education

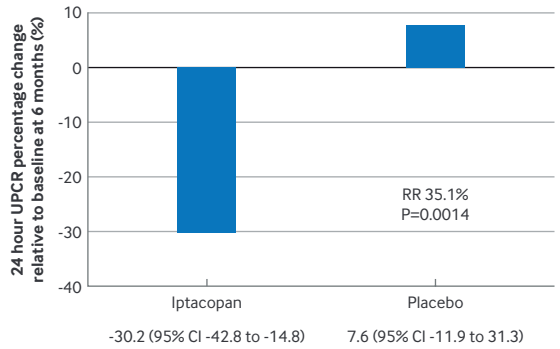
RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Aspirin for colorectal cancer

Colorectal cancer prevention and treatment has long been on aspirin's list of potential benefits. A new trial suggests that a subgroup of people with alterations in the PI3K pathway gene may be more likely to benefit than others. PI3K alterations were found in 37% of the 2980 people with

stage 1, 2, or 3 colorectal cancer recruited and tested for the study, which examined the effects of aspirin *v* placebo in those with group A and group B PI3K alterations separately. The risk of recurrence at three years was less than half in those allocated to receive aspirin albeit with wide 95% confidence intervals (7.7% *v* 14.1% for group A alterations (hazard ratio 0.49, 95% CI 0.24 to 0.98), 7.7% *v* 16.8% for group B alterations (0.42, 0.21 to 0.83)).

N Engl J Med doi: 10.1056/NEJMoa250465



Percentage change in proteinuria (24-h urine protein creatinine ratio) after treatment with iptacopan or placebo relative to baseline at six months

A complement for rare diseases

A trial of iptacopan therapy in patients with C3 glomerulopathy published in the *Lancet* shows that even ultra-rare kidney diseases can make it into the major medical journals. The study found a statistically significant relative reduction of proteinuria after 6 months' treatment with the oral complement inhibitor versus placebo (see figure). The study's sponsor was involved in design, analysis, and writing, and the surrogate endpoint was justified on the basis that the sample sizes in rare disease trials are too small to directly study delaying kidney failure.

Lancet doi:10.1016/S0140-6736(25)01148-1

Early days for multicancer detection tests

Multicancer detection (MCD) tests are available to buy—although may set you back more than a thousand pounds. Websites offering the tests, which usually detect fragments of DNA released by cancer cells, seem to imply an established evidence base for them, such as that they've been validated on over 40 000 participants. A systematic review suggests there is still a way to go: the authors searched for controlled studies in screening populations and found no controlled studies that report benefits of screening with MCD tests. The NHS-Galleri trial should change that and is expected to report its findings next year.

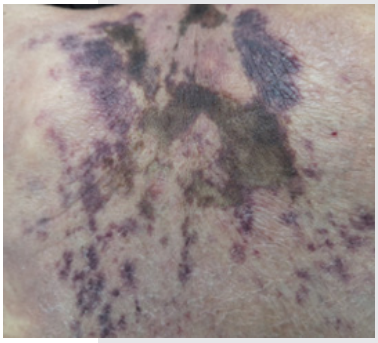
KAVANAGH D, BOMBACK AS, VIVARELLI M, ET AL. LANCET 2025; DOI:10.1016/S0140-6736(25)01148-1

Ann Intern Med doi:10.7326/ANNALS-25-01877

Low dose oral semaglutide for obesity

Countless headlines exalt the life changing benefits of newer obesity drugs such as tirzepatide, but there are far fewer about people who are left behind

CLINICAL PICTURE



Painful purpura in systemic lupus erythematosus

A woman in her late 50s presented with a two month history of a scattered macular rash on her back, which progressively merged into painful purpura. She had a history of systemic lupus erythematosus treated with prednisone and hydroxychloroquine. Physical examination showed violaceous, reticular purpura with dusky central discoloration (figure). Laboratory test results showed thrombocytopenia (platelets 34 × 10^9/L; reference range: 150-450 × 10^9/L) but were otherwise unremarkable. Skin biopsy demonstrated circumferential vascular calcifications in small to medium vessels of the deep dermis and subcutis. A diagnosis of non-uraemic calciphylaxis (NUC) was made.

Calciphylaxis is a rare condition characterised by skin necrosis secondary to microvascular calcification and thrombosis. It is most often seen in patients with end stage renal failure. More rarely, it occurs in patients with normal or mildly impaired kidney function, in which case it is known as NUC. Causes of NUC include malignancy, liver disease, primary hyperparathyroidism, warfarin

because they are unable to tolerate them. The landmark SURMOUNT-1 trial found between 4.3% and 7.1% of participants allocated to receive tirzepatide discontinued the drug owing to side effects, compared with 2.6% in the placebo group. Low dose oral semaglutide might be an alternative, and has been studied in a new randomised trial. The results showed that 25 mg once daily semaglutide plus a lifestyle intervention led to an average 13.6% weight loss after 64 weeks, compared with 2.2% in the lifestyle and placebo group. However, gastrointestinal side effects were still common (74.0% *v* 42.2%)

N Engl J Med doi:10.1056/NEJMoa2500969

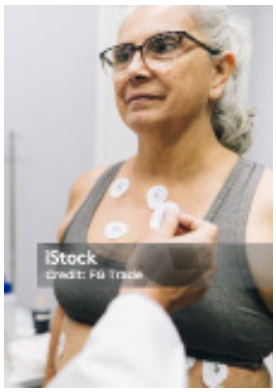
Cardiovascular disease risk and hormone replacement therapy

Criticism of the 2024 National Institute for Health and Care Excellence menopause guideline update included that important evidence was excluded on cardiovascular disease (CVD) outcomes in women who take hormone replacement therapy. A new secondary analysis of women's health initiative trials returns to this question, although is unlikely to have the final say. The study assessed the risk of atherosclerotic CVD in 27 347 postmenopausal women in the United States with vasomotor symptoms. No difference in CVD risk was found in women aged 50 to 59 years taking conjugated equine oestrogens with or without medroxyprogesterone acetate compared with placebo, but a higher risk was found in women over the age of 70.

JAMA Intern Med doi:10.1001/jamainternmed.2025.4510

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

Cite this as: *BMJ* 2025;391:r2050



use, and connective tissue disease. The one year mortality of calciphylaxis ranges from 45% to 80%, with sepsis caused by secondary infection of the necrosed lesions the most common cause of death. Despite meticulous wound care and maximal medical therapy, this patient died one month after presentation.

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Patient consent obtained.

Cite this as: *BMJ* 2025;391:r1901

MINERVA From the wider world of research

Childhood blood pressure

Many characteristics track from early life into adulthood. Tall children, for example, tend to grow into tall adults. The same seems to be true for raised blood pressure and its consequences. In a large sample of US children born between 1959 and 1966, higher blood pressure at age 7 carried an increased risk of cardiovascular mortality when they reached their mid 50s (*JAMA* doi:10.1001/jama.2025.14405).

How often should patients monitor their blood pressure?

Self-monitoring of blood pressure is now a routine part of the management of hypertension. How often should it be checked? Too often might overemphasise random fluctuations. Too rarely might lead to under treatment. Data from two trials in which participants measured their own blood pressure show that there was little change in mean blood pressure over a year, but a much larger variability within an individual's monthly readings (*Hypertens* doi:10.1097/HJH.0000000000004123). The conclusion is that, in the absence of a change in medication, annual measurement is enough.

Compression stockings for vasovagal syncope

Wearing thigh length compression stockings reduces venous pooling in the lower limbs and ought to be an effective way of preventing vasovagal syncope. Surprisingly, a randomised trial finds no benefit (*J Am Coll Cardiol* doi:10.1016/j.jacc.2025.05.049). But more than a third of participants discontinued treatment. The likely explanation isn't that elastic stockings don't work, but that people don't like wearing them.

Candesartan for migraine prevention

In a randomised trial in people with frequent migraines, candesartan (16 mg/day) reduced migraine days by two per month compared with a reduction of one per month with placebo (*Lancet Neurol* doi:10.1016/S1474-4422(25)00269-8). The treatment was generally well tolerated, with dizziness as the most often reported side effect. The question now is how candesartan compares with other preventive treatments for migraine such as beta blockers and anti-seizure drugs.

