education

FROM THE JOURNALS Edited highlights of weekly research reviews

Compression chamber

Training sessions on basic life support always relax a bit once everyone's had a go at chest compressions and debated which song should be sung to get the right tempo. The awkwardness remains but takes on a different quality—like an ambulance siren that sounds different once it's moving away from you. Speaking of blue-light ambulances, should they be going to A&E or straight to the catheter lab after an out-of-hospital cardiac arrest?

A multicentre, open-label, randomised trial enrolled 554 patients who had an out-of-hospital cardiac arrest without ST segment elevation to either immediate angiography or initial intensive care assessment (then delayed or selected angiography). It found no statistically significant difference in death at 30 days, with 54% dying in the immediate angiography group and 46% in the delayed group.

N Engl J Med doi:10.1056/NEJMoa2101909

I can't get no sleep

I've managed to repress most memories of hospital night shifts, but the sounds of a ward at night stick in my mind—along with the faces of patients unable to sleep from the sound of clinical waste bins closing, trolley wheels squeaking, and strangers' snores. As well as being another part of the misery of being in hospital, disturbed sleep is a common cause of delirium.

Might there be a digital solution to the sleep deprivation of hospital in-patients? Researchers in California devised a decision support tool driven by a "real-time prediction algorithm" to see if identifying inpatients on general wards who could safely forgo four hourly observations overnight would reduce the incidence of delirium. It didn't, but neither did they see any increase in intensive care admissions or resuscitation calls.

JAMA Intern Med doi:10.1001/jamainternmed.2021.7387

Clotting factors

When new evidence makes guideline recommendations out of date, it can take years for these to be updated. Living guidelines seek to address this, by updating parts of a guideline as needed. One example is the NICE rapid covid guideline, which has been updated 12 times since it was published in March 2021, but which currently offers no recommendations on thromboprophylaxis in patients discharged from hospital after covid-19.

An open-label randomised controlled trial recruited patients being discharged from hospital after covid-19 who were at high risk of venous thromboembolism (VTE). Three of the 159 people allocated to take rivaroxaban 10 mg for 35 days had a thrombotic event (symptomatic or fatal VTE, asymptomatic VTE, symptomatic arterial thromboembolism, and cardiovascular death), compared with nine of the 159-person control group (P=0·0293).

Although these findings seem promising, I suspect guideline groups will wait for other studies to report before making any recommendations: it's a relatively small study and the rates of VTE were much higher (5% of the control group had a symptomatic or fatal VTE) than observed elsewhere (it's typically 0.5-1.6% in people discharged from hospital after covid-19).

Lancet doi:10.1016/S0140-6736(21)02392-8

Going with the flow

The false positive rates of lateral flow tests are back in the spotlight after the change in policy in England so that people who do not have symptoms of covid-19 but do have a positive lateral flow test no longer need to have a confirmatory PCR test.

Researchers in Canada reviewed 903 408 rapid antigen tests conducted over 537 workplaces between January and October 2021. A remarkable 278 (60%) of the 462 false positive results occurred in two workplaces and were drawn from a single batch of lateral flow tests. The authors highlight the need to have systems in place that can quickly identify these issues. Fortunately, in the UK we have two systems for logging positive lateral flow tests: the gov.uk website and posting a photo of your positive test on social media along with a sad/shocked/masked face emoji.

JAMA doi:10.1001/jama.2021.24355

Article of no association

A cohort study in *JAMA* provides further evidence that use of maternal hormonal contraceptives does not explain a rise in the incidence of CNS tumours in children since the 1970s. This large, prospective, population based study found no association between the two. It included all live-born children born in Denmark between 1995 and 2014—a total of 1 185 063 children—thereby winning this week's prize for best population coverage in a research paper.

JAMA doi:10.1001/jama.2021.22482

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GUIDELINES

Prevention and non-surgical management of pelvic floor dysfunction: NICE guidance

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Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on bmj.com.

Pelvic floor dysfunction is a complex condition that is associated with urinary incontinence, emptying disorders of the bladder, pelvic organ prolapse, sexual dysfunction, chronic pelvic pain, faecal incontinence, and emptying disorders of the bowel.[1 2] Approximately five million women in the UK have experienced pelvic floor dysfunction.[3] Age has an important effect, as 6% of women in their 20s experience symptoms, with this increasing to 40% of women in their 60s.[4] These symptoms can have a notable impact on quality of life. In July 2020, the Independent Medicine and Medical Devices Safety Review highlighted the major complications women faced after surgical management with pelvic mesh.[5] Preventive and non-surgical strategies can reduce the number of women developing severe symptoms and needing invasive treatment.

This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) guideline on pelvic floor dysfunction: prevention and non-surgical management. The guideline applies to women aged 12 and older.[6] It uses the term "women" throughout, but this should be taken to include those who do not identify as women but who have female pelvic organs.

WHAT'S COVERED IN THE GUIDELINE?

- Strategies to prevent pelvic floor dysfunction
- Non-specialist care options for the management of pelvic floor dysfunction
- Symptom based referral criteria for supervised pelvic floor muscle training

CPD READING
0.5 HOURS

Preventive and non-surgical strategies can reduce the number of women developing severe symptoms and needing invasive treatment

WHAT YOU NEED TO KNOW

- Modifications to lifestyle, such as increasing physical activity, having a healthy diet, losing weight, stopping smoking, and controlling diabetes can help prevent and treat symptoms of pelvic floor dysfunction
- Encouraging women to start and continue training of the pelvic floor muscles in the long term can help prevent and treat symptoms
- Pelvic floor muscle training is an effective option to treat symptoms of pelvic floor dysfunction in women with pelvic organ prolapse, urinary incontinence, and faecal incontinence

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS GUIDELINE

Committee members involved in this guideline included three lay members who, with their personal experience of pelvic floor dysfunction and previous use of relevant services, contributed to the formulation of the recommendations summarised here.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

What is pelvic floor dysfunction?

