education

FROM THE JOURNALS Edited highlights of weekly research reviews on https://bit.ly/2PLtil8

No need to wait to conceive after a stillbirth

There is currently no guidance about the optimal interval between having a stillbirth and getting pregnant again. This international cohort study of 14 452 births used birth records from Finland, Norway, and Western Australia and found that the median inter-pregnancy interval was nine months, and 63% of the women who had previously had a stillbirth conceived within 12 months.

Getting pregnant again within a year of stillbirth did not increase the odds of a second stillbirth (2%), preterm birth (18%), or low birthweight baby (9%) compared with women who waited two to five years. Women who have had a stillbirth can be reassured that most will not have a problem conceiving again quickly, and that conceiving within one year does not increase the risk of adverse outcomes.

Lancet doi:10.1016/S0140-6736(18)32266-9

Peanut patches are no panacea

Peanut allergy is a growing problem. It affects 1-2% of US children. There is currently no treatment for peanut allergy. This randomised controlled trial found that daily treatment for a year with a patch containing peanut protein meant that children who are allergic to peanuts could tolerate a higher dose in a peanut challenge than those who had used a placebo patch. Unfortunately, the difference wasn't significant according to the trial's criteria, though it was statistically significant. Systemic allergic reactions were rare, and none was severe. This desensitisation treatment, known as epicutaneous immunotherapy, may yet hold some hope, but it's not ready to be rolled out yet.

JAMA doi:10.1001/jama.2019.1113

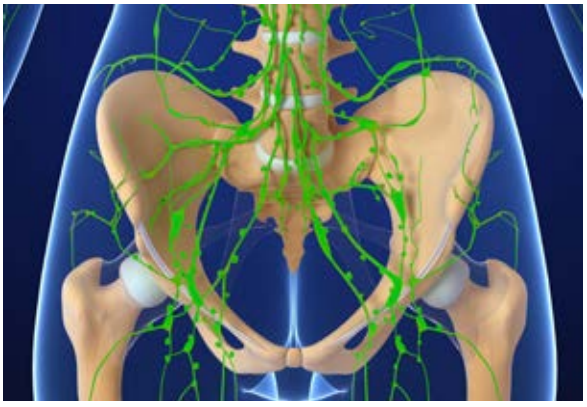
Lymphadenectomy in advanced ovarian cancer

Women with advanced (stage IIB-IV) ovarian cancer usually have their normal pelvic and paraaortic lymph nodes removed (lymphadenectomy) in addition to resection of all macroscopically visible tumour followed by chemotherapy. Is the lymphadenectomy justified?

This randomised controlled trial found that median overall survival was 69.2 months among women who didn't have lymphadenectomy and 65.5 months in those who did. Progression-free survival was the same in both groups (25.5 months). Predictably, the rate of serious postoperative complications, such as the need for a repeat laparotomy, was more likely among women who had had lymphadenectomy (12.4% *v* 6.5%). Mortality within 60 days of surgery was low, but higher in the lymphadenectomy group (3.1% *v* 0.9%).

On the other hand, women in both groups reported similar quality of life and global health status scores. The orthodoxy has been challenged and found wanting.

N Engl J Med doi:10.1056/NEJMoa1808424



Haemodialysis and depression: what helps?

The number of people receiving haemodialysis for end stage renal disease is increasing, and around a third of them are depressed. This study asked whether depressed patients would be more amenable to therapy if they had a specially designed session to encourage engagement and whether cognitive behavioural therapy (CBT) or the antidepressant drug sertraline is the more effective treatment. The results were rather disappointing.

The engagement interview was no better than a chat with a member of the research team in encouraging participation. And, although sertraline was more effective than CBT, neither treatment improved depression scores to a clinically important extent. This study did not compare sertraline and CBT with no treatment and didn't have long term follow-up. But at least it's a spotlight on the mental health needs of people living with chronic renal disease.

Ann Intern Med doi:10.7326/M18-2229

Bag for life

Lack of oxygen in the blood is the most common complication during intubation of critically ill adults and may increase the risk of cardiac arrest and death. Does positive-pressure ventilation via bag-mask ventilation during the 45-90 seconds between induction and laryngoscopy reduce the risk of hypoxaemia without increasing the risk of aspiration?