A Mediterranean diet for people with psoriasis

Weight loss is often beneficial in people with psoriasis, particularly among those who are overweight or obese. Eating a Mediterranean-type diet, characterised by a high intake of olive oil, vegetables, and cereals, and a low intake of dairy products and red meat, may also help. A small randomised controlled trial found a Mediterranean diet intervention, sustained for four months, substantially improved psoriasis severity in patients with mild to moderate disease (*JAMA Dermatol* doi:10.1001/jamadermatol.2025.3410).

Mortality among surgeons in the United States

In the US, mortality among surgeons is roughly 50% higher than that among physicians, although similar to that of other highly educated professionals such as lawyers, engineers, and scientists (*JAMA Surg* doi:10.1001/jamasurg.2025.2482). The leading causes of death were cancer and heart disease, but motor vehicle collisions and hypertension were commoner among surgeons than in other occupational groups.

Cite this as: *BMJ* 2025;391:r2046

EASILY MISSED?

HPV positive oropharyngeal cancer

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CPD READING
0.5 HOURS

What is HPV positive oropharyngeal cancer?

Squamous cell carcinoma is the most common malignancy affecting the oropharynx (fig 1), specifically the lymphoid tissue of the palatine tonsils and base of the tongue.[1] The causal association between HPV, particularly the HPV 16 subtype, and oropharyngeal squamous cell carcinoma (OPSCC) was recognised by the International Agency for Research against Cancer in 2007. This is a clinically and pathologically distinct disease entity from HPV negative OPSCC. It has a markedly different epidemiology, typically affecting younger male patients without the traditional head and neck cancer risk factors of long term tobacco and alcohol exposure.[2] During the past two decades, the incidence of OPSCC has risen sharply in the UK, US, New Zealand, and across many countries in Europe and Asia (box).[2] This trend is largely driven by the increasing prevalence of oropharyngeal HPV infection, which now accounts for more than 50% of OPSCC cases in the UK.[8]

WHAT YOU NEED TO KNOW

- The rising incidence of human papillomavirus (HPV) positive oropharyngeal squamous cell carcinoma (particularly in the UK, North America, and northern Europe) is driven by changing sexual behaviours, including increased oral sexual exposure.
- Compared with HPV negative disease, patients tend to be younger men with minimal exposure to tobacco or alcohol.
- Presentation is often with a painless neck lump due to early nodal metastasis; the primary tumour is usually small and located in the tonsil or the base of the tongue.
- Despite adverse pathological features, prognosis is good and response to treatment is favourable, although standard treatment regimens can result in substantial long term morbidity.
- Universal HPV vaccination is expected to reduce future incidence; education on the risks and consequences of HPV transmission, particularly by oral sexual contact, is important for both clinicians and the general public.

Why is it missed?

Patient demographics and clinical presentations that are different from other head and neck cancers can reduce the index of cancer suspicion in patients and GPs and contribute to delayed diagnoses.[6 9-11]

Initial misdiagnoses include tonsillitis or branchial cleft cysts.[17-19] OPSCC can present with lateral neck cystic nodal metastases that can closely resemble a branchial cleft cyst on clinical examination and cytology.[19 20]

Why does this matter?

HPV positive OPSCC has a more favourable prognosis than HPV negative OPSCC; however, early diagnosis can improve outcomes such as overall survival, risk of recurrence, and quality of life.[23 24] In the near future, treatment de-escalation protocols could also be available.[25]

Treatment of OPSCC, particularly when multimodal therapy such as chemoradiation is required, carries the risk of substantial long term adverse effects on speech, ability to swallow, and overall quality of life.

Incidence rates of OPSCC in the UK are projected to rise until 2040 after which a reduction in rates is expected owing to the impact of HPV vaccination (box 2).[36]

How is it diagnosed?

Key points on history

- Neck mass
  - Two thirds of patients with HPV positive OPSCC present with a painless cervical nodal mass. Bilateral cervical nodal involvement is possible in midline tumours at the base of the tongue.[5]
- Odynophagia, dysphagia, throat pain, and otalgia
  - Relate to the primary tumour and are less prevalent in HPV positive OPSCC.[5]
  - Direct questioning is important because throat symptoms might be subtle and patients could underestimate their significance.[6]
  - The absence of concomitant infectious symptoms, such as fever, should be noted and should increase the index of suspicion about a non-infectious aetiology.
- Altered tongue movement, bleeding, trismus, and weight loss
  - Signs of more advanced disease.[1]
- Nutritional status
  - Patients with OPSCC have a high risk of malnutrition, both from the disease and from oncological treatment.

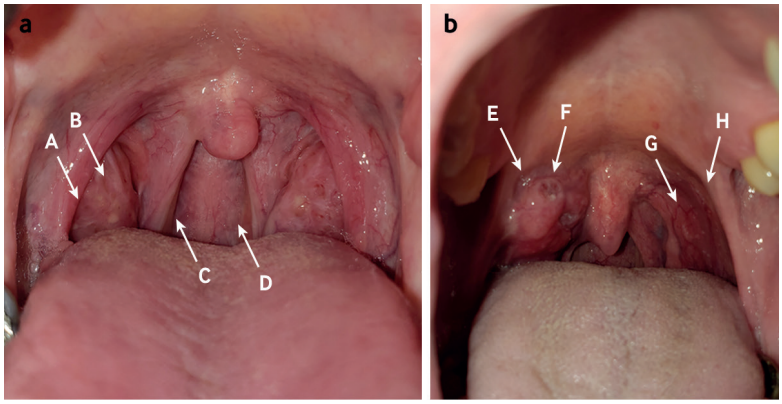


Fig 1 | Oropharynx (a). Right tonsil in a patient with HPV positive OPSCC (b). A=anterior tonsillar pillar; B= right palatine tonsil; C=posterior tonsillar pillar; D=posterior pharyngeal wall; E=asymmetrical irregular prominence of the superior pole of the right palatine tonsil, obscuring view of the anterior pillar; F=small superior mucosal surface ulcer; G=left palatine tonsil; H=left anterior tonsillar pillar

- Inquire about oral intake, unintentional weight loss, changes in diet texture, and swallowing difficulties (including coughing, choking, or prolonged mealtimes), because these might indicate nutritional compromise. Early dietitian and speech and language therapy involvement improves the tolerability of treatment.[37]

Key examination points

- Oral cavity
  - Oral cavity cancers usually present with visible mucosal lesions, ulcers, or pain. However, early presentations can be vague and overlap in symptoms with OPSCC.
  - Systematically assess eight subsites of the oral cavity for premalignant or malignant mucosal lesions. These include the inner mucosal surface of the lips, buccal mucosa, upper and lower alveolar ridges (bony edges where the teeth sit), retromolar trigone (small triangular mucosal area just behind the last lower molar), hard palate, floor of the mouth, and the anterior two thirds of the tongue, with particular attention to the lateral tongue margins.
  - White or red oral mucosal lesions might represent premalignant conditions such as leucoplakia, proliferative verrucous leucoplakia, erythroplakia, or lichen planus, all of which carry varying risks of malignant transformation into oral mucosal squamous cell carcinoma. Oral mucosal squamous cell carcinoma accounts for over 90% of all oral cancers and can present as a nodular mass or mimic the appearance of leucoplakia or erythroplakia in its early stages, underscoring the importance of thorough oral examination.[38]
- Oropharynx
  - Include tonsils, anterior and posterior tonsil pillars, soft palate, and posterior pharyngeal wall.
  - HPV positive OPSCC is typically small and located in the palatine tonsils (58%) or base of the tongue (37%). It might be submucosal and, therefore, not visible.[39]
  - HPV negative OPSCC, by contrast, is less likely to present with small T1 lesions. The primary tumour is usually larger relative to nodal disease and more prone to invade adjacent muscle, leading to more prominent symptoms such as pain, dysphagia, or trismus.
- Technique for palpation of tonsil and base of the tongue[16]
  - Begin with an explanation of the technique. It is usually well tolerated with only mild discomfort or transient gagging. Emesis is rare. Topical lidocaine spray can be used to improve comfort.
  - With the patient upright, use a gloved index finger to gently sweep two or three times across the base of the tongue from one side to the other, beginning just posterior to the circumvallate papillae. Likewise, the palatine tonsils can be gently palpated from superior to inferior (fig 2).
  - The normal tongue base feels smooth and pliant. Areas of induration or discrete nodules might indicate submucosal malignancy.[15]

How common is HPV positive OPSCC in the UK?