Pelvic floor dysfunction is a condition in which the pelvic floor muscles around the bladder, anal canal, and vagina do not work properly. Urinary incontinence, faecal incontinence, and pelvic organ prolapse are the three most common symptoms. Other symptoms include emptying disorders of the bladder, emptying disorders of the bowel, sexual dysfunction, and chronic pelvic pain.

Raising patient awareness of pelvic floor dysfunction

Patients may be reluctant to discuss pelvic floor dysfunction because of embarrassment. Increased awareness and understanding of the condition among healthcare practitioners can help encourage a preventive approach and support women with symptoms to seek help. Healthcare professionals may consider discussing pelvic floor dysfunction with women in primary and intermediate care services, care homes, supported living communities, and at postnatal appointments.

Good communication and sensitivity are crucial when assessing women for pelvic floor dysfunction because of the nature of the condition

Risk factors for pelvic floor dysfunction

Modifiable risk factors

- Body mass index (BMI) >25 kg/m^2
- Smoking
- Lack of exercise
- Constipation
- Diabetes

Non-modifiable risk factors

- Age (risk increases with age)
- Family history of urinary incontinence, overactive bladder, or faecal incontinence
- Gynaecological cancer and any treatments for this
- Gynaecological surgery (such as a hysterectomy)
- Fibromyalgia
- Chronic respiratory disease and cough (chronic cough may increase the risk of faecal incontinence and flatus incontinence)

Related to pregnancy

- Being over 30 when having a baby
- Having given birth before their current pregnancy

Related to labour

- Assisted vaginal birth (forceps or vacuum)
- A vaginal birth when the baby is lying face up (occipito-posterior)
- An active second stage of labour taking more than one hour
- Injury to the anal sphincter during birth.

Prevention of pelvic floor dysfunction

Improving strategies to prevent and manage pelvic floor dysfunction within the community and in primary care could potentially minimise the number of women requiring invasive surgical intervention in the future. Community based services may include physiotherapists, bladder and bowel team members, and continence advisers.

Relevant resources from Public Health England and NICE should be used by healthcare and allied health professionals to encourage women to modify their lifestyle. The resources include guidance on physical activity (for example, the UK Chief Medical Officer's guidance on physical activity[7]), weight loss (the NICE guideline on managing obesity,[8] and if relevant, the NICE guideline on weight management before, during, and after pregnancy[9]), diet (for example, the Public Health England Eatwell guide[10]), and smoking cessation (for example the NICE guidelines on stop smoking interventions and services[11]).

Pelvic floor muscle training should also be encouraged in all women (including in pregnancy), as it can prevent symptoms of pelvic floor dysfunction developing, however, adherence is key for long term effectiveness. Women can find guidance and support from the NHS website.

Assessment and diagnosis of pelvic floor dysfunction in primary care

Good communication and sensitivity are crucial when assessing women for pelvic floor dysfunction because of the nature of the condition.

Initial assessment

Depending on the symptoms described, carry out a focused history, clinical examination, and investigations to exclude other causes, such as:

- Pelvic masses
- Neurological disease
- Urinary tract infection
- Adverse effects of medication
- Diabetes
- Cancer (for further information see the NICE guideline on suspected cancer: recognition and referral[12])
- Fistula
- Inflammatory bowel or bladder conditions
- Endometriosis
- Mobility and cognitive impairment.

Ask women who have recently given birth about symptoms of pelvic floor dysfunction during routine postnatal care, in hospital, and in the community.

For women who are taking several medications, conduct a medication review. For guidance on how to do this, see the NICE guideline on medicines optimisation.[13]

Depending on the symptoms and the woman's preferences and circumstances, consider other clinical examinations. For example:

- Inspecting the woman's vulva and vagina for atrophy
- Asking them to bear down, to check for visible vaginal or rectal prolapse
- Rectal examination to check for impaction, for women who are at risk of this and who cannot give an accurate history of their symptoms (for example, women with cognitive impairments or dementia).

Managing pelvic floor dysfunction

Advise women with a BMI greater than 30 kg/m^2 that weight loss can help with the following symptoms associated with pelvic floor dysfunction:

- Urinary incontinence
- Overactive bladder
- Pelvic organ prolapse.

Do not wait for women to lose weight before starting other pelvic floor dysfunction management options.

- Explain how a balanced diet (following Public Health England's Eatwell Guide[10]) and appropriate fluid intake can improve stool consistency, which can help with their symptoms
- Advise women with overactive bladder or urinary incontinence associated with pelvic floor dysfunction to:
  - reduce their caffeine intake
  - modify their fluid intake (increasing if it is too low, decreasing if it is too high)
- For women who are doing supervised pelvic floor muscle training and want to be physically active, advise them that supervised exercise (for example, yoga) may help with their symptoms.

Pelvic floor muscle training

Pelvic floor muscle training is exercise which improves pelvic floor muscle strength, endurance, power, relaxation, or a combination of these. Unsupervised and supervised pelvic floor muscle training can improve several symptoms of pelvic floor dysfunction. For unsupervised pelvic floor muscle training, information can be obtained from sources such as leaflets, videos, and information on social media, online resources, and mobile applications. Supervised training can ensure that pelvic floor muscle contraction and relaxation is done correctly. Tailor training for each woman, to ensure that it is manageable and will meet their training goals.