This randomised trial found that the bag-mask ventilation group had a lower rate of aspiration (2.5% *v* 4%), better minimum oxygen saturation (96% *v* 93%), and fewer episodes of severe hypoxaemia (10.9% *v* 22.8%) compared with no ventilation. One caveat is that these were critically ill patients in intensive care units; the same findings might not hold for people who are being intubated in other settings.

N Engl J Med doi:10.1056/NEJMoa1812405

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PRACTICE POINTER

Assessing a disturbed person in the community

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CPD READING
0.5 HOURS

You are urgently called to reception where a 25 year old man is shouting about the building having been taken over by demons. He appears distressed and is not responding to attempts by reception staff to communicate with him. He shouts about his neighbours, that he needs to "sort them out." You see from his notes he has a history of psychotic episodes.

When a person in severe psychological distress presents like this to a general practice or community clinic it can be difficult to know what to do, particularly if they are behaving aggressively, or if they are refusing help.

The person may be experiencing a deterioration in their mental health, such as a psychotic episode, or it may be related to substance use or acute social stressors. Most patients who are acutely disturbed present no danger to others, however situations can evolve rapidly.

This article offers advice about an initial approach to a person who is acutely disturbed in a community setting, particularly focusing on those presenting with a suspected psychotic episode. Recently, the Mental Health Act in England and Wales has undergone some important changes, which this article takes into account, but the principles outlined here are generalisable to other settings.

WHAT YOU NEED TO KNOW

- Listen, acknowledge the person's feelings, reassure them that you wish to help, offer a quiet space to talk, a drink, and time to speak
- If there is an imminent physical risk to the person or others, use internal alarms to alert the rest of the practice, contact police, and consider evacuating the area
- Check for the presence of physical and mental health comorbidities, drug or alcohol use, or acute life stressors (relationships, housing, finances, access to services)
- Establish any risk factors, such as a history of aggression, self harm, or suicide attempts, recent psychiatric admission, or a forensic history
- If the situation cannot be safely de-escalated then Section 136 (S136) of the Mental Health Act is a police power in the UK to remove someone to a place of safety for assessment and can now be used in a general practice or community clinic

How to approach and assess the person

There is limited evidence about the frequency, cause, or management of severe behavioural disturbance in people presenting in community settings. These suggested approaches are based on accepted clinical practice and experience of authors.

Immediate actions

Attempt to de-escalate the situation. Use non-aggressive verbal and non-verbal communication, while monitoring the situation for potential risks to the person and to staff and other patients in the waiting area.[1]

Communication

- Focus on the person, listen to what they are saying
- Ask their name
- Present a calm demeanour
- Consider the potential physical risk to staff and patients and take action if the risk is high, by
  - using silent internal alarms to attract help;
  - considering evacuation of patients or staff at risk;
  - having other staff call the police (ideally out of earshot of the distressed person);
- Alert clinical staff that a rapid assessment of the person may be needed.

Safety

- Find a safe quiet area for the person to wait
- Get something for the person to drink
- Have someone sit with the person if it is safe to do so.

Positive actions

- Actively listen to the person and use summarising statements to show that you are listening
- Identify why they have presented here and now
- Be attentive to cues mentioned by the person
- Acknowledge the person's feelings and distress and build trust by reassuring the person that you wish to help, following the principles of patient centred care.[2]

Involve others

- Involve anyone at the practice who knows, and is trusted by, the person
- See if a relative/friend/carer can attend or provide collateral information
- Ask other staff members to access the clinical notes and provide a summary for the assessing clinician quickly.

Community settings should have (ideally silent) emergency communication systems to call for help from other staff. Encourage staff to call senior managers and clinicians for support in such situations, so that non-clinical and uninvolved clinical staff can manage the ongoing function of the reception and clinical areas. Intervening early and decisively could prevent a more extreme reaction later.

Clinical assessment

An acutely disturbed person needs urgent assessment. At the end of this initial assessment the clinician will need to decide how urgently the person needs to be assessed by a medical or psychiatric team and whether it is necessary to seek support from the police or emergency services to convey the patient to a safe place for assessment. Aim to form a differential diagnosis, assess capacity, complete a brief risk assessment, and develop a provisional management plan.