- In England, the incidence rate in men increased from 3.7 per 100 000 in 2000, to 12 per 100 000 in 2022, now exceeding the incidence rate of cervical cancer (9.2 per 100 000 in 2022)[3 4]
- A retrospective cohort study across 11 UK centres between 2002 and 2011 found that 51.8% of 1474 OPSCC cases were HPV positive, based on p16 immunohistochemistry and HPV DNA in situ hybridisation[5]
- The proportion of HPV positive disease as well as the overall incidence is expected to increase further in the UK in the next 20-30 years, until the expected benefits of universal HPV vaccination are seen[6 7]

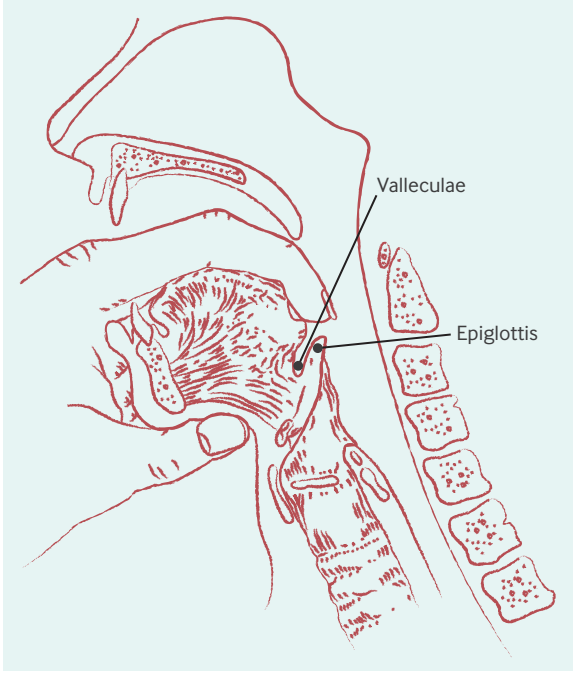


Fig 2 | Palpation of the base of the tongue

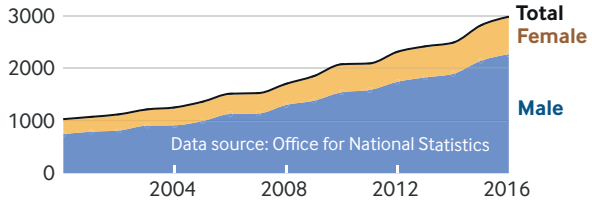
thebmj Visual summary

HPV positive oropharyngeal cancer

Key differences and examination points

Over recent decades, incidence of oropharyngeal cancer has risen rapidly due to an increase in oropharyngeal HPV infection. HPV positive cancers represent an epidemiologically distinct disease, often occurring without the traditional risk factors of long term tobacco and alcohol use. This visual summary highlights key differences in patient profile, clinical presentation, and examination compared with HPV negative oropharyngeal cancer

Incidence of oral cavity and oropharyngeal cancer in England



Key points on history

- Two thirds of people with HPV positive oropharyngeal cancer present with a painless cervical nodal mass
- Direct questioning is important because throat symptoms might be subtle and patients may underestimate their significance
- The absence of concomitant infectious symptoms should increase the index of suspicion regarding a non-infectious aetiology

Signs of more advanced disease

Bleeding · Weight loss · Altered tongue movement · Trismus

Why is it missed?

Patient demographics and clinical presentation differ from other head and neck cancers, reducing index of suspicion

Compared with HPV negative disease, people with HPV positive oropharyngeal cancer tend to have these characteristics:

Younger · More likely to be white · Less use of alcohol and tobacco

Common misdiagnoses

Tonsillitis

A 2014 study in Scotland found that 47% of patients referred for oropharyngeal cancer had been treated for tonsillitis an average of 1.9 times, with secondary care referral delayed on average 34 days from initial presentation

Branchial cleft cysts

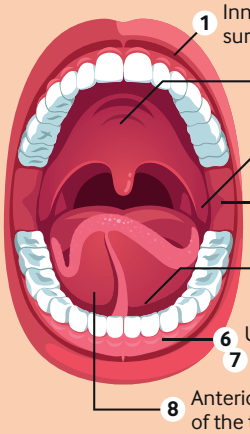
Oropharyngeal cancer may present with lateral neck cystic nodal metastases that can closely resemble a branchial cleft cyst on clinical examination and cytology

A new cystic neck mass in the upper aspect of the anterior triangle in an adult >40 years should be considered a nodal metastasis until proven otherwise

Key examination points

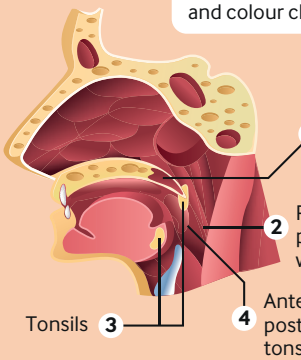
Oral cavity

Systematically assess eight subsites of the oral cavity for mucosal lesions



Oropharynx

Assess for masses, ulceration, asymmetry, and colour change



HPV positive oropharyngeal cancer is typically small and located in the palatine tonsils or base of tongue. It may be submucosal and therefore not visible and only evident on palpation

Neck

Expose neck to clavicle, examine from behind with neck slightly flexed to relax neck musculature

1. Palpate all cervical lymph nodes
2. Assess nodes for:
   - Size
   - Mobility
   - Consistency

   >1cm potentially pathological
3. Typical metastatic nodes will be non-tender and hard, with a horizontal dimension equal to or more than vertical dimension

HPV positive oropharyngeal cancer most commonly metastasises to the nodal group anterior to the upper part of the sternocleidomastoid muscle, located above the level of the hyoid bone within the anterior triangle

- Neck
  - Expose neck to clavicle, examine from behind with neck slightly flexed to relax neck musculature.
  - Palpate all cervical lymph nodes including those within the anterior triangle, posterior triangle, parotid, pre-auricular, and post-auricular regions.
  - HPV positive OPSCC most commonly metastasises to the nodal group anterior to the upper part of the sternocleidomastoid muscle, located above the level of the hyoid bone within the anterior triangle.[40]
  - Assess nodes for size (>1 cm potentially pathological), mobility, and consistency.
  - Typical metastatic nodes will be non-tender and hard, with a horizontal dimension equal to or more than the vertical dimension.[40]
- Flexible nasal endoscopy
  - Key tool in an otolaryngologist outpatient clinic. Not routinely used in primary care.
  - Allows high resolution examination of the nasal cavity, nasopharynx, oropharynx, larynx, and part of the hypopharynx.

Investigations

- Currently, the diagnostic investigation for OPSCC does not differ according to HPV status.
- Mass in the neck or lymph node
  - Ultrasound guided fine needle aspiration or core biopsy[42]
- Tumour staging[40 43]
  - Computed tomography or magnetic resonance imaging required for local staging depending on local multidisciplinary team preference
  - Histological confirmation is crucial and usually acquired during a general anaesthetic examination of the upper aerodigestive tract, although tonsil tumours might be amenable to biopsy in an ear, nose, and throat clinic under local anaesthetic.
- Confirmation of HPV
  - The 2024 Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines recommend confirmation of HPV status of in all cases of OPSCC.[43]
  - A combination of p16 immunohistochemistry (as a surrogate marker for HPV status) and HPV specific testing, such as DNA detection by polymerase chain reaction, is recommended to improve the accuracy of the diagnosis and prognosis.[43]
- Liquid biopsies
  - Interest in the use of liquid biopsies that assess for the presence of circulating cell free tumour DNA in the diagnosis and surveillance of HPV positive OPSCC, which allows for surveillance across all high risk HPV genotypes, is developing.[44]
  - A 2023 cohort study of 163 patients found a sensitivity of 91.5% and specificity of 100% in the diagnosis of HPV OPSCC.[45]
  - Prospective clinical validation studies with the aim of complementing or potentially reducing reliance on traditional tissue diagnosis which can be invasive, technically difficult in submucosal disease, and sometimes non-diagnostic, are ongoing.