- Pelvic floor muscle training programmes should be supervised by a physiotherapist or other healthcare professional with the appropriate expertise in pelvic floor muscle training.

When to consider supervised pelvic floor muscle training

Preventing symptoms

- Consider a three month programme of supervised pelvic floor muscle training:
  - From week 20 of pregnancy for pregnant women who have a first degree relative with pelvic floor dysfunction
  - During postnatal care, for women who have experienced any of the following risk factors during birth:
    - assisted vaginal birth (forceps or vacuum)
    - a vaginal birth when the baby is lying face up (occipito posterior)
    - injury to the anal sphincter.

Managing symptoms

- Consider a programme of supervised pelvic floor muscle training for at least four months for women with symptomatic pelvic organ prolapse that does not extend greater than 1 cm beyond the hymen upon straining.
- Offer a programme of supervised pelvic floor muscle training for at least three months to women (including pregnant women) with stress urinary incontinence or mixed urinary incontinence.
- Consider a programme of supervised pelvic floor muscle training for at least four months for women with faecal incontinence and co-existing pelvic organ prolapse.

Additional management options to consider

In women with pelvic floor dysfunction, devices can be placed into the vagina to provide additional support to the pelvic floor and relieve symptoms. Women can self-manage these devices in the community if they wish, with instruction and advice from clinicians regarding removal, cleaning, and re-insertion.

Intravaginal devices

In women with stress urinary incontinence, an intravaginal device can support the urethra and prevent urinary leakage. Several different intravaginal devices are available in the UK.

- Consider a trial of intravaginal devices for women with urinary incontinence, only if other non-surgical options have been unsuccessful.

Vaginal pessaries

In women with pelvic organ prolapse, a pessary can be placed into the vagina to support the areas displaced by pelvic organ prolapse.

- Consider pessaries for women who have symptomatic pelvic organ prolapse.

Pelvic floor muscle training is exercise which improves pelvic floor muscle strength, endurance, power, relaxation, or a combination of these

Implementation

Challenges to implementing this guidance are the availability of services within local areas—including physiotherapists and specialist nurses for supervised pelvic floor muscle training—and time constraints within appointments in primary care and in the community.

Competing interests: Available at link https://bit.ly/3FTJF8V.

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Find the full version with references at doi: 10.1136/bmj.n3049

FURTHER INFORMATION ON THE GUIDANCE

Methods

This guidance was developed by the National Guideline Alliance in accordance with NICE guideline methodology (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf).

A guideline committee was established by the National Guideline Alliance, which incorporated healthcare and allied healthcare professionals (one general practitioner, one urogynaecologist, one gynaecologist, one women's health physiotherapist, two urogynaecology nurses, one midwife, one psychologist, with co-opted members: one obstetrician, one colorectal surgeon, one geriatrician, one specialist continence nurse, one health visitor, one pain specialist, one care home manager, and three lay members.

Review questions were developed based on the key clinical areas of the guideline scope. The best available evidence and cost effectiveness evaluations were reviewed for all review questions. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. Original economic modelling was performed in prioritised areas.

The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment: the committee took all comments into consideration when producing the final version of the guideline.

NICE will conduct regular reviews after publication of the guidance, to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

What is not included in this summary

Please see the full NICE guideline6 for recommendations on community based multi-disciplinary teams, psychological interventions, and behavioural approaches, such as bladder retraining, pessaries, and intravaginal devices.

Future research questions

- What is the most effective way to provide pelvic floor muscle training (covering the type of training, the timing, and who should supervise it) to improve adherence and prevent pelvic floor dysfunction?
- Is pelvic floor muscle training for young women (aged 12-17) effective in preventing pelvic floor dysfunction?
- How effective is pelvic floor muscle training in preventing pelvic floor dysfunction during pregnancy in women who are at higher risk?
- What lifestyle factors reduce the risk of developing pelvic floor dysfunction (for example, diet, reducing intake of carbonated drinks and caffeine)?
- How effective are prediction tools for identifying women who are at risk of pelvic floor dysfunction?
- Is pelvic floor muscle training effective in preventing pelvic floor dysfunction for older women (aged 65 and over), and women in the perimenopausal or postmenopausal phases?
- What co-existing long term conditions (for example, chronic respiratory disorders) are associated with a higher risk of pelvic floor dysfunction?

Managing snakebite

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CPD READING
0.5 HOURS

Snakebite affects between 1.8 and 2.7 million people worldwide each year, and it is estimated to cause between 80 000 and 138 000 deaths.[1 2] Snakebite envenoming is more common in South and South-East Asia (2 million annually), sub-Saharan Africa (420 000) and Latin America (150 000).[1 2] These regions also report a high burden of deaths from snakebite (100 000, 32 000, and 5000 deaths respectively) possibly due to poor access to medical aid.[1 2] Delayed diagnosis and treatment can worsen prognosis.[8-11] The World Health Organization recognised snakebite as a neglected tropical disease in 2017 and called for concerted global action to reduce deaths and disability.[12]

Who is at risk of snakebite?

Rural communities in tropical countries are worst affected.[13-16] Agricultural workers, hunter-gatherers, herders, fishermen, and rural families living in precarious housing conditions with outdoor toilets have a higher risk of snakebite. Their living environments intersect with snake habitats.[12] Men between 10 and 40 years are more commonly affected.[4 15 17-20] Non-mechanised farming techniques, barefoot farming, and sleeping on the floor further increase the risk.[16 21] Bites are more common during wetter months, when agricultural activities and breeding season for snakes potentially converge.[15 17 20 22 23]

WHAT YOU NEED TO KNOW

- Bites from venomous snakes can result in bleeding, paralysis, long term disability, and death
- Immobilise the bitten limb when transporting the patient to a medical facility; the universal use of pressure immobilisation is controversial, and tourniquets are not recommended
- The 20 minute whole blood clotting test is a simple bedside test to screen for and monitor coagulopathy in resource limited settings
- Assess vital parameters and initiate resuscitation measures if the patient is clinically unstable with signs of bleeding, shock, paralysis, or respiratory distress
- Intravenous antivenom is recommended in patients with systemic symptoms; the dose and type depend on likely snake species, local guidelines, and availability

How does envenoming occur?

