastric or PEG tube feeding, then those terms are explicitly used.

The evidence for change

Outcomes and safety of enteral tube feeding in advanced dementia

A 2021 Cochrane Review assessed the safety and effectiveness of enteral tube feeding for advanced dementia including 14 controlled, non-randomised studies.[26] Enteral tube feeding was defined as the administration of food via a nasogastric tube, PEG tube, or jejunal post-pyloric feeding.[26] Although the certainty of evidence was low, the review found that enteral tube feeding did not substantially lengthen survival compared with standard care. There was no available evidence for any type of enteral feeding about the impact on quality of life, pain, nutrition, family or caregiver outcomes, or behavioural and psychological symptoms of dementia. The systematic review found some evidence of harm: a narrative synthesis found very low certainty evidence that enteral tube feeding was associated with an increased risk of pressure ulcers, and the balance of evidence suggested an increased risk of pneumonia.

Other reported complications of enteral tube feeding in advanced dementia include agitation, greater use of

International Choosing Wisely statements on enteral feeding tubes and advanced dementia

- Choosing Wisely Canada (last updated November 2022)[8]
  "Don't recommend percutaneous feeding tubes in patients with advanced dementia; instead offer oral feeding"
- Choosing Wisely and the American Geriatrics Society (last updated April 2015)[9]
  "Don't recommend percutaneous feeding tubes in patients with advanced dementia; instead offer oral assisted feeding"
- Choosing Wisely Germany (last updated October 2016)[10]
  "In patients with advanced dementia, nutrition should not be provided through a percutaneous endoscopic gastrostomy (PEG)"*
- Choosing Wisely Austria (last updated November 2018)[11]
  "Compared to support with eating, gastric tubes have no advantage for people with dementia, but they sometimes pose serious health risks"*
- Choosing Wisely Italy (last updated February 2022)[12]
  "Do not prescribe enteral artificial nutrition (PEG, percutaneous endoscopic gastrostomy, or nasogastric tube) to patients with advanced dementia, but instead favour manually assisted physiological feeding"*
- Choosing Wisely Switzerland (last updated June 2017)[13]
  "Do not recommend a percutaneous gastric tube in patients with advanced dementia; offer assisted oral feeding instead"*

*Translated to English

physical and chemical restraints, worsening urinary and faecal incontinence, intra-abdominal abscesses, refeeding syndrome, and increased use of acute care services (such as emergency department visits).[17]

Global trends in the use of enteral tube feeding

Choosing Wisely statements from multiple countries along with professional society guidelines recommend against insertion of enteral feeding tubes, and instead recommend offering oral assisted feeding.[8 9 14-17] Increased awareness of the harms of enteral tube feeding has developed alongside practice changes, decreasing the use of feeding tubes in patients with advanced dementia in the US, Canada, Europe, and UK.[27-30] In particular, between 2000 and 2014, the incidence of enteral feeding tube insertions among US nursing home residents with advanced dementia decreased by approximately 50% (from 11.7% to 5.7% of residents).[27] In Canada, the annual prevalence of enteral tube feeding among nursing home residents with advanced dementia decreased from 3.5% in 2006 to 1.7% in 2022.[28] Conversely, trends of enteral tube feeding use in patients with advanced dementia remain largely stable in other countries including Israel, Japan, and Taiwan.[31-34]

Even in countries where rates have decreased, there are still persistent differences in rates of enteral tube feeding. In the US, an observational study between 2000 and 2014 of more than 70 000 nursing home residents with advanced dementia found that African-American residents were consistently more than five times more likely than white residents to receive tube feeding.[27] Further, there is marked geographical and socioeconomic variation in enteral tube feeding in US nursing homes, with homes located in urban versus rural areas, and those in poorer regions having higher rates.[35 36] In Canada, there is a higher prevalence of enteral feeding tubes among non-English speaking and non-French speaking nursing home residents with advanced dementia.[28]

A palliative approach to dementia care has the potential to address differences in quality of care, including the use of enteral tube feeding

Barriers to change

Clinical barriers

In the advanced stages of dementia, the patient's best interest may be increasingly served by prioritising comfort, which often aligns with the patient's and caregiver's goals of care. A randomised controlled trial of US nursing home residents living with dementia found that comfort is the primary goal of care for most (67%), with only 7% wanting life prolonging care, and the remaining 26% opting for basic medical care only (treatment including antibiotics, parenteral therapy, and hospitalisation, but not cardiopulmonary resuscitation, intubation, enteral tube feeding, or intensive care).[38-40] Despite this, many people living with advanced dementia receive measures aimed at prolonging life towards the end of life—including enteral tube feeding—which may not improve comfort, and are often distressing to both patients and caregivers.[4 7 41]

Given the often protracted and gradual decline associated with dementia, family members commonly do not realise that dementia is a terminal illness, and, further, healthcare professionals often find it challenging to identify the final phase of the disease and consider dementia as a "cause" of death.[42 43] Clinicians may also be challenged by the fact that prognosis in dementia can be unpredictable, and the trajectory of the disease can vary.[43 44] In the case of feeding difficulties, a US cohort study of nursing home residents with advanced dementia who developed an eating problem had a 38.6% mortality after six months even after adjusting for age, sex, and disease duration.[7]

Non-clinical barriers

Financial and administrative incentives within many healthcare systems are not well aligned with the scientific evidence against enteral tube feeding in advanced dementia. The relative ease and availability of PEG procedures in hospital settings, particularly in high income settings, time constraints for discussion and education of substitute decision-makers, and fear of litigation may contribute to clinicians offering enteral tube feeding.[43 48 49]

How should we change our practice?