Differential diagnosis

Consider whether any of the following factors are contributing to the presentation:

- A reaction to stressors (relationships, housing, finances, access to services)
  You might ask
  - what are the person's main concerns?
  - has anything happened to precipitate this presentation?
- Intoxication with, or withdrawal from, alcohol or recreational drugs
  You might consider whether this is intoxication or withdrawal, either alone or with psychological comorbidities
- A history of medication use
  You might ask if the person has been taking the medication as prescribed
- A first episode or relapsing psychosis
  You might ask or investigate
  - is there a history of mental health problems (diagnosis, severity, admissions, treatment)?
  - when, how, and why symptoms may have changed?
  - has there been any history of recent contact with emergency and/or psychiatric services?
- Other organic causes (adverse medication reactions, infections, neurological illnesses, metabolic and endocrine disorders)
- Other psychiatric comorbidities—eg, acute stress reaction in the context of an emotionally unstable or dissocial personality disorder.

Prevalence data on presentations of disturbed persons to primary care are not available. Acute psychological stressors and factors related to substance abuse may be common causes, and if there is judged to be no acute risk to practice staff and patients, would normally be managed by primary care clinicians, using non-acute established pathways. People seeking drugs may have a history of dependence and may show signs of withdrawal. It is very rare for such patients to threaten staff or patients, but if so, then the practice can alert the police, as for any patient who is being intimidating in the context of intoxication alone.

Suspected psychosis

It can be more challenging to manage and arrange urgent support for an acutely psychotic patient in a community setting.

Psychotic illnesses are common; with an annual prevalence of an active psychotic disorder of 4 in 1000 adults.[3] It is not known how many people present in primary care or the community when experiencing an acute psychotic episode. However, rates of patients detained by the police on S136 in the UK have risen, which might suggest an increase in acutely disturbed presentations in community settings. Figures from NHS digital 2015-16 show a rise of 18% from the previous year, to 22 965.[4] During this period, 17.8% of people detained on S136 subsequently went on to be detained under Section 2 or Section 3.[4]

A person experiencing a psychotic episode will often lack insight[5] and therefore may not present asking for help. If services are alerted by family or friends asking for help, then a planned response by primary care or psychiatry teams (including domiciliary visits) may be most appropriate. Sometimes relatives may persuade a person to go to the GP or the emergency department. However, in an acute presentation, with no warning, there are different options for managing the situation depending on where the patient is, and whether they are known to mental health services already.

In a suspected psychotic episode, assess:

- delusions
- hallucinations
- disordered thinking or speech (including content and nature of the patient's beliefs)
- impact of patient's beliefs on their past and potential actions.

Usually, most assessments of a person at first presentation would also include questioning the validity of their beliefs, but this may not be appropriate in an acute presentation in a community setting.[6]

Risk assessment

Carry out a brief assessment of the risk of harm the patient might pose to themselves or others. The box below outlines red flag symptoms and signs that might increase risk.

Key risks include self harm, accidental injury, vulnerability to assault from others, and harm to others.

In known patients, any serious risk history should be known to the practice.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

A person who has had experience of being sectioned commented on and approved the final draft of the article and has provided a patient account.

Referral

If you suspect an underlying mental health cause and the patient calms, consider contacting local psychiatry services, who can provide the person's recent history (in some areas of psychiatry electronic records are available to primary care). Local psychiatry services may offer urgent assessment. If there are any concerns about physical health problems (such as alcohol withdrawal) then assessment at an emergency department may be most appropriate. Mental health services available could be the local community mental health team/home treatment team/liaison psychiatry/street triage/single point of access service (depending on local arrangements). If the person is a known patient, they may have a "crisis plan" or advanced directive in their records, which will inform care planning.

Ask the person:

- Do they have a crisis plan?
- Would they agree to be seen by the specialist mental health team—for example at the local emergency department, street triage, or the local crisis team, depending on local options?
- Do they have a care coordinator that they would like to see?

What options are available if the person refuses to be assessed?

No immediate risk

If the assessment suggests there are no immediate risks and the patient calms down, but the initial assessment suggests that there is mental disorder and the patient is still refusing immediate help, then a Mental Health Act assessment can sometimes be organised, depending on local protocols. In the UK this would be a Section 4, but is more likely to be a Section 2 or a Section 3 organised with the local approved mental health professional and police over the following few days (see bmj.com for details on types of section) (in locations where demand is high and resources are low there can be longer waiting times for community Mental Health Act assessments).