PATIENT EXPERIENCE

When I attended my GP with a lump under my jaw, it didn't even cross my mind that this could be cancer. It was only after I attended the ear, nose, and throat surgeon for the results of my biopsy and I was asked by the nurse specialist "Is there anyone with you?" that I knew the news was not going to be good. I had not even thought to bring anyone with me—it was just a small lump in my neck.

When I was told that I had tonsil cancer caused by a virus I was surprisingly reassured because the surgeon said it usually responds well to treatment. My mother, father, and sister all had passed away from cancer, but they were told that it was serious right from the first consultation. I had never heard of tonsil cancer or HPV although I wondered how I got it and why I wasn't offered a vaccination when I was younger. As the disease was in my lymph nodes, I required radiation and chemotherapy. The first couple of weeks of treatment were ok. By the third week I had serious difficulty swallowing food or still water. I lost my sense of taste and both my throat and neck burned. I lost hair at the back of my head, and my neck and face became swollen. I lost my self-confidence and rarely left the house. I lived on moist soft food such as rice pudding. After my treatment, my fatigue continued to worsen, and I gained weight (particularly around my neck and face). I was referred by my GP to the lymphoedema physiotherapist, but she suggested it might be low thyroid levels. When this was treated by my GP, I began to feel much better.

My dry mouth is now a constant companion that I have grown used to. I purchase 15 L of water every week and always have a bottle of water with me. This gives me confidence during conversations and allows me to eat food socially. Artificial saliva mouthwash, particularly at night, helps me sleep. Without the mouthwash my mouth is like sandpaper when I wake up. I always have my moisturising mouth spray with me. I now know what foods to avoid. I do miss coffee but unfortunately caffeine greatly worsens my symptoms. I now can only chew my food on one side of my mouth because I needed to have two teeth removed before my treatment.

I found returning to my work as a chef initially difficult. Although my taste had returned to normal, I doubted myself and had to squash the urge to over-season food. I was lucky to have very supportive colleagues, and my confidence has now fully returned.

My family were very supportive, and I wonder how I would have coped without them. I would tell anyone going through this journey that you are not alone. There are numerous avenues of support available to you—but it is important that you just ask. Although the treatment side effects are difficult at the start, they do get better over time and you will find treatment that works for you.

How is it managed?

Although treatment is similar for HPV positive and HPV negative OPSCC, outcomes are considerably better for patients with HPV positive OPSCC.

Radiotherapy is the primary treatment for both HPV positive and negative OPSCC, particularly in European centres. Intensity modulated radiotherapy has largely replaced open surgery, offering improved quality of life with lower morbidity and mortality.[48]

Competing interests: None declared.

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Find the full version with references at doi: 10.1136/bmj-2025-086142

EDUCATION INTO PRACTICE

- In a patient over 40 years of age presenting with a sore throat and a neck lump, what symptoms and signs would prompt a red flag referral to an ear, nose, and throat clinic?
- How would you assess and investigate a cystic neck mass in a patient over 40 years of age?
- When might you consider engaging members of the multidisciplinary team, recognising that early involvement could improve treatment tolerability and long term outcomes?

OPINION Jonna Kuntsi

We need greater awareness of the ADHD continuum

The debate around attention deficit/hyperactivity disorder (ADHD), in the media and the clinical-scientific world, has recently reached new heights. This is partly due to many countries seeing a large increase in the number of people seeking ADHD assessment and diagnosis. One aspect of the discourse that is leading to confusion and misunderstanding is the lack of awareness that ADHD exists on a continuum. While the existence of autism on a spectrum is now widely accepted, understanding of the ADHD continuum lags behind.

There is strong evidence, including genetic evidence, that ADHD is the extreme of quantitative traits. The dimensionality of ADHD is already reflected in the diagnostic process: how ADHD is measured and diagnosed relies on quantitative measures of symptoms and how impairing they are. Diagnosis represents a cut-off on a dimension: the number of symptoms required to reach an ADHD diagnosis has varied in different versions of the diagnostic classification systems over time. For example, the latest version of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) lowered the number of symptoms required to meet diagnosis in adults, from six to five symptoms, in either the inattention or the hyperactivity-impulsivity domain. Changes over time show how the diagnostic cut-off is not set in stone and can be adjusted along the ADHD continuum, when new evidence emerges among specific age groups about the extent of symptoms and impairment that are considered severe enough to require treatment.

Clear acknowledgment and open discussion about the ADHD continuum should help us better understand the condition, target interventions, and consider the broader social context. Some people being assessed for ADHD will have symptoms that severely impair their daily lives. But others will unavoidably be close to the diagnostic cut-off, given the dimensional nature of how we measure ADHD. This also means that different people with an ADHD diagnosis can vary in the severity of their symptoms and how impairing they are.

In addition, the same person can also show substantial fluctuations in symptom severity over time. While ADHD is linked partly to genetic and biological underpinnings, how symptoms are expressed and how impairing they are can vary depending on the social and environmental context. We need more research on how best to target interventions to different severities of ADHD symptoms.

Context dependence

When people with ADHD are compared with people without the condition, differences are observed at all levels of investigation, from genetics and neurotransmitters to brain structure and cognitive performance. However, such correlates also vary on a continuum. We can consider cognitive performance as an example: if we ask a large group of people with and without ADHD to perform a cognitive task measuring attention, we will observe a range of scores in both groups. Although the mean score among people with ADHD will be towards one end of the scale, there will be some overlap in the scores in the two groups.

The extent to which a person's ADHD symptoms—inattention, hyperactivity, and impulsivity—are an impairment in everyday life is dependent on the societal context. A child's restlessness and challenges in concentrating are not likely to cause major problems when playing in a playground, but they can emerge as a cause for concern at the start of school because of the expectations of focused academic work in the classroom. Acknowledging the role of social context can help to indicate when the need for intervention and support is greatest: when there's a mismatch between the environmental demands and the characteristics of the person with ADHD.

Recognising people who fall just above or below the diagnostic cut-off helps us interpret multinational research evidence for the "relative age" effect for ADHD. Children who are the youngest in their class are more likely to be rated as high for ADHD symptoms and to receive an ADHD diagnosis than older children in the same class. Here, we need to keep in mind that ADHD in children is rated and diagnosed relative to others of the same age and that the symptoms must be inappropriate for their developmental level. Children who are younger in their class with "borderline" levels of ADHD symptoms may be more likely, if they are inappropriately compared with their older peers, to be referred for a diagnostic assessment and therefore also to receive a diagnosis.

Increased awareness and acknowledgment that we all fall somewhere along the ADHD continuum—as we do along the spectrum of autism or levels of anxiety—could help reduce stigma and misunderstandings that are still pervasive in many media and clinical-scientific debates. The language we use matters: how health professionals, researchers, teachers, and the media describe ADHD and interpret or communicate research findings is a powerful tool. Greater awareness of the ADHD continuum—of the varying severity and how impairment is linked to the societal context—can also inform better targeted interventions.

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STATE OF THE ART REVIEW

Atypical diabetic neuropathies

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This is a summary of Clinical Review Atypical diabetic neuropathies. The full version can be read here: https://www.bmj.com/content/390/bmj-2024-081109

CPD READING
0.5 HOURS

Peripheral neuropathy, manifesting as a distal, symmetric polyneuropathy, is estimated to occur in up to half of patients with diabetes.[1] However, diabetes is also associated with development of several other peripheral nerve manifestations, which we collectively refer to as "atypical diabetic neuropathies." These conditions include treatment induced neuropathy of diabetes, radiculoplexus neuropathy, mononeuropathies, and the special case of chronic inflammatory demyelinating polyneuropathy, which may be associated with diabetes but is not an atypical diabetic neuropathy in itself.