Promoting a palliative approach to feeding problems in advanced dementia

A palliative approach to dementia care, especially in the advanced stages, has the potential to address differences in quality of care, including the use of enteral tube feeding.[51]

A Cochrane review on the impact of palliative care interventions in advanced dementia found that

WHAT HEALTHCARE PROFESSIONALS NEED TO KNOW

- Eating can be an emotive issue for family caregivers, who may have concerns about starvation. They may see an enteral feeding tube as the way to ensure this does not happen.
- Time must be taken at the earlier stages of dementia to have a conversation with the patient and family explaining the course of dementia and that eating difficulties may arise, particularly in the advanced stage of the condition. The risks of enteral feeding should be explained.

advance care planning interventions increased the documentation of advance directives (including orders for no enteral tube feeding) and discussions of goals of care, which may increase provision of goal-concordant care. The same review suggested that changes to the organisation and delivery of care for people with advanced dementia may lead to improvements in comfort in dying (including reduced rates of enteral tube feeding, both percutaneous and nasogastric). However, overall, the evidence was limited in quantity and certainty.[44]

This uncertainty of evidence, however, does not mean that palliative interventions, including advance care planning, do not improve care for patients with advanced dementia.[52]

Recognising the need for palliative care and the limitations of existing evidence, consensus-based methodology has been used to define optimal palliative care for people with dementia.[37] This includes practising shared decision making to allow patients and caregivers to clarify the clinical situation and:

- Set goals of care and engage in advance care planning[4] that anticipates feeding problems
- Start early and actively involve patients while they are capable of expressing their values and goals[37 50 53]
- Designate a substitute or surrogate decision maker in anticipation of the person with dementia losing capacity
- Encourage regular review of goals and update the plan throughout the disease course; consider using structured communication tools such as the Serious Illness Conversation Guide and the Conversation Project from the Institute for Healthcare Improvement[54 55]
- Align treatment options (enteral tube versus careful oral assisted feeding) with preferred level or goal of care.

If patients and their caregivers do not accept the recommendation for oral feeding, treatment discussions should be guided by the goals of care, and patients, substitute decision-makers and providers, including

Set goals of care and engage in advance care planning that anticipates feeding problems

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

JT, a coauthor on this article, is a family caregiver and patient advocate focusing on the care of frail older adults. For six years, she was a public member of the British Columbia Polypharmacy Risk Reduction Initiative and an honorary lecturer for the Department of Family Practice in the Faculty of Medicine at the University of British Columbia. She teaches as a guest lecturer for the PharmD programme at the University of British Columbia. She is a member of the Oversight Committee for the Therapeutics Initiative and is on the Executive Committee of the Canadian Medication Appropriateness and Deprescribing Network (CADeN). She was involved at every stage of writing, drafted the section on patient perspectives, and provided critical review of all manuscript sections.

EDUCATION INTO PRACTICE

- When might you begin discussions about feeding difficulties with patients who have a diagnosis of dementia?
- What information would you provide to patients and family caregivers and how might you arrive at a treatment decision?

members of the multidisciplinary healthcare team (such as dietitians and speech language pathologists), should contribute to the decision making.[4] Decision aid tools can support substitute decision-makers by increasing knowledge of feeding options and by reducing decisional conflict.[56]

Steps include:

- Clarifying the clinical situation and education about advanced dementia and feeding problems
- Establishing the preferred level or goal of care (comprehensive comfort *v* life-prolonging *v* basic medical care only) based on patient preferences and any available advance care planning
- Aligning treatment options (enteral tube *v* careful oral assisted feeding) with preferred level or goal of care.

Education for healthcare providers

Healthcare providers may benefit from more education and support.[57] A 2017 survey of internal medicine physicians across seven New York hospitals reported that 38% were unsure of what the American Board of Internal Medicine/American Geriatrics Society Choosing Wisely recommendations advised on this topic.[48] All members of healthcare teams need to understand the terminal nature and limited life expectancy of advanced dementia as well as the management of feeding problems, including relevant guidelines that recommend against enteral tube feeding.[37 50]

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EDITORIAL

Harms of enteral tube feeding

Multiple complexities in decision making require a careful approach

Eating and drinking are core aspects of human experience and more than just the intake of fluid and calories, bringing social interaction, enjoyment and expression of individuality, and social and cultural values.[1] Difficulties with food and fluid intake can occur through all stages of dementia and are often more problematic in the advanced stages.[2]

Enteral tube feeding, including nasogastric tube and percutaneous endoscopic gastrostomy (PEG) tube feeding, was initially viewed as an intervention to provide nutritional support for those with dementia who were experiencing difficulties with eating and drinking and were unable to take in sufficient food or fluids orally. Not providing nutrition might be perceived as an indicator of neglect— allowing someone to "starve to death."[3] Increasingly though, research has shown enteral tube feeding has minimal or lack of benefit, no evidence of increased survival, and a higher risk of harm, including development of pressure ulcers and aspiration.[4] This is reflected in clinical practice where better understanding has led to a decline in the use of enteral tube feeding in the United Kingdom and United States.[5,6]

The linked article from Stall and colleagues (p 210)[7] provides updates on the use of enteral tube feeding in people with dementia, highlighting lack of evidence that enteral tube feeding improves outcomes, including mortality, survival, and quality of life.[4]

In the UK the National Institute for Health and Care Excellence, British Medical Association, and General Medical Council do not recommend tube feeding for people with severe dementia[8,9] when eating problems are due to disease progression. Current guidance focuses on comfort feeding, or "at risk" feeding, which involves careful hand feeding with food the individual takes pleasure from, acknowledging the risk the person may aspirate. This is supported by guidance from the European Society for Clinical Nutrition and Metabolism.[2]

Clinicians may feel unease witholding enteral feeding fearing they are not taking action

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In the UK, many decisions around managing eating and drinking problems in people with dementia take place in acute hospitals after an unplanned emergency admission.[10] Optimal care is led by multidisciplinary teams, but, understandably, some clinicians may still feel unease about not initiating enteral feeding. This might stem from concerns about not doing something[11] and uncertainty around how long a patient may live, whether feeding might prolong life or improve quality of life, or how families will respond.[12-15] However, more evidence and better awareness is leading to a decline in use of tube feeding.[4-16] The UK's multidisciplinary and Comprehensive Geriatric Assessment approach is particularly valuable in bringing together healthcare teams with families and carers.

Complexities of decision making

A key clinical dilemma in the acute hospital setting is whether the cause is reversible or related to the progression of dementia.[2-18] Potentially reversible or temporary causes include infection and constipation, which must be dealt with before considering enteral feeding. Stall and colleagues' article[7] does not discuss that, in carefully selected cases, such as after severe traumatic injury, temporary feeding using a nasogastric tube could provide interim support.[8,9]

Stall and colleagues highlight the need for a palliative care approach, which includes regular review of an individual's goals of care and communication through advance care planning.[19,20] Although this is considered good practice in the UK,[8] implementation varies by case and locality, partly because of a limited evidence base and available resources.[21] Considerations such as staff training, availability of speech and language therapy, feeding risk policies, and capacity for shared decision making can vary substantially, which is not explored in the article. Furthermore, in the UK, not everyone with dementia has an advance care plan or wants to discuss future care—it is estimated that over a quarter of patients more generally do not have a care plan,[22] resulting in critical decisions being made in real time without documented wishes.[23]

Given the complexity of decision making for people with advanced dementia, UK based resources have been developed to support professionals and family in managing nutrition and hydration. These include a clinical decision guide,[24] a framework to streamline end-of-life decision making for professionals,[25] and targeted materials for families.[26,27] Given the inherent difficulties in managing nutrition during advanced dementia, these tools offer invaluable practical guidance. We need to start collecting accurate information on the use of enteral tube feeding in people with dementia across all settings and countries to help improve our understanding of the clinical landscape and where we need to target support.