A Mental Health Act assessment can take time to organise, and most practices are not resourced to manage a disturbed person safely in the meantime. In this case the best option might be for the person to be seen in the emergency department of a hospital if they agree to go, while acknowledging that the security and environment may not be ideal. It is a matter of determining, as best as is practicable, what the safest option for the person might be.

In some situations it may be better, if safe, for the person to return home and wait for input from the mental health team you have contacted.

Different types of Mental Health Act sections

A person may be detained under section if they are suffering from a mental disorder of a nature (chronicity, prognosis, previous response to treatment) and/or degree (current manifestation of the illness—eg severity of current symptoms, impact on functioning etc) that warrants:

- **Section 2** Assessment for up to 28 days in hospital
- **Section 3** Medical treatment for up to 6 months in hospital
- **Sections 2 & 3** require two doctors to make recommendations and the application is made by an approved mental health professional (often a social worker)
- **Section 4** An emergency application for detention for up to 72 hours, which requires one doctor's recommendation and a recommendation from an approved mental health professional
- **Section 135 (1)** - Gives the police the power to remove a person from a dwelling (ie, any private property). It lasts up to 24 hours and requires a warrant to have first been obtained from a magistrates' court
- **Section 136** Gives the police the power to remove a person from a public place, when they appear to be suffering from a mental disorder and are in need of care or control, to a place of safety. It lasts up to 24 hours
- **Section 5(2)** A temporary hold of a patient already receiving treatment in a hospital, applied by any doctor for up to 72 hours.

Risk factors for harm to the patient or others[7]

- Recent (within last 2 weeks) discharge from inpatient services[8]
- History of self harm or suicide attempts, hopelessness, suicidal ideation/plan
- Current alcohol or drug misuse
- Notable forensic history (such as serious assault)
- Delusions focusing on an individual
- History of carrying weapons

EDUCATION INTO PRACTICE

- Think about the last time you assessed a patient who was acutely distressed. What aspects of the risk assessment might you do differently? Did you feel confident about the legal framework or services available for getting the person additional physical and mental health support?
- What training might be useful for staff in your setting to increase confidence when assessing a patient who is acutely distressed?
- How might the recent changes to Section 136 affect your practice?

Immediate risk—call the police

If a person is unwilling to engage in any form of assessment at the surgery, is refusing to go to another setting, and you have immediate concerns about risk to self or others, then it may be necessary to call the police.

The police can use their powers under S136 of the Mental Health Act. S136 is a police power to remove someone they feel is in immediate need of care or control to a place of safety, for the purpose of assessment. There will be designated places of safety locally, which are usually based in psychiatric hospitals. Emergency departments can also be used. Recent changes to S136 clarify the use of police powers in such a situation.[9]

Removal from the statute of the link between the operation of S136 and "a place to which the public have access" has clarified some previously grey areas. There had been some debate about whether S136 powers could be used, for example, in treatment areas of the emergency department or GP consulting rooms. It is now clear that police will be able to exercise these powers in these settings if the criteria to do so are fulfilled. Police can use S136 powers in all areas of a GP practice. They can only not use S136 powers in a private residence or the private garden or buildings associated with a private residence. For a summary of recent changes to S136 see box 3.

If the person leaves the practice before anything can be organised then the police and the patient's family can be alerted if concerns about risk remain. Alternatively, the local mental health services could be contacted to ask for an urgent assessment, depending on local systems.

ANTHONY DEVLIN/SHUTTERSTOCK

Changes to the S136 in the Police and Crime Act 2017

- Police should consult a registered medical practitioner, a registered nurse, or an approved mental health professional, if practicable, before using S136.
- S136 can be used in any place other than a private dwelling or its private garden. The new legislation has removed reference to a place to which the public have access—so these powers can be used in all areas of a GP practice.
- A child may not, under any circumstances, be removed to a police station as a place of safety.
- Police stations can only be used as a place of safety for adults in limited circumstances (imminent risk of serious injury or death, when nowhere else can reasonably manage the risk). Given that a person is in a mental health crisis and there may be an accompanying physical disorder including intoxication with alcohol and drugs, it is recommended that the person be assessed in a healthcare setting.
- There is a reduction in the permitted period of detention from 72 hours to 24 hours with the possibility of a 12 hour extension (if not practicable to complete the assessment for example in 24 hours for example because of intoxication).