Epidemiology

Diabetes affects 9.3% of the world's population,[3] and diabetic polyneuropathy may occur in up to a half of all patients with diabetes.[1] With the possible exception of diabetic mononeuropathies, the individual forms of atypical diabetic neuropathies are much less common. Carpal tunnel syndrome is the most common atypical diabetic neuropathy, affecting approximately 20-30% of the diabetes population.[4 5] Cranial neuropathies occur in about 1% of patients with diabetes, representing a 10-fold higher frequency than in the general population.[6]

Although the overall risk of treatment induced neuropathy of diabetes is not well established, results from a single large diabetes centre estimated an incidence of around 10% in patients with diabetes over a five year period.[11] The yearly incidence of lumbosacral radiculoplexus neuropathy is around 4 per 100 000 and estimated lifetime incidence in patients with diabetes is approximately 1%.[4 12] Chronic inflammatory demyelinating polyneuropathy is a rare disorder, with prevalence estimates ranging from 0.7 to 10.3 cases per 100 000 people.[13]

WHAT YOU NEED TO KNOW

- Roughly half of all patients with diabetes will develop a typical distal, symmetric polyneuropathy, but several other atypical peripheral nerve conditions can also occur
- Treatment induced neuropathy of diabetes is an acute and severely painful small fibre neuropathy that occurs in association with a precipitous drop in glycated haemoglobin levels
- Radiculoplexus neuropathies include lumbosacral, cervical, and thoracic forms in which pain and weight loss are followed by weakness and sensory loss in the distribution of a single anatomical region
- Monophasic cranial mononeuropathies are caused by non-inflammatory microvascular ischaemia and present acutely followed by slow improvement. Patients with diabetes are also at increased risk for compressive neuropathies
- Increased prevalence of chronic inflammatory demyelinating polyneuropathy in patients with diabetes is suspected, although definitive diagnosis is challenging in the setting of diabetes

Treatment induced neuropathy of diabetes

Pathophysiology

The pathophysiology of treatment induced neuropathy of diabetes is not well understood. Skin biopsies from affected patients show borderline or reduced intraepidermal nerve fibre density with small and medium sized nerve fibre swellings.[2] Treatment induced neuropathy of diabetes is associated with a high rate of concurrent microvascular complications, especially onset and/or progression of retinopathy and nephropathy.[2 11] These observations suggest a likely primary contribution of microvascular dysfunction underlying development of treatment induced neuropathy of diabetes (figure).[2 11]

Proposed mechanisms driving microvascular disease include neuronal ischaemia, potentially in the setting of arterio-venous shunting or hypoglycaemia induced neuronal microvascular damage, as well as inflammatory injury due to cytokine release.[2]

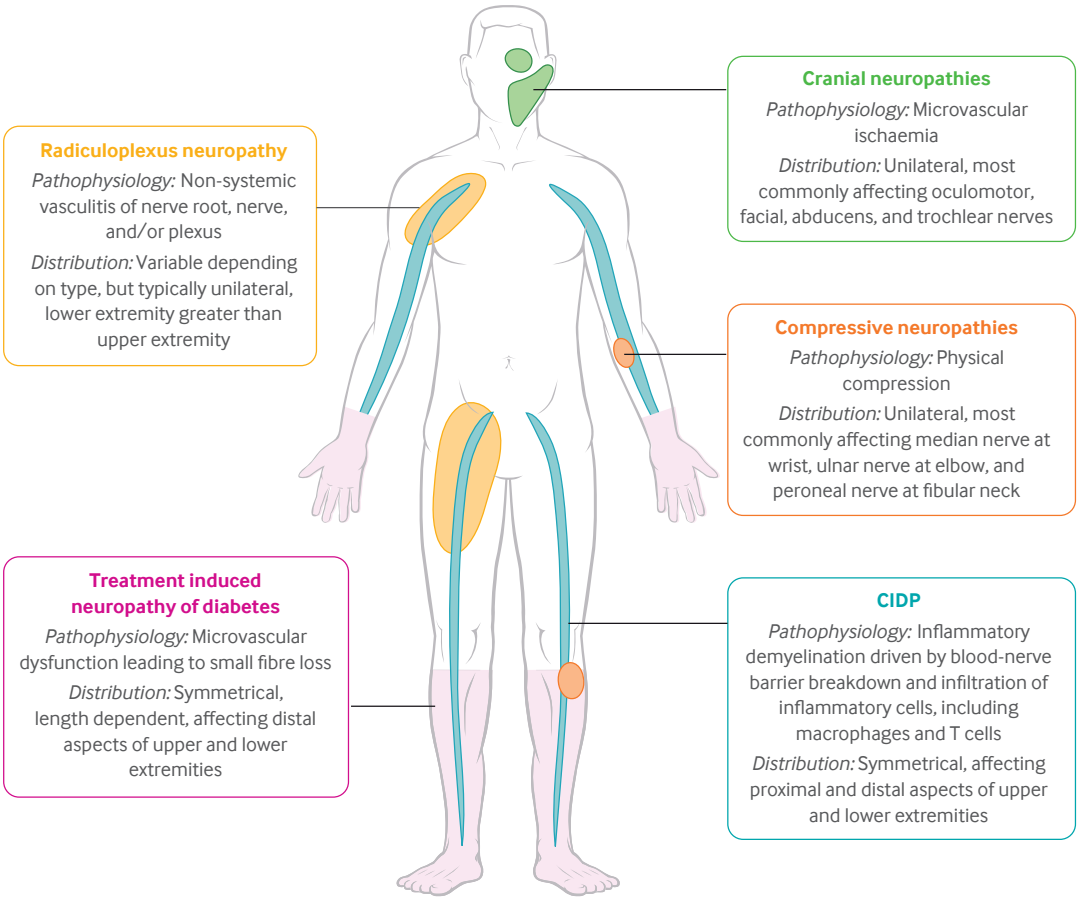
Clinical features

The key precipitant of treatment induced neuropathy of diabetes is a rapid improvement in glucose control occurring over a period of less than three months.[2 11 19] In addition to pain, autonomic features are also prominent, including orthostasis, gastrointestinal dysfunction, and sexual dysfunction. Patients with type 2 diabetes account for more than 70% of cases.[11] Longstanding hyperglycaemia is a prerequisite for development of treatment induced neuropathy of diabetes, it has not been observed in patients with abnormal glucose concentrations for less than six months.

Mean age at onset is 25 years in type 1 diabetes and 51 years in type 2 diabetes, and female patients account for 79% and 46% in type 1 and type 2 diabetes, respectively.[11] Risk of treatment induced neuropathy of diabetes is directly proportional to the rate of decline of the percentage of glycated haemoglobin.[11]

Diagnosis

Diagnosis of treatment induced neuropathy of diabetes rests on recognising the typical clinical presentation of acute, severe, primarily length-dependent pain and sensory disturbances in the upper and lower extremities occurring within six to eight weeks of rapid correction of glycated haemoglobin levels.[2] Tracking previous



Pathophysiology and distribution of atypical diabetic neuropathies. Radiculoplexus neuropathies result from inflammatory vasculitis and can affect nerves/roots/plexi of the lower extremities, upper extremities, or thoracic segment. Treatment induced neuropathy of diabetes is due to microvascular dysfunction and causes a length dependent sensory neuropathy. Cranial neuropathies are caused by non-inflammatory microvascular ischaemia most commonly affecting the oculomotor, facial, abducens, and trochlear nerves. Compressive neuropathies are caused by mechanical compression and most commonly affect the median, ulnar, and peroneal nerves. Chronic inflammatory demyelinating polyneuropathy (CIDP) is an inflammatory demyelinating neuropathy that affects proximal and distal segments of nerves leading to sensory loss and weakness of the extremities

HbA_{1c} levels is often all that is needed to diagnose this condition.

Neuropathic pain is the primary feature and generally occurs in a stocking-glove distribution affecting the distal aspects of the legs and hands, although more diffuse and proximal distributions can occur. Hyperalgesia, allodynia, and paraesthesia in the same regions as neuropathic pain are frequently reported.

In most patients, neurological examinations show length-dependent reductions in pain and thermal sensation with variable reduction in vibratory sensation. Motor function is uniformly unaffected, except in cases of recurrent treatment induced neuropathy of diabetes. Autonomic features are prominent, with patients reporting orthostatic symptoms (lightheadedness, dizziness, presyncope, syncope), gastrointestinal symptoms (nausea, vomiting, diarrhoea, loss of appetite, early satiety), and sexual dysfunction.[2 11]

Treatment

Pain management and prevention of future episodes are the primary treatments. Pain is typically severe and refractory to drugs for neuropathic pain. Even with combinations of two or three drugs at maximal doses, most patients experience a prolonged period of persistent and debilitating pain.[2] Tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, gabapentinoids, and sodium channel blockers are used.[20]

Longitudinal data indicate that stable glycaemic control is an important aspect of long term management of treatment induced neuropathy of diabetes.