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PRACTICE POINTER

Assessment and investigation of thunderclap headache

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CPD READING

0.5 HOURS

A 63 year old man presents to the emergency department with severe, sudden onset headache eight hours before arrival. He appears uncomfortable but is alert and oriented. His blood pressure is 165/110 mm Hg, otherwise his vital signs are normal. He has a history of depression, for which he takes escitalopram.

Undifferentiated headache is one of the most common neurological symptoms presenting to primary care and emergency departments worldwide.[1 2] Headache represents 1-4% of all emergency department presentations and thunderclap headache accounts for about 14% of those cases, according to a multinational observational study performed across high and middle income countries.[3]

Thunderclap headache refers to severe headache of sudden onset. Whereas some studies define sudden onset as reaching maximum intensity immediately, within one minute or less, and lasting for five minutes or longer, studies investigating diagnoses associated with increased risk of acute morbidity and/or mortality, related to an acute headache, have tended to use a time of up to one hour until maximum intensity.[4-7] As such, we believe that the assessment of patients suspected of having a thunderclap headache should not be limited to those whose maximum intensity peaks within one minute, but rather up to one hour.

In this article, we provide guidance on the assessment of adult patients presenting with thunderclap headache, including of the most common dangerous causes, and a targeted approach to investigations.

WHAT YOU NEED TO KNOW

- Thunderclap headache is associated with high risk aetiologies, such as subarachnoid haemorrhage and intracranial haemorrhage
- Delayed diagnosis is associated with worse clinical outcomes
- The Ottawa subarachnoid haemorrhage rule has a high sensitivity and low specificity. It can help identify patients who are at low risk for non-traumatic subarachnoid haemorrhage and reduce unnecessary investigations
- Early imaging (non-contrast CT (computed tomography) within 6 hours) and, if necessary, lumbar puncture, are first line diagnostic investigations
- CT angiography for subarachnoid haemorrhage can identify vascular causes of thunderclap headache and could be an alternative to lumbar puncture in select cases

What are the differential diagnoses to consider?

Dangerous causes of thunderclap headache require timely diagnosis and intervention. These include subarachnoid haemorrhage, intracranial haemorrhage, acute ischaemic stroke, intracranial or extracranial arterial dissection, reversible cerebral vasoconstriction syndrome, meningitis, and acute angle closure glaucoma.[8] In the table (see bmj.com), we provide a comprehensive list of differential diagnoses and recommended investigations; however, we could not identify estimates of the proportion of thunderclap headaches that correspond to each diagnosis.

Although the International Headache Society recognises an entity known as primary thunderclap headache, where no underlying cause is identified, this is not a diagnosis that is usually made in the acute setting, even when using specialist investigations and imaging.[7] A diagnosis of primary thunderclap headache should be considered only when all other causes have been demonstrably excluded.

Subarachnoid haemorrhage

Subarachnoid haemorrhage occurs when there is bleeding into the subarachnoid space, which is normally filled with cerebrospinal fluid. Non-traumatic subarachnoid haemorrhage is most often caused by the rupture of a cerebral aneurysm, but it can also result from arteriovenous malformations, and other vascular abnormalities.[9]

One meta-analysis and systematic review of 20 population based cohort studies published between 2000 and 2017 found a mortality of 34-38% in patients who had subarachnoid haemorrhage, along with a high risk of disability among survivors, with only 39-51% of survivors recovering to be functionally independent at 12 months.[29 30] A single centre retrospective study found that patients with aneurysmal subarachnoid haemorrhage were at higher risk of death in hospital compared with non-traumatic non-aneurysmal subarachnoid haemorrhage (16.8% *v* 1%, respectively).[31]

Consider a diagnosis of subarachnoid haemorrhage in patients who present with thunderclap headache. About 40-50% of subarachnoid haemorrhage patients are alert and oriented at presentation with only a severe headache and no other symptoms or neurological abnormalities.[32] Ask patients about high risk features, including onset of headache during exertion, subjective neck pain or stiffness, and/or witnessed loss of consciousness.[33] However, be aware that 4-8% of patients with subarachnoid

thebmj Visual summary

Thunderclap headache

Initial assessment and investigation

This graphic presents a proposed algorithm for diagnosis of subarachnoid haemorrhage. It can be applied to patients with sudden onset headache reaching peak intensity immediately, but also to patients presenting with headaches reaching peak intensity within one hour. The priority for clinicians in the acute management of thunderclap headache is to consider and investigate for potentially dangerous diagnoses appropriately. Further details about differential diagnoses can be found in the full article by Hans Rosenberg and co-authors in *The BMJ*.

Patient with suspected thunderclap headache

Presents with severe, sudden onset headache

History and physical exam

Timing · Severity · Quality

Ottawa subarachnoid haemorrhage rule

Patients with thunderclap headache require further investigation if any of the following six criteria are met:

- Symptoms of neck pain or stiffness
- Onset during exertion
- Peak intensity immediately
- ≥40 years old
- Witnessed loss of consciousness
- Limited neck flexion on exam

Apply Ottawa subarachnoid haemorrhage rule

Positive

Negative

Non-contrast CT (computed tomography) head

Laboratory tests

- Full blood count
- Electrolytes
- Creatinine
- Coagulation studies, if applicable

Negative CT head

Headache duration:
>6 hours
<1 week
OR
Haemoglobin: <100 g/L

Headache duration:
≤6 hours
AND
Haemoglobin:
≥100 g/L

Subarachnoid haemorrhage still suspected

Subarachnoid haemorrhage on CT

Lumbar puncture

CT angiogram head and neck

Red blood cell count: >0.002 x 10^{12}/L

Xanthochromia

Neither

Consider alternative diagnosis

CT angiogram shows aneurysm?

Yes

No

Aneurysmal subarachnoid haemorrhage

Non-aneurysmal subarachnoid haemorrhage

Did the patient have xanthochromia?