How to involve carers and relatives

The person may make it clear that they don't want you to discuss their care with their family, which can be difficult. In this situation, if your considered assessment is that the patient lacks capacity to make this decision, confidentiality may be breached if failure to do so may expose the person or others to a risk or if you judge it is in the person's best interests.[10] If the person has capacity and refuses to consent to information being shared, then confidentiality maybe breached if certain conditions are met, such as risk to carers, relatives, or others.[11]

Importantly, carers and relatives can always give information to clinicians, with no release of information by clinicians to them.

If the person agrees, carers can give collateral history and support the person during the assessment. Carers may need support themselves—guide them towards local carer support groups if interested.

If a patient is placed on S136 in the practice, inform any involved carer or family member as soon as possible.

Post-presentation follow-up

Care governance

Review the care provided in the acute setting soon after the incident, and identify any gaps in facilities, staffing, or staff training, which could improve future care and dignity for similarly distressed patients. Staff members can find situations like this quite distressing—offer an opportunity to speak individually to the practice manager or other appropriate senior team member to check whether they need support.

Communication between teams

The mental health team should inform the primary care team of the consequences of assessment (use of any section, admission, treatment, home treatment team, routine community follow-up, crisis plan).

Patient follow-up

Mental health

It is good practice for the GP to contact patients after discharge from inpatient or other care, to invite them for a non-urgent face to face, or telephone, discussion of progress. This would provide an opportunity for patients to discuss their crisis plan if presenting to primary care in future, and how events were managed when they presented in crisis.

Promoting physical health

Patients with serious mental illness have 15-20 years reduced life expectancy[12] so it is useful to consider a physical health review (opportunistically or planned), including cardiovascular disease risk factors. Offer referral to the smoking cessation adviser. Arrange relevant blood tests or electrocardiogram as required by identified behavioural risks or medication review.

Crisis plan and relapse indicators

Review the patient's "crisis plan" (or recommend this is discussed with a care coordinator). Discuss relapse indicators (or early signs of relapse) and set out what might be done if there should be a relapse in future, including information about medication and who to contact in an emergency.

Competing interests: None declared.

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Treatment refractory hypothyroidism

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This is part of a series of occasional articles on common problems in primary care. *The BMJ* welcomes contributions from GPs

CPD READING
0.5 HOURS

A 40 year old woman complains of tiredness over the past few weeks. She had a total thyroidectomy three years ago for Graves' thyrotoxicosis and has been taking levothyroxine since then. She weighs 80 kg and is taking 150 µg daily. A blood test done in the previous week showed thyroid stimulating hormone (TSH) levels above 30 mU/L (reference range 0.4-4.5 mU/L).

Some hypothyroid patients continue to have symptoms or biochemical evidence of hypothyroidism (serum TSH above the upper laboratory reference range) despite standard thyroid replacement therapy. The prevalence of treatment refractory hypothyroidism is not established. Studies in different populations report about a third of patients taking thyroid medications have TSH levels above the reference range, suggesting inadequate thyroid hormone replacement.[1 2]

Further dose increases may not always be appropriate. Patients may not be taking the treatment regularly as advised. Conditions that decrease absorption or increase demand for thyroxine may also be responsible. A recent expert consensus report recommends identifying and addressing the likely cause before increasing the daily dose of levothyroxine above 1.9 µg/kg body weight.[3]

WHAT YOU NEED TO KNOW

- Persistent symptoms of hypothyroidism or raised serum levels of thyroid stimulating hormone (TSH) despite optimum thyroid hormone replacement (up to 2.0g/kg body weight of levothyroxine) suggest treatment-refractory hypothyroidism
- Explore adherence to treatment and conditions that impair absorption (taking the drug with medications or food, coeliac disease, etc) or increase demand (pregnancy, other medications)
- Discuss measures such as taking the tablet on an empty stomach in the morning an hour before other food or medications and using reminders, such as dosette boxes, to improve adherence

What you should cover

Look for possible causes

- Ask about adherence to treatment. Is the patient taking the levothyroxine tablets regularly?
- Is she taking levothyroxine alongside other medications or with meals? Several foods and medications interfere with the absorption of levothyroxine in the intestine. Certain medications increase the metabolism of levothyroxine.
- Review her medication list, tablet box, and prescription history.
- If the patient acknowledges non-adherence, explore the reasons for it in the context of her life. What else is going on in her life? Is she stressed? Does she understand what the tablets are for? Has she searched for information on the internet? Has she any concerns about side effects? Does she miss tablets because she finds it hard to wake up and because it says take on an empty stomach? Is the drug well tolerated?
- Is the patient pregnant? Pregnancy increases the demand for levothyroxine.
- Has the patient got any symptoms or signs to suggest malabsorption? Vomiting, diarrhoea, or weight loss accompanied by anaemia can suggest malabsorption. However, many patients have no symptoms.