Most medically important snakes in these regions belong to two taxonomic families[24-27]:

- *Viperidae*—African adders and bush vipers, Asian pit vipers, mamushis, habus, and New World rattlesnakes, moccasins, bushmasters, and lanceheads
- *Elapidae*—African and Asian cobras, African mambas, African rinkhals, Asian kraits, Australian and Papuan venomous snakes, Asian and New World coral snakes and sea snakes

Venomous snakes inject venom during a bite using specialised grooved or hollow fangs that are connected to venom glands on each side of the upper jaw via a duct.[28] Viperids usually have long foldable front fangs, while those in elapids are short and fixed (fig 1).[28] Depending on fang length, venom is introduced either subcutaneously or intramuscularly.[3]

Some snakes with fangs towards the back of the mouth (such as African boomslang and vine snakes, South American racers, and Asian yamakagashis) and the burrowing asps (or stiletto snakes) can also cause envenoming.[3 28 29] Spitting cobras and rinkhals can eject venom over several metres, often delivering venom droplets into the eyes of the animal or human perceived to be a threat.[30-32]

What are the clinical effects of snakebite?

Clinical manifestations vary between species of snakes (see box 1 on bmj.com).[3] Some toxins in venom exert local effects such as swelling, blistering, bruising, and necrosis at the bite site.[24 25] Common systemic effects include bleeding, paralysis, generalised rhabdomyolysis, and acute kidney injury. Venom injection deep into a limb can cause tissue swelling in the tightly constrained space and compromise neurovascular function.[54 55] This manifests as "acute compartment syndrome."[24 25 31]

How do patients present?

Patients usually give a history of being bitten by a snake, except those who experience painless nocturnal bites by kraits while asleep.[22 56 57] Patients are often fearful and anxious. Occasionally, painful bites may be mistaken for a puncture wound from a thorn or sharp stone and be ignored initially.[58] Some patients, especially children, bitten by highly venomous snakes, may present with cardiovascular collapse, unconsciousness, bleeding, paralysis, or respiratory failure and may not provide a clear history of snakebite.[44 59]

Fig 1 | Difference in fangs between elapids and viperids. A) Elapids have short, fixed, front fangs. B&C) Vipers have much longer and retractable front fangs. (Photos courtesy of Ahmad Khaldun Ismail)

What first aid can be provided?

Reassure the person about prompt first aid and medical assistance to allay fears. Arrange for rapid transport to the nearest medical facility, preferably with access to antivenom and critical care support.[60]

Immobilise the person, and especially the bitten limb to slow venom spread.[24] Remove rings and other tight objects around the limb.[61] A systematic review identified pressure immobilisation with an elastic bandage or pad (at a comfortable pressure) at the bite site as an effective first aid measure to slow venom spread, but the quality of evidence was very low.[62 63] Its use is variable, and it is discouraged in most practice and guidelines because of the uncertainty of benefit and possibility of worsening local tissue damage.[15 29 62 64-67] However, pressure immobilisation is generally recommended for neurotoxic elapid bites in some regions.[68]

Tourniquets can cause severe local damage and gangrene and must not be used.[24 25] It is common for communities to resort to traditional therapies such as wound incisions, cauterisation, and application of herbs, minerals, or animal excrement. These can delay access to effective treatment and may cause more harm.[15 71 72] Irrigate eyes with copious amounts of water if there is exposure to venom.[31]

EDUCATION INTO PRACTICE

- Think about the last time you treated a patient with snakebite. Reflect on the challenges you encountered while diagnosing and treating envenoming. What changes, if any, might you make to your approach next time?
- How do you review a snakebite patient as an outpatient discharge? To what extent was the patient able to share difficulties in returning to routine life?

Tourniquets can cause severe local damage and gangrene and must not be used

What to cover on initial assessment?

Rural and remote primary care centres are often the first point of medical aid for people with a snakebite. Laboratory and intensive care services at such facilities are often limited. A competent clinical assessment is vital to guide management and referral decisions.[14 73-76]

Snakebite envenoming can quickly worsen into a life-threatening emergency. Assess vital parameters to identify if the patient is critical or at risk for shock, respiratory failure, and cardiac arrest.[24 25] The Glasgow coma scale score and pupillary reactions can be misleading in patients with advanced paralysis and should be avoided.[24]

History

Reassure clinically stable patients. Ask about their symptoms to determine the presence, nature, and extent of envenoming. Details about the site, circumstances, and timing of the bite can reflect distinctive features of epidemiology, habitats, and periods of activity of medically important snakes locally and help infer likely biting species.[3 24 25]

Inquire about medications, substance use, and comorbidities as these can influence diagnosis and outcomes. Recent ethanol or recreational drug use may modify presenting symptoms. Antiplatelets or anticoagulants may worsen bleeding and interfere with key blood tests. Shock in patients with pre-existing coronary artery disease can precipitate a myocardial infarction.[3]