Yes

No

Likely traumatic initial lumbar puncture

Consider alternative diagnosis

Alternative diagnoses

May be determined before or during investigations for subarachnoid haemorrhage, or may require further investigations guided by clinical assessment

- Cerebral venous sinus thrombosis
- Intracranial or extracranial arterial dissection
- Acute ischaemic stroke
- Meningitis
- Acute angle closure glaucoma
- Reversible cerebral vasoconstriction syndrome
- Intracranial haemorrhage

haemorrhage might present without headache at onset.[34 35] Additional symptoms of subarachnoid haemorrhage to assess for include focal neurological symptoms and an altered level of consciousness.

In a 2008 prospective cohort study of 401 patients with subarachnoid haemorrhage, 26% of patients were not correctly identified as having a subarachnoid haemorrhage at first contact with a doctor.[34] Furthermore, misdiagnosis was strongly associated with poorer outcomes, defined as modified Rankin scale score of 3-6.

Intracranial haemorrhage

Intracranial haemorrhage is spontaneous, non-traumatic bleeding that occurs in the brain parenchyma, and accounts for 10-20% of cerebrovascular events.[36] It is associated with a high 30 day mortality of 35-52%, with only one in five survivors expected to achieve full functional recovery at six months.[11] These patients can present with general neurological symptoms, such as headache, vomiting, seizures, altered level of consciousness, and/or focal neurological symptoms such as hemiplegia, aphasia, and ataxia.

Acute ischaemic stroke

Acute ischaemic stroke is a condition in which a sudden loss of blood flow to a region of the brain results in tissue damage and neurological deficits. According to a narrative review of 22 observational studies on headache in acute stroke, the prevalence of headache attributed to ischaemic stroke was between 7.4% and 34%, with 21-50% of these headaches being sudden onset.[37]

Acute ischaemic stroke represents the majority (65%) of acute cerebrovascular events and is typified by focal neurological symptoms such as unilateral facial palsy, unilateral upper or lower extremity weakness, aphasia, dysarthria, diplopia, and/or ataxia.[38] These neurological signs and symptoms can be seen in isolation or in combination as part of recognised stroke syndromes, depending on the size of the vascular region(s) affected.[39]

Intracranial or extracranial arterial dissection

Arterial dissection is a condition in which a tear occurs in the inner lining (intima) of an artery. When it involves the carotid or vertebral arteries, and less commonly the basilar or intracranial arteries, it can be associated with thunderclap headache in a minority of cases.[40] Additionally, it could present with associated pain involving the face and ipsilateral anterolateral neck (carotid dissection), or the occiput and posterior neck (vertebral dissection). Intracranial dissection in the distal internal carotid or distal vertebral artery is less common, but can present with sudden onset headache as well. Pain usually persists for hours or days and might precede focal neurological symptoms if the dissection flap causes thromboembolism and subsequent ischaemic stroke.[15]

Reversible cerebral vasoconstriction syndrome

Reversible cerebral vasoconstriction syndrome is characterised by a sudden thunderclap headache owing to reversible vasoconstriction of the cerebral arteries. It is an uncommon condition and rare cause of hospital admission, with one US administrative data study showing an overall hospital admission rate of 2.7 per million hospital admissions.[41] In this study, hospital admission rate was four times higher in women than in men. Unlike most of the other diagnoses listed in this article, it often presents with recurrent similar episodes of thunderclap headache over days or weeks.[7] In rare cases, it can present with acute complications such as seizure, haemorrhage, ischaemic stroke, and posterior reversible encephalopathy syndrome.[16]

Meningitis

Meningitis is an inflammation of the meninges, and can be caused by viruses, bacteria, fungi, parasites, and some non-infectious conditions. The classic triad of fever, neck stiffness, and altered level of consciousness is seen concurrently in only about 50% of patients; however, 95% have at least two of the four symptoms of headache, fever, neck stiffness, or altered mental status.[42] If an infectious cause of meningitis is suspected, investigations (such as CT head) to rule out subarachnoid haemorrhage should not delay early administration of antibiotics, antivirals, or steroids.[43]

Acute angle closure glaucoma

Acute angle closure glaucoma is an ophthalmological emergency in which the fluid drainage system of the anterior eye, formed by the angle where the cornea and iris meet, suddenly becomes blocked, usually owing to pupil dilation in a patient with an anatomically shallow anterior chamber. This blockage prevents the aqueous humour from draining properly, causing a rapid increase in intraocular pressure (>30 mm Hg). Acute angle closure glaucoma presents with a sudden unilateral headache, associated with decreased visual acuity, eye pain, photophobia, and a mid-dilated pupil. The pain associated with acute angle closure glaucoma can be abrupt in onset and generalised in nature, with some patients complaining of unilateral thunderclap headache.[19] Without prompt treatment, this is a vision threatening emergency.

How to diagnose subarachnoid haemorrhage in a patient with thunderclap headache

The infographic includes an algorithm for assessment and investigation, focusing on subarachnoid haemorrhage, in patients who present with sudden onset headache. The initial diagnostic approach includes a focused history and physical exam.

Ask about high risk headache features, including:

- Sudden onset, maximal within minutes (up to one hour)
- Severe intensity
- Location, including laterality
- Association with exertion, vomiting, or loss of consciousness
- Presence of any neck pain and focal neurological symptoms such as weakness, numbness, speech difficulties, and visual changes.

Box 1 | Ottawa subarachnoid haemorrhage rule

The Ottawa subarachnoid haemorrhage rule is for alert patients >15 years old with new severe non-traumatic headache reaching maximum intensity within one hour.

It is not appropriate for patients with new neurological deficits, history of previous aneurysms, or history of similar headaches (≥3 episodes over ≥6 months).

Patients require investigation if one or more finding is present:

- Symptoms of neck pain or stiffness
- Age ≥40 years old
- Witnessed loss of consciousness
- Onset during exertion
- Thunderclap headache (peak intensity immediately)
- Limited neck flexion on exam

During physical exam, assess:

- Level of consciousness
- Presence of meningism (neck stiffness with flexion)
- Presence of focal neurological symptoms by using a screening neurological exam with particular attention paid to cranial nerve palsies, which can be subtle
- For signs of increased intracranial pressure and subhyaloid haemorrhage by using fundoscopy, which is seen in about 20% of patients with subarachnoid haemorrhage.[44]

Ottawa subarachnoid haemorrhage rule

The Ottawa subarachnoid haemorrhage rule is a clinical decision tool that has been designed to help doctors in the emergency department identify patients at low risk for non-traumatic subarachnoid haemorrhage (box 1). If negative, and dangerous differential diagnoses for sudden headache have been ruled out, then treat the patient with appropriate analgesia and symptom control. However, if subarachnoid haemorrhage remains a differential diagnosis after history and examination, then further testing is needed.