Prognosis

The underlying neuropathy and associated symptoms improve greatly in most cases, with patients reporting gradual improvements in pain over 18-36 months and an average time to 50% reduction in pain of 15 months.[2 19] In this setting, most patients are able to tolerate weaning off neuropathic pain drugs, and autonomic symptoms generally improve concurrently with resolution of pain. The gradual improvement in symptoms is dependent on stable glycaemic control.

Patients with fluctuations of glycaemic control outside of the ideal range of HbA_{1c} are at risk of additional episodes associated with acute recurrences of neuropathic pain. Recurrent treatment induced neuropathy in type 1 diabetes seems to be commonly associated with development of motor neuropathy in addition to the typical autonomic and sensory neuropathy features.[19] Furthermore, these patients experience severe retinopathy, nephropathy, and sometimes lower extremity ulcerations, highlighting the importance of avoiding further episodes.

Radiculoplexus neuropathy

Pathophysiology

Radiculoplexus neuropathy in all forms, including diabetic, is caused by a non-systemic vasculitis of the affected nerve roots, plexus, and/or individual nerves (figure).[21] Perivascular inflammation is the hallmark on nerve biopsy, with most cases showing inflammatory

changes to the vessel wall, haemosiderin deposition, and neovascularisation.[22 23] However, the inciting event that leads to microvasculitis is not well understood.

Clinical features

Radiculoplexus neuropathy classically presents with preceding significant weight loss and acute to subacute lancinating pain, followed weeks later by muscle atrophy, weakness, and areflexia of the associated limb.[21] Although cervical, thoracic, or lumbosacral regions can be affected, radiculoplexus neuropathy most commonly affects the lower extremities, referred to as lumbosacral radiculoplexus neuropathy. Pain is a hallmark feature, but it can be absent in approximately 10% of lumbosacral presentations and 20% of cervical presentations.[26]

Diabetes is the most significant risk factor for developing lumbosacral radiculoplexus neuropathy, with an eightfold higher risk.[12] Severity and duration of diabetes do not seem to correlate well with risk of developing radiculoplexus neuropathy,[12] although rapid glycaemic control is a predisposing factor.[12] Diabetic lumbosacral radiculoplexus neuropathy is typically heralded by drastic weight loss and unilateral proximal leg pain. Over weeks to months, the pain begins to subside, but weakness develops in the proximal leg before spreading to distal myotomes, the contralateral leg (30-90%), and sometimes to the thoracic (12-14%) or cervical segments (10-15%). Around one third of patients have distal symptoms at onset, such as foot drop.[28] Paraesthesias, sensory loss, and autonomic dysfunction may also occur.[12 28-30]

Diabetic cervical radiculoplexus neuropathy presents unilaterally in most cases, with spread to the contralateral side occurring in only a minority of cases.[22] Cervical radiculoplexus neuropathy may spread to other body segments and nerves including the lumbosacral segment (24%), thoracic segment (19%), phrenic nerves (6%), cranial nerves (2%), and sympathetic chain (1%).[22] Diabetic cervical radiculoplexus neuropathy affects each trunk of the brachial plexus at a similar frequency, but it can also cause a pan-plexopathy affecting all trunks in a third of cases.[22]

Diabetic thoracic radiculoneuropathy presents with burning pain and paraesthesias in a band-like thoracic dermatomal distribution radiating around the abdomen, either unilaterally or bilaterally.[21 30] Abdominal muscle weakness can occur, resulting in focal out-pouching of the abdominal wall.[21] Significant associated weight loss is a hallmark feature.

Postsurgical inflammatory neuropathy is typically defined as a neuropathy occurring within 30 days of a surgical event and is, by definition, not directly related to surgery, positioning, or anaesthesia.[27 35] Although the overall incidence of postsurgical inflammatory neuropathy has not been established, diabetes was the most common pre-morbid risk factor, present in 33% of cases.[27]

Finally, patients with diabetes can rarely develop a form of multiple mononeuropathies, also known as mononeuritis multiplex of diabetes.[24 25] Patients typically show preferential involvement of the peroneal and ulnar nerves with limited proximal weakness,[36] creating at least some clinical distinction from typical radiculoplexus neuropathy. Furthermore, some patients with multifocal diabetic neuropathy have a relapsing clinical course.[24]

Diagnosis

Although the diagnosis of radiculoplexus neuropathy is based on clinical history and examination, electrodiagnostic testing can aid in the localisation of the nerve injury to the nerve roots and plexus, which dramatically narrows the differential diagnosis. Magnetic resonance imaging of the involved nerve roots and plexus can be supportive and can serve an essential role in evaluating alternative diagnoses such as mechanical compression, infiltrative malignancy, post-radiation neuropathy, infectious radiculitis, amyloidosis, sarcoidosis, and vasculitis/connective tissue disorders.[37] Notably, clinical improvement following the subacute phase is typical of radiculoplexus neuropathy but not its disease mimics. Routine serological testing for the above mimics should be considered in suspected cases. Laboratory findings may include non-specific elevation of erythrocyte sedimentation rate, rheumatoid factor, and antinuclear antibody titres.[28] Lumbar puncture and nerve biopsy can be considered to rule out other diagnoses. Cerebrospinal fluid studies often show elevated protein without cells or oligoclonal bands.[28]

For suspected mononeuritis multiplex of diabetes, definitive diagnosis requires nerve biopsy for confirmation of typical pathological features of microvasculitis.[24 25]

Treatment

Treatment is supportive, including physical therapy, pain control, bracing where appropriate, and treatment of depression as needed. Drug therapy for neuropathic pain should be offered.[28 39] Maintaining good diabetic control is an important component of management.[37]

Given limited data on mononeuritis multiplex of diabetes, whether treatment for such patients should be similar to that for radiculoplexus neuropathy or to that for non-systemic vasculitis without diabetes is unclear.

Prognosis

Diabetic radiculoplexus neuropathy affecting any anatomical region is usually monophasic and self-limited. Nearly all patients recover, although the extent of recovery is variable. Symptoms continue to worsen for an average of two to three months and up to 18 months before stabilising and then improving.[22 27-29] Pain typically improves before weakness does. Morbidity from radiculoplexus neuropathy is due to severity of pain and weakness leading to functional impairments. In lumbosacral radiculoplexus neuropathy, 25-50% of affected patients will need to use a wheelchair at some point, with this number improving to 10-15% at follow-up.[28 29] Foot drop is the most common residual deficit.[28] Estimates of relapse in radiculoplexus neuropathy vary, ranging

from 5% to 20% of diabetic lumbosacral radiculoplexus neuropathy and 21% of cervical radiculoplexus neuropathy.[12 22 30] In mononeuritis multiplex of diabetes, pain usually resolves within weeks, especially in patients who receive corticosteroids. Motor deficits typically improve gradually over several months, with minor to moderate residual deficits remaining in approximately 50% of patients.[24]

Mononeuropathy

Pathophysiology

Mononeuropathies in diabetes can be related to entrapment or microvascular nerve ischaemia (figure). The risk of nerve entrapment in diabetes is increased through several metabolic and structural mechanisms. Hyperglycaemia itself leads to inappropriate osmolyte and sorbitol accumulation, glucose driven oxidative stress, and cell damage due to protein glycation.[51] The combination of up regulation of vascular endothelial growth factor resulting in increased vascular permeability and angiogenesis as well as hyperosmotic effects of sorbitol and other products can also cause nerve oedema, predisposing to nerve compression.[52 53] Furthermore, accumulation of advanced glycation end products in the extracellular matrix leads to mechanical stiffening of connective tissue and increased susceptibility to nerve compression and trauma.[54]

In contrast to entrapment neuropathies, the pathological findings and association with risk factors for cardiovascular diseases and ischaemic stroke indicate that facial and cranial nerve palsies result from non-inflammatory microvascular ischaemia.[55 56] In oculomotor mononeuropathy, for example, studies have shown axonal degeneration limited to the central portion of the nerve trunk, hyalinisation of the vessel walls, and narrowing of the lumen of the intraneural arterioles in very short segments of the nerve, but no evidence of inflammation.[57-59]