SOURCES AND SELECTION CRITERIA

We used an expert consensus report for diagnosis and management of treatment refractory hypothyroidism (www.ncbi.nlm.nih.gov/pmc/articles/PMC5680379/). We have drawn recommendations during pregnancy from guidelines of the American Thyroid Association. We also referred to previous case reports and drew from experience at our centre.

LIFE IN VIEW/SPL

Causes of treatment refractory hypothyroidism

Decreased bioavailability

- Non-adherence to, or tolerability of, levothyroxine therapy
- Substances that interfere with intestinal absorption (such as proton pump inhibitor therapy, coffee, food (when tablet taken alongside), soya, kelp, iron, calcium, aluminium hydroxide, chromium picolinate, cholestyramine, colestipol, grapefruit juice, sevelamer hydrochloride, sucralfate, raloxifene, multivitamins)
- Intestinal malabsorption (such as short bowel syndrome, lactose intolerance, gluten enteropathy, inflammatory bowel disease, infiltrative enteropathy, infection with *Giardia* or *Helicobacter pylori*)

Increased need for levothyroxine

- Weight gain
- Pregnancy
- Increased metabolism of levothyroxine due to increased hepatic metabolism by cytochrome P450 enzymes, induced by drugs (such as phenobarbital, phenytoin, carbamazepine, rifampicin, tyrosine kinase inhibitors, rexinoid compounds)

Others

- Assay interference from heterophilic antibodies and biotin-containing medications

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We interviewed two patients taking levothyroxine for hypothyroidism. Both thought they had not been adequately informed on how to take the tablets and why they must take them regularly. One of the patients noted that it was important that doctors listen to the patient to come to a shared management plan, recognising that one size would not fit all. We have attempted to cover these points in the article. A patient with hypothyroidism also reviewed this paper for *The BMJ* and found the tips to improve absorption of levothyroxine useful. We thank these patients for their contribution.

EDUCATION INTO PRACTICE

- How would you explore adherence to taking levothyroxine?
- What measures will you suggest to a patient to improve adherence to treatment?
- What tests will you consider in a patient with treatment refractory hypothyroidism?

What you should do

Explain why regular treatment is important and how it is to be taken

Draw up a shared management plan that incorporates the patient's goals and preferences. Inform patients that not taking recommended levothyroxine replacement puts them at risk of weight gain, raised cholesterol levels, tiredness, depression, and, over a longer time period, myxoedema coma, which can be fatal.[4]

Explain that the absorption of levothyroxine tablets can be affected by other substances taken at the same time. Advise the patient to take levothyroxine on an empty stomach with water at least an hour before breakfast or any other tablets in the morning. This has been shown to optimise absorption.[5]

Discuss other ways to improve adherence (such as a dosette box, alarms or reminders on phone, tablet counting, etc). Measures such as taking levothyroxine at bedtime, trying a different preparation of levothyroxine (brand, liquid formulation), or supervised weekly dose may be considered in patients who find it hard to adhere to treatment, but there is no evidence to support these.

Dose increase

Levothyroxine dose increment of 25-50 µg may be appropriate for patients taking other medications that decrease its bioavailability. Increasing the dose by 25-50 µg is also advised in pregnant women taking levothyroxine for optimal fetal growth and development. Monitor serum TSH every 6-8 weeks, aiming to keep it <2.5 mU/L throughout pregnancy.[6]

Assess the effect of advised changes

Offer the patient an initial full thyroid function test (TSH and free thyroxine levels in the blood) as well as simple screening tests for malabsorption (such as full blood count, serum levels of vitamin B_{12}, folate, ferritin, calcium, and albumin, and coeliac antibody test). Recheck thyroid function after six weeks to see the effect of the above changes.