The Ottawa subarachnoid haemorrhage rule has a sensitivity for subarachnoid haemorrhage of 100% (95% confidence interval 97% to 100%) on initial derivation and consistent performance in prospective validation studies.[6 45 46] However, the rule has low specificity (13-15%) and as such, is only useful to rule out subarachnoid haemorrhage.[6 45] If subarachnoid haemorrhage cannot be ruled out with the Ottawa subarachnoid haemorrhage rule assessment, then investigate further.

Blood testing

Blood testing is not necessary for all patients who present with a thunderclap headache but it might be useful in those with concerning features on history or examination, helping to direct further investigation for potentially dangerous causes. In the case of suspected subarachnoid haemorrhage specifically, initial laboratory testing should include:

- A full blood count to assess for anaemia, which decreases the sensitivity of CT head for the presence of blood
- Creatinine to assess renal function
- Coagulation studies, particularly for patients treated with anticoagulants.

Computed tomography

A non-contrast CT head is the first neuroimaging test in most patients who undergo investigation for subarachnoid haemorrhage, especially if onset of the headache was within six hours (fig 1, A).[9 47 48] A 2011 prospective cohort study showed a sensitivity of 100% for subarachnoid haemorrhage when a non-contrast CT head was performed within six hours of onset.[5]

Based on our experience, we suggest that if the patient does not have a visible subarachnoid haemorrhage on non-contrast CT performed within six hours after onset and the patient does not have known anaemia (haemoglobin <100 g/L can reduce the sensitivity of CT), the diagnosis of subarachnoid haemorrhage can be ruled out.[50]

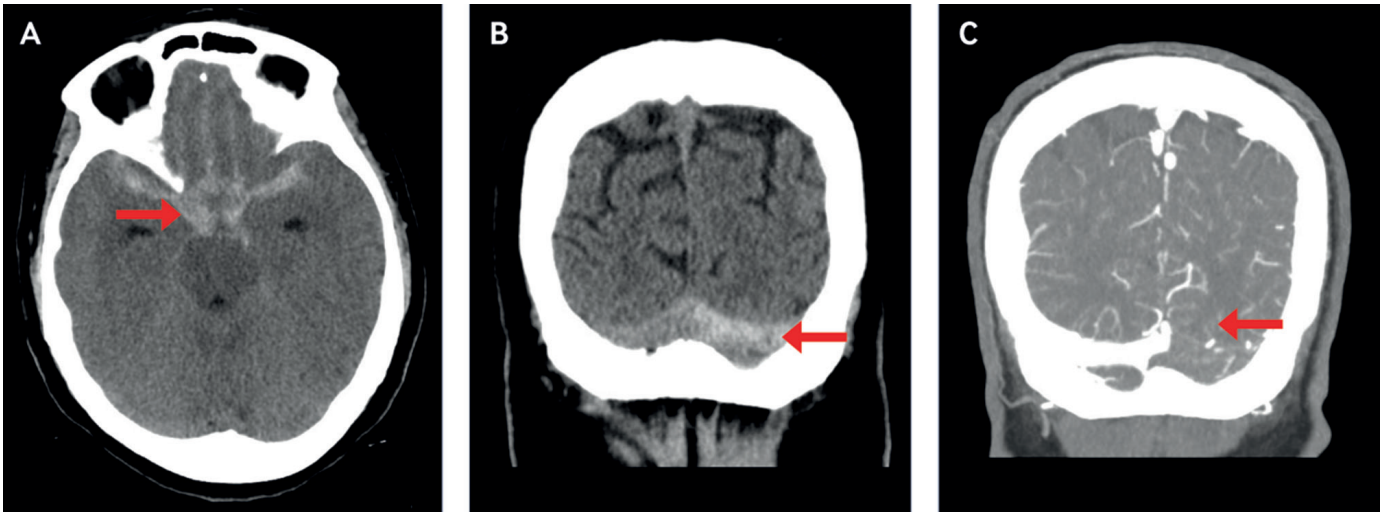

Fig 1 | CT findings of subarachnoid haemorrhage (A) and cerebral venous sinus thrombosis (B/C). A: Acute subarachnoid haemorrhage most prominent in the prepontine, suprasellar, bilateral cisterns of the lateral cerebral fossa. Axial images using 5 mm slices. B: Non-contrast CT head showing increased density along the left transverse sinus suggestive of acute venous sinus thrombosis. Coronal images using 5 mm slices. C: CT venogram of the head showing non-opacification of the left transverse sinus. Coronal images using 0.63 mm slices

Box 3 | Focused investigations for the differential of non-subarachnoid haemorrhage causes of thunderclap headache

- Intracranial haemorrhage is initially assessed by non-contrast CT head. Once the haemorrhage is identified, discussion with specialists and suspicion for the aetiology of the haemorrhage might lead to further imaging, including CT angiography or MRI.[12]
- Acute ischaemic stroke is usually assessed with non-contrast CT paired with CT angiography (where accessible). Some hospitals might also use MRI in the assessment to guide immediate reperfusion therapies, but this is not necessary in the initial acute assessment.[57]
- Suspected cervical, vertebral, and basilar artery dissection should be assessed with CT angiography.
- The initial imaging for reversible cerebral vasoconstriction syndrome is also CT angiography (fig 2); however, MRI is an alternative.[16 58] Additionally, the reversible cerebral vasoconstriction syndrome 2 ($RCVS_2$) score can be used to assist clinicians in diagnosis.[59]
- Meningitis necessitates a lumbar puncture for definitive diagnosis (unless contraindications are present), with a preceding non-contrast CT head only necessary in patients with immunocompromise, history of central nervous system disease, papilloedema, suspected raised intracranial pressure, or focal neurological signs.[43] Maintain a low threshold to pursue lumbar puncture testing in patients who have fever or persistent altered mental status, even after negative initial neuroimaging.
- Acute angle closure glaucoma is more likely in a patient with unilateral headache. It is diagnosed with a detailed ophthalmological exam, including inspection, visual acuity assessment, fundoscopy, and measurement of intraocular pressures.[19]

If thunderclap headache has occurred in a patient without neurological signs more than six hours before a non-contrast CT head or the patient has anaemia (haemoglobin <100 g/L), then a negative non-contrast CT head alone might not be sufficient to rule out subarachnoid haemorrhage. A discussion with the patient, or designated alternate decision maker, should explore the risks and benefits of next line investigations, including potential lumbar puncture, CT angiography of the brain, or both.