Clinical features

Nerve entrapment is the main cause of focal mononeuropathies in diabetes. It can occur at any stage of the disease and may be asymptomatic.[60] Such entrapment neuropathies include median neuropathy at the wrist, ulnar neuropathy at the elbow, and peroneal neuropathy at the knee, with wrist neuropathy being the most prevalent.[60 61] A recent meta-analysis of 42 observational studies showed that diabetes was a risk factor for symptomatic carpal tunnel syndrome with an odds ratio of 1.68 (95% confidence interval 1.45 to 1.94).[62]

Asymptomatic median neuropathy at the wrist is also common in patients with diabetes, with a reported prevalence of 25-30%.[4 63 64] On the other hand, the association between ulnar neuropathy at the elbow and diabetes is not as well established. The prevalence of peroneal neuropathy at the knee varies widely among individuals with diabetes, ranging from 3% to 60%.[68-70]

Cranial neuropathies also occur as complication of diabetes. The oculomotor and facial nerves are the most frequently affected, followed by the abducens and trochlear nerves.[6 7]

Diagnosis

Recognition of symptoms and signs in a particular nerve distribution is the first step for diagnosis. Entrapment neuropathies have a gradual onset, progress slowly, and persist without intervention.[60] Electrodiagnostic testing aids in localising neuropathy at compression sites and differentiates it from other conditions with similar symptoms, such as radiculopathies.[74] Ultrasonography is a cost effective diagnostic method that is particularly useful in cases with atypical presentations and when electrodiagnosis cannot localise the entrapment.[75] Cranial mononeuropathies have an acute onset, do not progress, and are diagnosed on the basis of clinical presentation.[76]

Treatment

Management of entrapment neuropathies is largely dictated by severity. Mild to moderate cases are amenable to conservative measures such as wrist splinting for carpal tunnel syndrome. For refractory and severe cases of carpal tunnel syndrome, local corticosteroid injection at the wrist and surgical decompression are recommended.[7] Surgical intervention may be considered for refractory and severe cases of ulnar neuropathy at the elbow.[77]

Management of oculomotor neuropathies is conservative, focusing on the control of cardiovascular risk factors, the use of eye patches to reduce diplopia, and adhesive tape to prevent corneal injury due to incomplete eyelid closure.[78] For facial mononeuropathy, a short course of oral corticosteroids starting within 72 hours from onset may improve recovery.[79]

Prognosis

Most patients with carpal tunnel syndrome experience significant improvement with non-surgical measures or surgical decompression.[80] Some studies have reported slower improvement and worse outcomes in patients with diabetes[81-83]; however, a meta-analysis of 10 studies concluded that improvement of patient reported outcomes following carpal tunnel release did not differ between patients with and without diabetes.[84] For ulnar neuropathy at the elbow, 89%, 67%, and 38% of mild, moderate, and severe cases, respectively, improve with non-surgical treatment.[85] However, patients with diabetes show worse patient reported outcomes after surgery for cubital tunnel syndrome versus patients without diabetes.[86]

Oculomotor mononeuropathy has a monophasic course, with most patients experiencing either complete or partial improvement.[87 88] The presence of diabetes does not seem to affect recovery from facial neuropathy.[89] Poor prognostic factors include the severity of facial weakness at the time of maximum deficit and a low compound muscle action potential on electrodiagnostic studies.[90]

Chronic inflammatory demyelinating polyneuropathy and potential association with diabetes

Pathophysiology

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune mediated polyradiculoneuropathy that involves cellular, humoral, and complement mediated pathomechanisms in the setting of a likely but unidentified antigenic trigger (figure).[91] Upstream, breakdown of the blood-nerve barrier occurs, which allows for passage of inflammatory cells into the peripheral nervous system.[92]

Multiple possible reasons are posited for why diabetes may predispose to CIDP. However, limited, if any, human data exist on the underlying pathophysiology.

Clinical features

CIDP is a chronic, painless, and progressive demyelinating disorder of motor and sensory large fibre nerves characterised by symmetrical proximal and distal weakness with associated hyporeflexia or areflexia. It is a clinical diagnosis supported by concordant electrodiagnostic criteria.[105] In contrast to the previously discussed atypical diabetic neuropathies, the relation between CIDP and diabetes remains controversial, but it is an important diagnostic consideration in patients presenting with atypical diabetic neuropathies.

Diagnosis

The diagnosis of CIDP requires electrodiagnostic testing. However, it is often incorrectly diagnosed, with 32-45% of patients with CIDP being found to be misdiagnosed after careful review.[116-118] Recognition is particularly challenging in patients with diabetes (so called CIDP-diabetes), especially those with concurrent diabetic polyneuropathy. Clinical diagnostic criteria for CIDP stipulate the presence of proximal and distal weakness in the setting of hyporeflexia or areflexia in all limbs and progression over at least eight weeks.[97]

By contrast, diabetic polyneuropathy is typically sensory predominant and slowly progressive and carries minimal motor deficits beyond weakness of toe extension.[119] The presence of proximal arm and leg weakness is particularly important as it is a hallmark of CIDP and absent in typical diabetic polyneuropathy. Patients in whom CIDP is ultimately diagnosed on electrodiagnostic testing rarely present at disease onset with a distal symmetric polyneuropathy pattern as is typical in diabetic polyneuropathy.[121]

An additional challenge in diagnosing CIDP-diabetes is that diabetes itself can induce conduction velocity slowing on nerve conduction studies.[122] Protein concentrations in cerebrospinal fluid, which are often helpful in the diagnosis of CIDP, are hard to interpret in patients with diabetes and suspected CIDP as diabetes alone often leads to elevated cerebrospinal fluid protein.[124 125]

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS MANUSCRIPT

A person with type 1 diabetes and diabetic polyneuropathy reviewed a draft of the manuscript and offered input on the content. They asked specific questions to clarify the risk factors for treatment induced neuropathy of diabetes and whether patients can develop more than one neurological complication of diabetes concurrently. We edited the manuscript to cover these and other specific points raised by the patient reviewer.

Prognosis

When patients with combined CIDP-diabetes are compared with patients with diabetes and a distal only (diabetic polyneuropathy) demyelinating phenotype, patients with CIDP-diabetes are older,[124] have a shorter duration of diabetes, and have more severe disease.[132] The increased disease severity in the combined CIDP-diabetes group is despite better glycaemic control. A retrospective European cohort from Serbia and the UK also found combined CIDP-diabetes to present later in life than CIDP only (59 *v* 52 years), although with similar baseline disease severity and with comparable treatment responses.[109] An Italian study of 393 patients with CIDP found that patients with diabetes generally had more severe disability scores, worse quality of life, and less frequent treatment response, with comorbidity having an effect on treatment choice in nearly half of cases.[110] At six month follow-up, patients with CIDP seemed to respond better to immunotherapy than did patients with CIDP-diabetes.[125] However, the potential long term therapeutic benefit of intravenous immunoglobulin in CIDP-diabetes should not be overlooked, as patients can benefit considerably. In one longitudinal study, neuropathy impairment scores improved from 38 to 16 by 40 months' follow-up.[133]

Emerging treatments

The use of glucagon-like peptide 1 (GLP-1) based therapies for the treatment of diabetes, weight management, and non-alcoholic steatohepatitis is rapidly increasing. These agents are highly effective in reducing HbA_{1c} levels in patients with type 2 diabetes.[134] Regarding an effect of GLP-1 based therapies on modifying risk of developing of diabetic polyneuropathy, a study of more than 5000 patients with type 2 diabetes treated with one of two GLP-1 agonists versus insulin glargine or glimeperide (each in combination with metformin) found no significant difference in the incidence of neuropathy over five years of follow-up.[144] Understanding how the next generation of GLP-1 based therapies affects typical and atypical diabetic neuropathy will be an important focus for future research.

Competing interests: See bmj.com.