Examination

Bite site—Look for fang marks, retained fangs, bleeding, swelling, bruising, discoloration, and blisters.[24] Fang marks do not confirm snakebite since bites by lizards, fish, rodents, large spiders, and some insects and thorns also leave paired punctures.[3] Their absence does not preclude envenoming, as many snake species produce faint or undetectable bites.[22 24 25 56 77 78] Raised vertical, red, tender streaks on the bitten limb suggest lymphangitis.[3 24 25] Regional lymph nodes may be enlarged and tender with bruised overlying skin.[3 24 25] Note any tourniquets, ligatures, wound incisions or cauterisation, and local traditional remedies as these may lead to specific complications requiring management.[24 25] For instance, tourniquets and ligatures, if left on for long, can cause severe local damage including ischaemia, necrosis, and gangrene. Similarly, incisions and local applications can lead to local bacterial infections, sepsis, and tetanus.[18 79 80]

Systemic examination—Look for signs of coagulopathy such as sub-conjunctival, retinal, nasal, and gingivobuccal bleeds, ecchymoses and internal haemorrhage (such as intracranial, pericardial, pleural, and retroperitoneal).[24 25] Assess

extraocular movements, bulbar function, and muscle power.[24 25] Look for ptosis, muscle tenderness, and jaw stiffness.[24 25] Jaw stiffness is a prominent but often overlooked feature in sea snake envenoming that, unlike trismus, can be reduced by sustained pressure on the lower jaw.[81]

Identifying snake species—Occasionally patients or accompanying persons may bring the killed snake for identification or have a picture of it. Identification of snakes based on description by victims or recognition from pictures is often unreliable.[29 82 83] Identifying biting species helps avoid unnecessary antivenom in patients bitten by non-venomous snakes or by species whose venoms are not neutralised by available products. It can help select appropriate antivenom in countries with products specific against single species and anticipate clinical progression. However, delaying emergency treatment until the species is identified is unnecessary.

What tests can be performed?

Perform a baseline 20 minute whole blood clotting test (20WBCT) to screen for coagulopathy in patients without overt bleeding. The 20WBCT is a simple, rapid, and inexpensive bedside test to screen for and monitor coagulopathy in areas with limited access to emergency laboratory facilities.[29 86 87] Collect a sample of venous blood from the patient and place a few millilitres into a clean dry test tube. Leave it undisturbed for 20 minutes at ambient temperature. Unclotted blood that runs out or a friable clot that readily breaks down on tipping the tube at 20 minutes indicates a possible clotting disorder.[24 25]

Most clinical validation studies on the 20WBCT report a sensitivity of 82-89% and specificity of 82-98%. One study indicated that the test might potentially miss one of every five coagulopathic patients.[88 89]

In settings with laboratory support, additional tests might include a complete blood count, coagulation studies, and biochemical assays.[3]

How is snakebite managed?

Resuscitation and supportive care

Admit all snakebite patients for observation for a minimum of 24 hours. The onset of symptoms may be delayed but can worsen rapidly. Inform patients and/or their relatives about potential complications, treatment, and critical care measures using simple language, after emergency medical stabilisation. If required, explain the need for referral clearly.

Promptly manage airway obstruction, respiratory paralysis, and shock by restoring airway, oxygen, intubation, and assisted ventilation as needed, and intravenous fluids. Figure 2 summarises the management of snakebite. Choose sites of venous access such as the hands, wrists, and in some cases the feet where haemostasis by external pressure is most likely to succeed.[24] Avoid central venous or arterial punctures before establishing a negative 20WBCT.[24] Ensure that an intravenous line and resuscitation facilities are in place before releasing tourniquets, since this may trigger pronounced clinical deterioration.[92] Avoid aspirin or other NSAIDs to control pain as they can exacerbate bleeding diathesis.[3]

Monitor vital parameters and urine output at regular intervals in all patients. The 20WBCT can be repeated as it is sometimes negative initially, and coagulopathy may be detected later.[24 25]

Antivenom

Antivenoms are whole or fragmented immunoglobulins fractionated from the plasma of domesticated animals hyper-immunised with venom from one or more snake species over variable periods.[93] They are highly specific and will neutralise only the venoms used in their production and those of a few closely related species.[93] Polyspecific antivenoms are raised against a mixture of venoms from more than one species.

Early administration of antivenom prevents or limits haemodynamic alterations, progression of coagulopathy to clinically overt bleeding, postsynaptic neurotoxicity, myotoxicity, acute kidney injury, and local tissue damage.[24 25 94] Physiological levels of clotting factors are at least partially restored within a median of six hours with sufficient doses of specific antivenoms.[45 95-101]

Robust clinical data on the safe and effective initial dose of antivenom are lacking for most products.[102] We suggest following national protocols or standard regional guidelines for dose.[24 25] Administration is always intravenous, as bolus or diluted in saline solution over 10-60 minutes, at the same dose for adults and children.[24] Repeat administration of antivenom if bleeding persists, if weakness or cardiovascular signs worsen within two hours, or if a 20WBCT is positive at six hours after antivenom administration.[3]

Other treatments

Neostigmine with atropine is a potentially useful adjunct in patients bitten by snakes such as some cobras with postsynaptic neurotoxins in their venom.