The utility of non-contrast CT head might also aid in the diagnosis of intracranial haemorrhage, acute ischaemic stroke, pituitary apoplexy, cerebral venous sinus thrombosis (fig 1, B and C), hydrocephalus, and intracranial mass lesions, which can all be associated with a thunderclap headache. Additionally, the presence of intracranial mass lesions, signs of raised intracranial pressure, or both would be an important contraindication to lumbar puncture.

Lumbar puncture

If the non-contrast CT head does not show a subarachnoid haemorrhage or alternative structural cause for the thunderclap headache, then lumbar puncture for cerebrospinal fluid analysis is usually the next recommended test.[47 48 52] There is a lack of evidence regarding how long a lumbar puncture remains accurate after the index headache. In our experience, lumbar puncture is a useful investigation up to one week after headache onset, but after this, the diagnostic accuracy of a lumbar puncture decreases. In addition to aiding in the diagnosis of subarachnoid haemorrhage, lumbar puncture can also help diagnose meningitis, and cerebrospinal fluid leak causing intracranial hypotension.

Cerebrospinal fluid is diagnostic for subarachnoid haemorrhage if spectrophotometry assessment is positive, if there is xanthochromia detected on visual inspection, or if there are more than $0.000\,005\times10^{12}$ red blood cells per litre in the final tube and an aneurysm is found on a concurrent CT angiogram.[53] Data from a Canadian prospective cohort study in patients aged 15 and older presenting with acute non-traumatic headache undergoing lumbar puncture testing suggests that the absence of xanthochromia and a red blood cell count less than 0.002×10^{12}/L in the final tube can safely exclude the diagnosis of aneurysmal subarachnoid haemorrhage with a sensitivity of 100% (95% confidence interval 74.7% to 100%).[53] However, if red blood cell count is between $0.000\,005\times10^{12}$/L and 0.002×10^{12}/L and the patient is at very high risk for subarachnoid haemorrhage, then we would suggest, based on our expert opinion, to proceed to CT angiogram for these patients. When interpreting

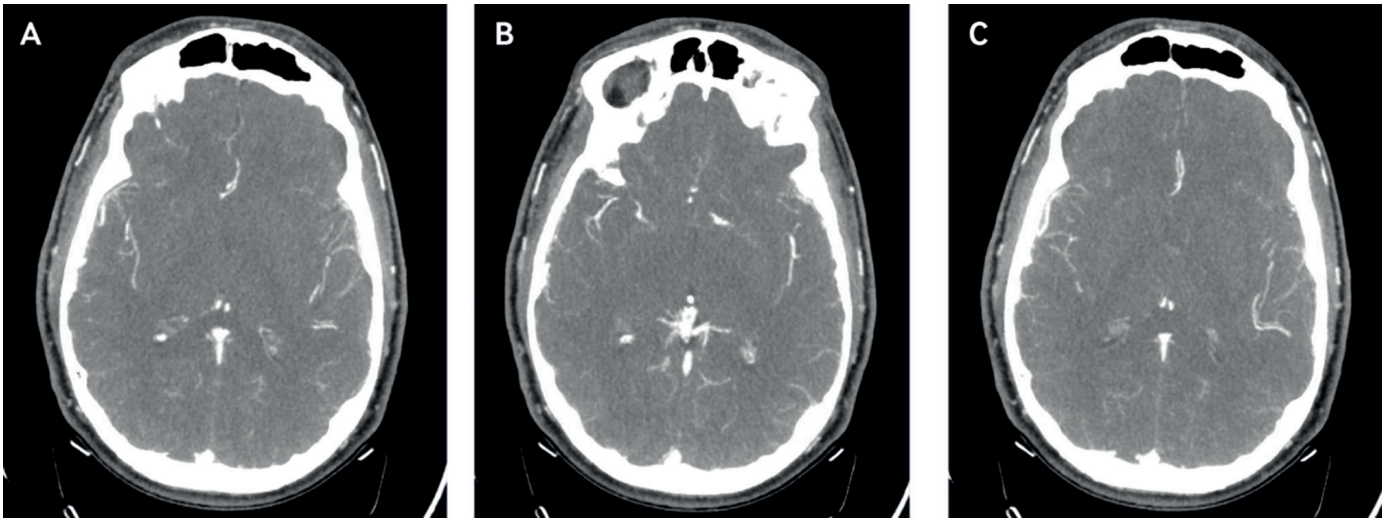

Fig 2 | CT angiogram findings of reversible cerebral vasoconstriction syndrome. Irregularity of the intracranial arteries with multifocal narrowing, more conspicuous at the M1 segment of the right middle cerebral artery (A), M2 branches of the right middle cerebral artery (B), A1 and A2 segment of both anterior cerebral arteries (C). Axial images using 0.63 mm slices

Box 4 | Definitive management for thunderclap headache

Management is dependent on diagnosis, and comprehensive treatments specific to aetiology are outside the scope of this article. Broadly, these include:

- Reduce the risk of re-bleeding from aneurysms and other vascular abnormalities by early neurosurgical consultation for source control, reversal of any active anticoagulation, and supportive care measures (avoid severe hypertension and raised intracranial pressure) for patients with subarachnoid haemorrhage.[9]
- Initiate appropriate antibiotic drugs, antiviral drugs, or both, in accordance with guidelines to manage infectious meningitis.[43]
- Refer to neurology for consideration of secondary prevention strategies for patients with arterial dissection and reversible cerebral vasoconstriction syndrome.[17 58]
- Refer to ophthalmology to initiate intraocular pressure lowering therapies and consider definitive management with iridotomy drainage for patients with acute angle closure glaucoma.[19]
- Nimodipine (administered orally or intravenously) might be an option for the treatment of primary thunderclap headache, but the evidence is limited.[60]

the presence of xanthochromia, spectrophotometry and visual assessment are both highly specific, with spectrophotometry being more sensitive, but also liable to reporting more false positives.[54]

Obtain consent from patients undergoing lumbar puncture and inform them of the risks such as infection, bleeding, and post-lumbar puncture headache. With strict adherence to sterile technique and appropriate selection of patients considering bleeding risk, the risk of infection and substantial bleeding when performing a lumbar puncture is low (<0.1%).[55] Follow consensus guidelines that detail procedure and equipment related factors to minimise the risk of post-lumbar puncture headache.[55]

CT angiogram

If the diagnosis of subarachnoid haemorrhage is established via a positive non-contrast CT head or a lumbar puncture that is considered positive or equivocal, then proceed to a CT angiogram of the brain to confirm the diagnosis and to guide definitive management.