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When chest pain tells an emotional truth

Helen Watkins shares the physical symptoms brought on by heartache and what healthcare professionals can do to recognise a person's emotional pain

Six years ago, I went to the emergency department with chest pain. I had experienced severe pain during the previous night, pain which radiated to my back and ears. I didn't disturb my husband, as we had arrived home in the UK from Australia only a few days earlier and were both still tired with jetlag. I told him the next morning, and we decided I should see my GP that day. The GP sent me to hospital to have my heart and troponin levels checked. My ECG showed no evidence of a heart attack and the blood tests were fine. I was discharged with a diagnosis of chest pain with an unknown cause, with a secondary provisional diagnosis of acid reflux. But I knew the real diagnosis was, quite simply, heartache.

When I had entered my GP's surgery, I explained my symptoms. I said I thought they were probably due to "heartache." And I explained the reasons why. I realised a heart attack should be ruled out, so I understood the need to send me to hospital and to ensure my physical safety, which I greatly appreciated.

Appreciating emotional pain

When I left Australia a few days earlier, I had left behind our daughter, son-in-law, one month old first grandchild, and our son. I wasn't expecting to see any of them again for at least a year. I felt bereaved. I tried to tell the health professionals in the hospital the social and emotional context for my pain. It was relevant to them as well as to me. It simply didn't appear to register with them or factor in their process of coming to a diagnosis. Physical signs and symptoms obviously need to be given priority and investigated, but emotional components can also be important.

It seemed that, once they were satisfied that the pain had not been cardiac in origin, they needed to find another plausible physical reason. I had become a checklist rather than an individual. If they had considered me to be an integral part of the diagnostic team, I would have felt heard and valued, with my physical and emotional pain both given validity. I knew the health professionals could not cure my heartache and I did not expect them to. I just wish their thoughtful care for my physical symptoms had extended to me as a whole person by acknowledging the pain I was feeling due to leaving my family.

PRIYA SUNDRAM

CPD READING
0.5 HOURS

Physical and emotional connections

Our language is rich in adages that can point to an emotional truth hiding behind, or prompting the manifestation of, a physical symptom. Feelings are so often given visible life and embodied. Think of some of the phrases commonly used: "I was gutted," "My heart was in my mouth," "My legs turned to jelly." They are all associated with stressful events, with anxiety, with shock. I had temporarily been "heartbroken."

I am blessed, or cursed, with a very explicit and often exaggerated connection between my feelings and their demonstration in the form of bodily symptoms. For example, I get symptoms of irritable bowel syndrome after episodes when I have been stressed. I suppose adrenaline gets me through the event, then when I relax, the bloating and abdominal pain briefly manifest. My emotional state is closely bound up with my physical state.

So, the next time someone presents with a physical symptom, please pay heed to the language with which they describe it. It is relevant. The words used, however commonplace they may sound, can reveal more of the iceberg, below the tip which is easily seen during a consultation. Active listening may add significantly to your appreciation of their feelings and dilemma. It may enhance the quality of the care you provide, and thus your professional satisfaction. And your patient will really feel heard.

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WHAT YOU NEED TO KNOW

- Actively listen to possible emotional causes for physical symptoms. They can provide you with key insights when formulating a diagnosis.
- Do not focus only on physical signs and symptoms which you can easily measure and assess. Keep an open mind about other, wider possibilities.
- Briefly acknowledge any emotional distress that a patient shares with you. It is a privilege to be trusted in this way and can ensure the patient feels heard and supported.

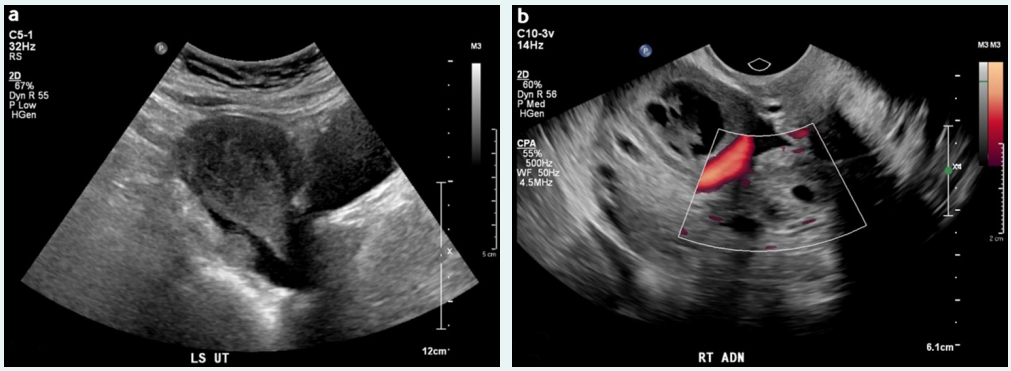
EDUCATION IN PRACTICE

- How could you ask about and acknowledge any emotional pain a patient is experiencing?
- What can you do to ensure patients feel they are heard, when sharing their reasoning about a possible diagnosis?

SPOT DIAGNOSIS

Acute abdominal pain in a young woman

A woman in her 20s presented to the emergency department with a one day history of severe lower abdominal pain and vaginal bleeding. Her previous menstrual period was 5 weeks earlier. She was not using any form of contraception, and had no relevant medical, gynaecological, or surgical history apart from a previous caesarean section. On admission, her temperature was 37.4°C. Her heart rate was 100 bpm with a blood pressure of 102/65 mm Hg. Abdominal examination revealed tenderness over the suprapubic region on deep palpation. Speculum examination showed a closed cervical os with no bleeding or retained product of conception. A urine pregnancy test was positive and her serum β human chorionic gonadotropin (hCG) level was 1724.2 IU/L (normal range <5 IU/L). Other laboratory tests showed a haemoglobin level of 114 g/L (normal range 120-160 g/L), white blood cell count of 17.27×10^9/L ($4.0\text{-}10.0\times10^9$/L), and platelet count of 311×10^9/L ($140\text{-}440\times10^9$/L). Urgent transabdominal and transvaginal pelvic ultrasonography were performed (figure).



Selected transabdominal (a) and transvaginal (b) pelvic ultrasonography images

What is the diagnosis?

Submitted by Wenwen Ni and Timothy Shao Ern Tan

Patient consent obtained.

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answers

SPOT DIAGNOSIS **Acute abdominal pain in a young woman**

What is the diagnosis?

A ruptured right tubal ectopic pregnancy with haemoperitoneum. An ectopic pregnancy occurs when a fertilised egg implants outside the uterus and is potentially life threatening if missed. Approximately one in 100 pregnancies are ectopic. Although the most common location is in the fallopian tube (~96%), ectopic pregnancy can also occur in the interstitial portion of the fallopian tube, cervix, ovary, caesarean scar, or abdominal cavity. Risk factors include previous ectopic pregnancy, pelvic inflammatory disease, pelvic and tubal surgery, use of intrauterine device, in vitro fertilisation, and smoking.

Patients might present with lower abdominal pain and might report a missed menstrual period or vaginal bleeding. Dizziness and fainting due to blood loss could indicate a ruptured ectopic pregnancy. However, history and physical examination alone are insufficient to confirm or exclude the diagnosis because up to one in three affected patients might have no frank clinical features such as severe abdominal pain or adnexal tenderness.

Transvaginal ultrasonography is the preferred imaging modality for diagnosis, with a high sensitivity and specificity. The most common finding of a tubal ectopic pregnancy seen in 95% (range 89% to 100%) of patients is an extraovarian adnexal mass. Colour Doppler ultrasonography might show peripheral hypervascularity surrounding the adnexal mass—the ring of fire sign. When the ring of fire sign is seen in an extraovarian location, especially in the presence of an adnexal mass, tubal ectopic pregnancy can be confidently diagnosed.

According to the latest National Institute for Health and Care Excellence guidelines, management of tubal ectopic pregnancy can be expectant, medical (with methotrexate), or surgical, depending on the patient's clinical status, ultrasound findings, and serum β-hCG levels. Patients opting for expectant management should undergo close monitoring with serial β-hCG measurements and be appropriately counselled on signs of rupture.

LEARNING POINTS

- Ectopic pregnancy is a potentially life threatening condition that must be considered in a patient of reproductive age presenting with acute abdominal pain.
- Transvaginal ultrasonography is the first line imaging modality used to evaluate for tubal ectopic pregnancy, with high sensitivity and specificity.
- Management of ectopic pregnancy can employ expectant, medical, or surgical approaches and should be individualised based on clinical presentation, imaging findings, and serial serum β-hCG levels.

PATIENT OUTCOME

See bmj.com.

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