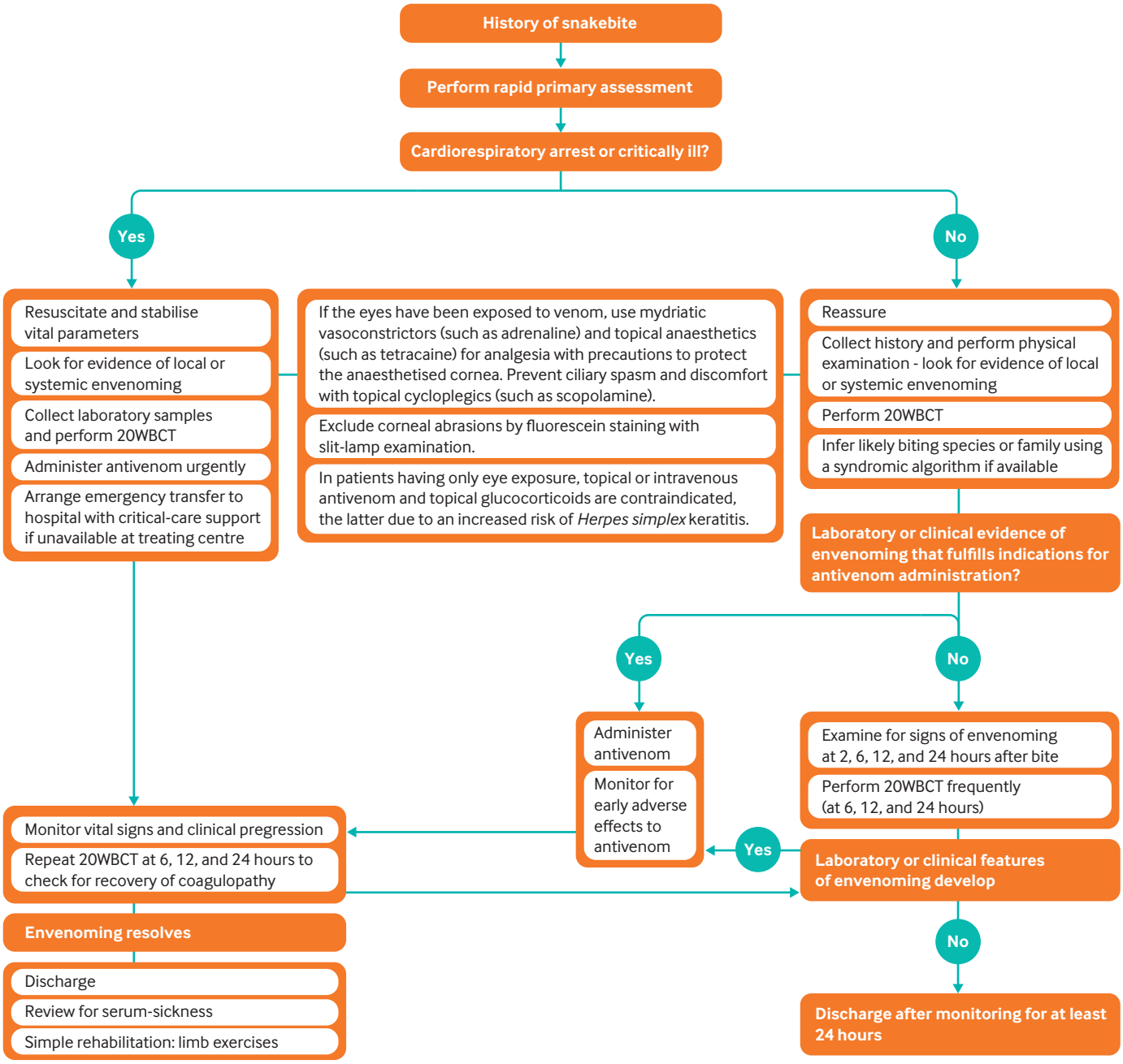
Administer a tetanus toxoid booster in all patients except in those with coagulopathy, in which case injection is postponed until haemostasis is achieved.[3] Aspirate large tense bullae to facilitate nursing the bitten limb, pre-empt spontaneous rupture, and prevent secondary infection. Broad spectrum antibiotics are indicated only if the wound has been incised or there are signs of necrosis, wound infection, or abscess formation.[3] Surgical debridement or amputation of gangrenous digits or limbs and skin grafting may be needed.[24 25] Fasciotomies are rarely justified since compartment pressures usually remain within normal limits.[3 107]

Risk of adverse reactions with antivenom

Monitor patients for adverse reactions in the first two hours of antivenom administration.[29] Anaphylaxis or pyrogenic reactions occur early (within minutes or hours). Mechanistic studies suggest that most events are not IgE mediated and thus cannot be accurately predicted by skin tests for immediate hypersensitivity.[109] However, their incidence and severity can be reduced by a prophylactic subcutaneous injection of low dose adrenaline.[108 110] Pyrogenic reactions result from product contamination during manufacture.[111]

Treat anaphylaxis at the earliest sign.[24 25] Suspend antivenom administration and inject adrenaline intramuscularly, ideally into the upper lateral thigh.[24 25] Additional treatment includes intravenous antihistamines and glucocorticoids and inhaled bronchodilators for bronchospasm.[24 25] Anaphylaxis can recur, and glucocorticoids do not prevent recurrence.[112] On resolution of the episode, cautiously resume antivenom in patients with a definite indication for continued treatment.[24 25]

Late reactions may manifest a week after administration.[108 111 113]



20WBCT = 20-minute whole blood clotting test

Fig 2 | Flowchart for the management of snakebite

What are the long term sequelae of snakebite?

Amputations following snakebite-related soft tissue injuries range from 5908 to 14 614 annually in sub-Saharan Africa.[4] Even in patients not requiring amputations, tissue loss may result in chronic ulcers, malignant transformation, and scarring.[29] Musculoskeletal sequelae such as contractures, wasting, and joint stiffness affected up to 3% of snakebite survivors in a study of 816 patients in Sri Lanka.[115] Cerebrovascular accidents result in persisting limb weakness and visual or cognitive impairment.[29] Eye exposure to venom can result in blindness.[31] Some patients with acute kidney injury may progress to chronic renal failure.[116-120] Limited data from South Asia indicate that chronic hypopituitarism, a sequel of acute pituitary haemorrhage, can present as late as 10 years after the bite.[37 91 121-123]

Even without amputation, tissue loss may result in chronic ulcers and malignant transformation

Competing interests: None declared.
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HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

No patients were involved in the creation of this article.