Generally, in the scenario where a non-contrast CT does not establish the diagnosis of subarachnoid haemorrhage, a lumbar puncture should be the next diagnostic test, based on consensus guidelines and our expert opinion.[47 48] Alternatively, the American College of Emergency Physicians supports the use of CT angiogram rather than lumbar puncture as the next step following a negative non-contrast CT.[50]

CT angiography can be a useful and often appropriate investigation in patients presenting with thunderclap headache. Circumstances where we recommend that CT angiography should be considered are given in box 2 (see bmj.com).[47 48]

CT angiography might not be available, especially in non-tertiary care centres, such as community hospitals and rural settings. Even when CT angiography is readily accessible, it could miss small aneurysms (<3 mm in size), identify incidental aneurysms that are present in about 2-3% of the background population, and expose patients to the risks of iodinated contrast media reactions, contrast induced nephropathy, and ionising radiation.[9 47] If incidental aneurysms <5 mm are found, it could result in invasive follow-up investigations with

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

For this article, a patient who had a subarachnoid haemorrhage that presented atypically without thunderclap headache, reviewed the manuscript. Although the focus of the article is thunderclap headache, the patient wanted to highlight to readers that there are atypical presentations of subarachnoid haemorrhage. Furthermore, the patient wanted to emphasise the importance of a standardised diagnostic pathway for primary care providers, to evaluate potential cerebrovascular events and to ensure timely recognition and referral of cases with subtle but concerning symptoms.

EDUCATION INTO PRACTICE

- In your practice, how many patients presenting with thunderclap headache have lumbar punctures performed as opposed to CT angiography, when ruling out subarachnoid haemorrhage?
- Once you have successfully ruled out subarachnoid haemorrhage in patients, how do you continue your investigations for other diagnoses?

the potential for unnecessary harm, including coiling or neurosurgical repair, and its associated risks.[56] Furthermore, anxiety associated with the diagnosis might have mental health impacts on patients and lead to higher use of healthcare resources by additional clinic or emergency department visits.

How to diagnose non-subarachnoid haemorrhage causes of thunderclap headache

The approach to history and physical exam for non-subarachnoid haemorrhage causes of thunderclap headache is similar to that of subarachnoid haemorrhage. Laboratory investigations should include full blood count, biochemistry, and clotting profiles. In addition, blood cultures should be considered in the case of suspected meningitis.

A summary of diagnostic tests is in the table (see bmj.com), and focused investigations, guided by the working differential diagnosis, are summarised in box 3.

What are the management principles?

The priority for clinicians in the acute management of thunderclap headache is to consider and investigate for potentially dangerous diagnoses appropriately, provide symptomatic and supportive care, and engage appropriate healthcare professionals early to initiate management and follow-up. Most patients with thunderclap headache require urgent or emergency specialist consultation that might include neurology, neurosurgery, and/or ophthalmology depending on local pathways (box 4).

Competing interests: See bmj.com.

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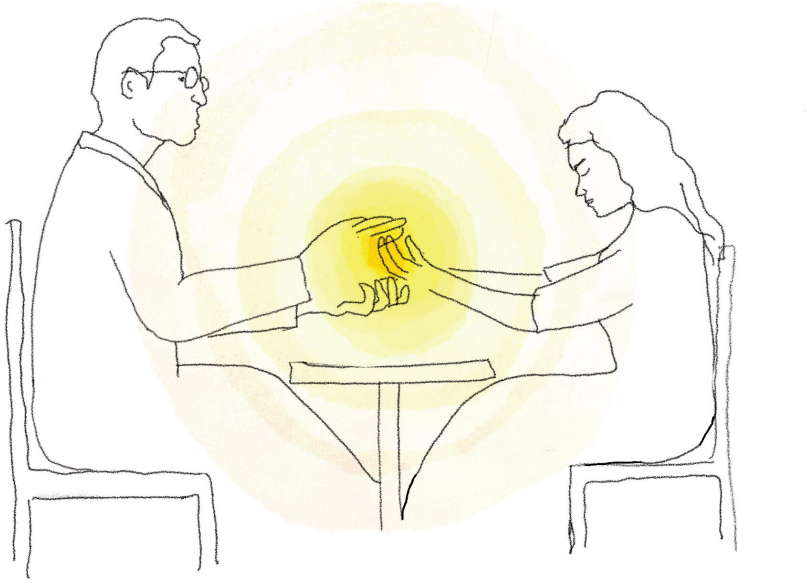
WHAT YOUR PATIENT IS THINKING

CPD READING 0.5 HOURS

Finding wise hope beyond a cure

Catherine Shteynberg calls for health professionals to use clear language when delivering a diagnosis of incurable cancer



PRIYA SUNDRAM

Delivering the devastating news of an incurable cancer diagnosis is one of the most important tasks oncologists face. Yet many cancer patients, as I've learnt through experience, support groups, and recent studies, don't always fully understand what their diagnosis means.

Confusing language

I received the diagnosis of an incurable low grade glioma in 2016. My surgeon was clear and compassionate, explaining that my cancer was incurable while remaining positive about treatments to prolong life. However, another health professional I saw described my cancer as a "tumour," and emphasised the need for genetic testing and regular magnetic resonance imaging. I turned to reputable resources like the website for the American Brain Tumor Association, but nowhere did it use the word "incurable," even in articles about the most aggressive brain tumours, glioblastomas. Instead, the terms used were "malignant," "life threatening," and "recurrence," but never "incurable." The only mention of the word I found was in sections on research.

Confusing communication from clinicians, loved ones, and trusted sources meant it took more than a year for me to accept that my disease would likely be fatal, if slow growing. Once I had accepted this, I began journalling, practising mindfulness, seeking acupuncture and massage, and having difficult conversations with my husband, friends, and family about my fate.

Facing the often invisible challenges

After two craniotomies, radiation, and chemotherapies, my hair grew back. The invisible nature of my ongoing disease led to inconsistent reactions from those around me. Friends, family, and colleagues said they were "so glad my cancer was gone" and that I "looked like nothing had happened." Meanwhile I was grappling with seizures, memory issues, and sadness about my deteriorating health. Accepting death is a lifetime's work, but for those with incurable cancer, facing early death, missing milestones, redefining identity after giving up work, and dealing with the potential future loss of mental capacity are especially hard. Comments like "everyone will die" or "no one knows their time" dismiss the daily challenges cancer patients face in confronting their mortality.

WHAT YOU NEED TO KNOW

- Language used when delivering a cancer diagnosis can be confusing and can make acceptance much harder
- Having to navigate unrealistic societal expectations of treatment and cure can be isolating and draining
- Focusing on acceptance while gaining a sense of "wise hope" can allow patients to focus on what matters to them

EDUCATION IN PRACTICE

- How can you ensure that a patient understands their diagnosis, especially someone with incurable cancer?
- What could you do to help someone navigate acceptance of this diagnosis and help them find peace and hope?

Finding wise hope

I'm not in a battle with my incurable cancer, nor do I see myself as a warrior or a fighter. That kind of violent, militarised language can be harmful—it creates unrealistic expectations and can make patients feel they've failed if their illness doesn't go away, even when a cure simply isn't possible. My incurable cancer doesn't make me a failure—it's the result of rogue cells in my body. Yet much of the discourse around cancer suggests hope only means a cure. I resonate more with the ideas of healing and "wise hope" shared by Buddhist teachers. While hope can be tied to specific outcomes—like "beating" cancer—wise hope is rooted in acceptance, recognising that we cannot predict the future. It offers a sense of potential, regardless of a cancer patient's outcome.

Despite doctors' communications about incurable conditions, some patients believe treatments like chemo or radiation therapies will cure them. Others may prefer not to know the truth. For me, knowing my cancer is incurable has brought me peace. I feel calmer and happier. I focus on travelling and writing now, before seizures and cognitive changes make that difficult. I reassess my life each month to ensure I'm doing what makes me and my family happy. I am grateful for the honest communication with my oncology team, which has been crucial in navigating this journey.

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CASE REVIEW

Auricular swelling and tenderness with multiple pulmonary nodules

A woman in her 40s presented with a one month history of swelling and tenderness of the ears (fig 1), along with pain in her palms and fingers, and mild chest tightness. She had no history of chronic infections or occupational exposures. On examination, both pinnae exhibited firm, nodular swelling with erythema, tenderness, and warmth. Tenderness was also noted in the metacarpophalangeal and phalangeal joints bilaterally. Audiometric and vestibular evaluations demonstrated no abnormalities. No murmurs, gallops, or adventitious breath sounds were detected on examination of the cardiac and respiratory systems. A chest CT (computed tomography) scan was performed, which revealed multiple pulmonary nodules and bilateral mediastinal lymphadenopathy (fig 2). Laboratory investigations revealed a negative Mantoux test and T-spot, with serum angiotensin converting enzyme and calcium levels within normal ranges. A biopsy of the ear tissue was recommended but the patient declined.

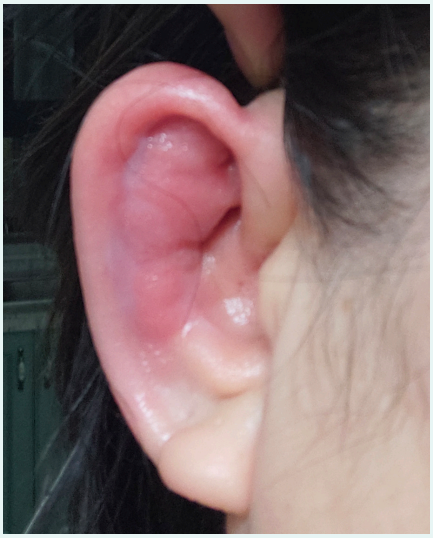

Fig 1 | Photograph shows warm, tender, swollen ear, with exception of the earlobe

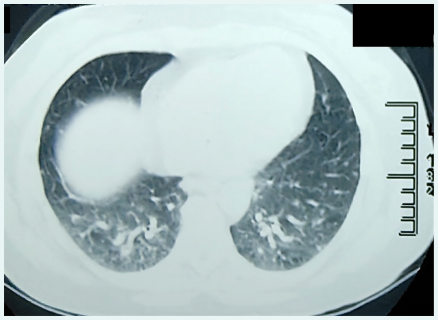

Fig 2 | CT image of the lung window shows ground glass attenuation and multiple lung nodules in the lower lobes

1 What are the differential diagnoses?
2 What is the most likely diagnosis?
3 How would you manage this patient?

Submitted by Chenhan Jia, Wanyi Lin, Hanlin Yin, and Liangjing Lu

Patient consent obtained.

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answers

CASE REVIEW **Auricular swelling and tenderness with multiple pulmonary nodules**

1 What are the differential diagnoses?

The differential diagnoses include relapsing polychondritis, tuberculous lymphadenitis, silicosis, and sarcoidosis. Relapsing polychondritis can affect various anatomical sites such as the ears, nose, respiratory tract, and thoracic wall but rarely affects the lungs. Tuberculous lymphadenitis is often associated with a positive Mantoux test or T-spot assay, and typically results in unilateral hilar lymph node enlargement, which is visible on CT imaging.

The clinical presentation of silicosis includes cough, sputum production, chest tightness, and dyspnoea, often with a history of occupational exposure. Sarcoidosis typically presents with pulmonary symptoms such as chest tightness, cough, and sputum production, which might be accompanied by extrapulmonary manifestations (eg, skin, cartilage, or joints affected) and has non-caseating granulomas on histology.

2 What is the most likely diagnosis?

Sarcoidosis, an inflammatory, multisystem disease characterised by the formation of non-caseating granulomas in affected organs. Risk factors for sarcoidosis include genetic susceptibility and environmental triggers such as mould exposure, insecticide use, and agricultural occupations.

Patients commonly present with subacute or chronic respiratory symptoms such as cough, shortness of breath, and chest pain. The second most affected organ is skin (approximately 25% to 40% of cases reported); primary manifestations include papules, nodules, plaques, and lupus pernio.

3. How would you manage this patient?

Oral glucocorticoid drugs are the preferred treatment for sarcoidosis in most patients. The European Respiratory Society guidelines recommend initiating drug treatment with 20 mg of prednisone or prednisolone daily. For those who respond to steroid treatment, the dose should be tapered over 1-3 months to 5-10 mg daily or every other day. Treatment should be continued for a minimum of 12 months.

PATIENT OUTCOME

See bmj.com.

LEARNING POINTS

- Sarcoidosis is a multisystem inflammatory disease that can affect any organ of the body.
- Serum angiotensin converting enzyme and calcium level tests are not specific but can be used to support the diagnosis of sarcoidosis.
- The preferred treatment for sarcoidosis is oral glucocorticoid drugs, which can be combined with immunosuppressant drugs such as methotrexate and leflunomide.

CPD READING
0.5 HOURS

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

LEARNING MODULE

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