CASE REVIEW

Hemiparesis and facial droop in an older woman

A woman in her early 80s presented to the emergency department with a 30 minute history of right sided weakness, dysarthria, dizziness, and confusion. She was taking irbesartan 75 mg/day for hypertension and the sulfonylurea glimepiride 4 mg/day and metformin 500 mg/day for type 2 diabetes. Physical examination revealed right sided facial droop involving the corner of the mouth (figure), right sided hemiparesis, and slurred speech. The patient scored 23 (range 0-42) on the National Institute of Health Stroke scale.

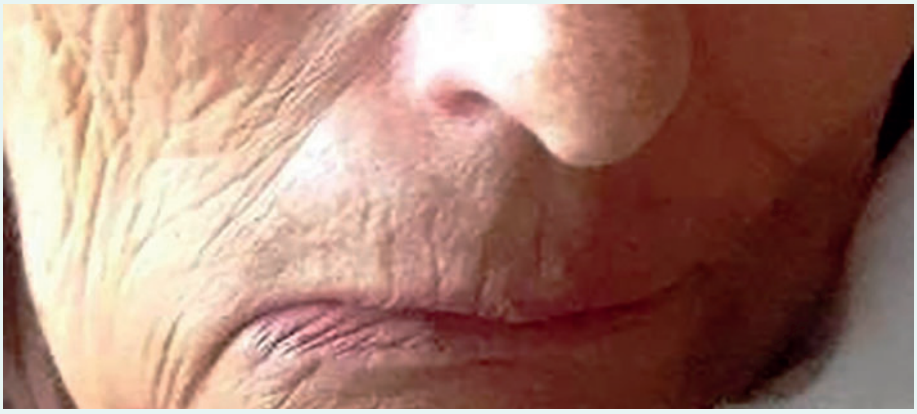
Findings on computed tomography (CT) of the brain were normal, with no visible acute or chronic lesions indicative of haemorrhage or infarcts. Finger stick blood glucose was 2.3 mmol/L (4-7 mmol/L).

Routine serum blood tests were performed (table).

1 **What are the differential diagnoses of hemiparesis and facial droop?**

2 **Which diagnosis is most likely in this case and why?**

3 **How would you manage this patient?**



Right sided facial droop

Serum blood test results

Investigation	Result	Normal range
Serum blood glucose (mmol/L)	2.2	4-6
Haemoglobin A_{1c} (mmol/mol)	45	40-42
Creatinine (µmol/L)	97.2	62-106
Urea (mmol/L)	15.4	3.6-18
Sodium (mmol/L)	139	135-148
Potassium (mmol/L)	4.5	3.5-5.3

Submitted by Dimitrios Anyfantakis and Serafim Kastanakis

Patient consent obtained.

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answers

CASE REVIEW **Hemiparesis and facial droop in an older woman**

1 What are the differential diagnoses of hemiparesis and facial droop?

A wide range of diagnoses that resemble stroke but have a different aetiology are called "stroke mimics." Hypoglycaemia, focal seizures leading to postictal Todd's paresis, and malignant tumours of the cerebellar pontine angle are the most likely differential diagnoses. Hemiplegic migraine and sepsis are other less common causes of hemiparesis and facial droop.

2 Which diagnosis is most likely in this case and why?

Hypoglycaemic hemiparesis—hypoglycaemia is a common stroke mimic, and the cause in 2% of presentations for hemiparesis. A serum blood glucose concentration <3.0 mmol/L is indicative of severe hypoglycaemia, which, if neglected, results in brain damage, coma, or death. Confusion, dysarthria, and drowsiness might also be present. Sulfonylureas stimulate the secretion of insulin, increasing the risk of hypoglycaemia. Glimepiride metabolites in patients being treated for renal disease take longer to be excreted, which can lead to severe hypoglycaemia that lasts >24 hours.

3 How would you manage this patient?

Intravenous dextrose infusion is recommended to correct hypoglycaemia. Hemiparesis resolves after normalisation of blood glucose levels. A CT scan of the brain is necessary to rule out transient ischaemic stroke.

PATIENT OUTCOME

On correction of the patient's hypoglycaemia with dextrose infusion, the right sided weakness and facial droop resolved. She reported a median of two non-severe hypoglycaemic events each month in the past year, presenting as autonomic symptoms lasting about 15 minutes. She had no previous episodes of hemiparesis. Glimepiride was discontinued to avoid future hypoglycaemic events.

LEARNING POINTS

- Hypoglycaemia is a potential reversible cause of focal neurological symptoms
- Timely recognition of hypoglycaemia is essential to prevent irreversible neurological deficits and avoid unnecessary investigations (brain CT) or treatments (intravenous thrombolysis, aspirin)
- Stroke mimics include hypoglycaemia, seizures, sepsis, migraine, brain tumours.

CPD READING
0.5 HOURS

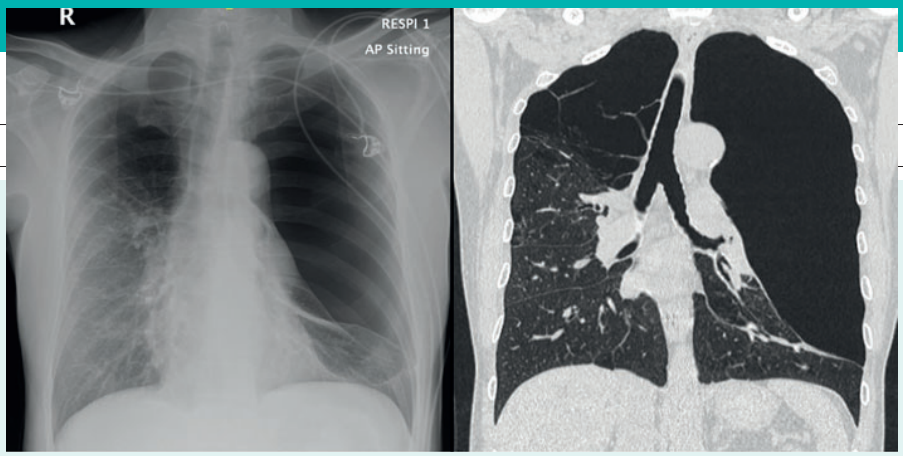
You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

Articles with a "learning module" logo have a linked BMJ Learning module at http://learning.bmj.com.

MINERVA

Vanishing lung syndrome mimicking tension pneumothorax



This is a chest radiograph of a man in his 50s with vanishing lung syndrome.

The patient presented with dyspnoea—on examination his trachea was deviated to the right and there was reduced air entry on the left side of his chest suggestive of pneumothorax. Tension pneumothorax seemed unlikely as his observations were normal so chest x ray was performed showing absent pulmonary markings on the left and a mediastinal shift to the right. However, no discernible visceral pleural line needed to diagnose pneumothorax was present.

No pneumothorax was detected on high resolution computed tomography (CT), but a giant left sided bulla occupied more than one third of the lung. Vanishing lung syndrome, or idiopathic giant bullous emphysema, was diagnosed. This condition is commonly caused by alpha 1 antitrypsin deficiency, smoking marijuana, and covid-19.

Inspection for pleural lines on chest radiographs is necessary when patients present with symptoms and signs of pneumothorax. If pleural lines are not visible, volumetric high resolution CT should be correlated with clinical status to avoid inappropriate thoracocentesis and potential iatrogenic pneumothorax, bronchopleural fistula, or haemothorax.

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Patient consent obtained.

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

Strategies to end the pandemic

Rather than trying to beat SARS-CoV-2 using one booster vaccine at a time, it would be better to build systems and pursue policies that protect the health of communities. These might include paid sick leave, protection for essential workers, better masks, improved ventilation, rapid test availability, places where sick people can easily isolate, social distancing, and ways of retaining an exhausted healthcare workforce. The writer was discussing the situation in the US, but his analysis is surely relevant in many countries (www.theatlantic.com/health/archive/2021/12/america-omicron-variant-surge-booster/621027).

Identifying triggers of paroxysmal atrial fibrillation

In a series of n-of-1 trials, 400 people at risk of paroxysmal atrial fibrillation either exposed themselves to or avoided self-selected triggers. Potential triggers included caffeine, alcohol, reduced sleep, exercise, lying on left side, and dehydration. Although avoidance of triggers reduced the number of arrhythmias, a meta-analysis of the individual trials found that alcohol was the only exposure significantly associated with an increased risk of atrial fibrillation (*JAMA Cardiol* doi:10.1001/jamacardio.2021.5010).

Alcohol was the only exposure significantly associated with an increased risk of atrial fibrillation

Apathy in Alzheimer's disease

Apathy, manifested by diminished volition and initiative, is a frequent feature of Alzheimer's disease, adding to disability and the burden on caregivers. Results from a randomised controlled trial suggest that methylphenidate helps a little, reducing apathy scores compared with placebo (*JAMA Neurol* doi:10.1001/jamaneurol.2021.3356). However, the trial found no improvements in measures of caregiver distress or patients' activities of daily living.

Therapeutics of Alzheimer's disease

Over the past 20 years, most new treatments for Alzheimer's disease have focused on slowing the accumulation of amyloid β and τ proteins in the brain. It's fair to say that the results have been disappointing. Perhaps it's time to reconsider and view the build-up of these proteins as a by-product of neuronal damage rather than as a central part of pathogenesis. If this view is correct, we've been aiming at the wrong targets (*Am J Psychiatry* doi:10.1176/appi.ajp.2021.19080873).

Cerebellar neurons that curb food consumption

It's generally thought that food intake is regulated by the hypothalamus. But functional magnetic resonance imaging in people with Prader-Willi syndrome, a genetic condition characterised by an insatiable appetite, has located a region within the cerebellum that also responds to food related stimuli. The idea that the cerebellum is involved in signalling satiety gets support from animal experiments in which artificial activation of neurons in the lateral deep cerebellar nuclei led to a striking reduction in food intake (*Nature* doi:10.1038/d41586-021-03383-9).

Healthcare avoidance

Primary care consultations and referrals to specialist care have declined over the past two years. A questionnaire survey from the Netherlands reports that part of the reason is that many people avoided contact with healthcare providers despite having potentially urgent symptoms. Healthcare avoidance was most strongly associated with female sex, poor appreciation of health, and high levels of depression and anxiety (*PLoS Med* doi:10.1371/journal.pmed.1003854).

Blood pressure during the pandemic

Blood pressure has risen during the pandemic, according to a longitudinal study from the US. Among nearly half a million participants, mean systolic pressure was 2 to 3 mmHg higher during the second half of 2020 than it had been in the previous year. Possible reasons include increased alcohol consumption, reduced physical activity, and poorer medical care (*Circulation* doi:10.1161/CIRCULATIONAHA.121.057075).

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