Referral

Consider referral to an endocrinologist if:

- TSH levels remain elevated after six weeks despite the above advice and changes in the absence of malabsorption. An endocrinologist may perform levothyroxine absorption challenge tests to differentiate true malabsorption from non-adherence to treatment (pseudomalabsorption).[3 7 8] Paired blood samples may need to be sent to an alternative laboratory to rule out TSH assay interference.
- Symptoms or blood test results suggest true malabsorption (for example, deficiencies of vitamin B_{12}, folate, ferritin, or calcium and positive coeliac antibody test).

Competing interests: None declared.

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What advice do you typically offer those with mild hypertension?

The study

Benefits and harms of antihypertensive treatment in low-risk patients with mild hypertension

Sheppard JP, Stevens S, Stevens R, Martin U, Mant J, Hobbs R, McManus R

Published on 1 December 2018 *JAMA Intern Med* 2018;178:1626-34. This project was funded by a grant from the National Institute for Health Research (NIHR-RP-R2-12-015) and the Medical Research Council (MRC) Strategic Skills Postdoctoral Fellowship

Why was this study needed?

Hypertension is the third biggest risk factor for all disease in the UK, closely following smoking and poor diet. It costs the NHS more than £2.1 billion every year.

Clinical guidelines for the treatment of hypertension across the world are inconsistent. American College of Cardiology/American Heart Association guidelines recommend the use of antihypertensive drug treatment in high risk patients with a blood pressure of 130/80 mm Hg or higher, or for individuals with blood pressure of 140/90 mm Hg or higher, regardless of cardiovascular risk. However, recommendations for the use of antihypertensives in patients with low cardiovascular risk has sparked debate, as there is a lack of clinical trial evidence to support the initiation of drug treatment for mild hypertension. This UK study aimed to address this gap.

What did this study do?

This retrospective longitudinal cohort study examined electronic health record data from the Clinical Practice Research Datalink of 38 286 low risk adults (average age 55) with mild hypertension. It compared rates of mortality and risk of cardiovascular disease between two groups: patients who received antihypertensive treatment and those who did not.

Mild hypertension was defined as three consecutive blood pressure readings of 140/90-159/99 mm Hg within 12 months.

The study defined cardiovascular risk by comorbidities rather than cardiovascular risk score because of concerns about missing data in the records. People with a previous history of cardiovascular disease or cardiovascular risk factors were excluded.

Patients were analysed in the two groups regardless of whether they subsequently started or stopped treatment during follow-up. Average follow-up was only 5.8 years, and a longer follow-up could have been useful.

What did it find?

- Overall, 1641 deaths occurred during the 5.8 years of follow-up: 4.49% of those on antihypertensives and 4.08% of those not on treatment. No statistically significant difference was observed between the groups (hazard ratio 1.02, 95% confidence interval 0.88 to 1.17).
- Similarly, no statistically significant associations were found between antihypertensive treatment and cardiovascular disease (hazard ratio 1.09, 95% confidence interval 0.96 to 1.25).
- The study did, however, find that treatment was linked to an increased risk of adverse events such as low blood pressure (hazard ratio 1.69, 95% confidence interval 1.30 to 2.20) and fainting (hazard ratio 1.28, 95% confidence interval 1.10 to 1.50).

What does current guidance say on this issue?

NICE 2011 guidelines on adult hypertension recommend using a formal method of estimating cardiovascular risk to discuss both prognosis and healthcare options for people with hypertension. This applies for not just raised blood pressure but also other modifiable risk factors.

The guidelines recommend offering lifestyle advice initially and then periodically before looking for pharmacological treatment in mild hypertension.

The NICE guideline *Hypertension in adults: diagnosis and management* is in development, with an expected publication date of August 2019.

Competing interests: *The BMJ* has judged that there are no disqualifying financial ties to commercial companies.
Further details of other interests, disclaimers, and permissions can be found on bmj.com

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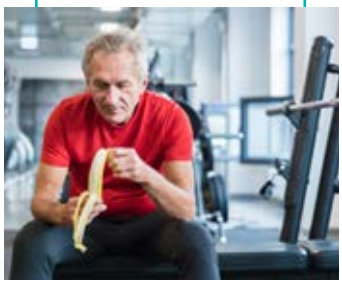
What are the implications?

This study found no evidence to support recommendations outlined in US clinical guidelines for the initiation of treatment in low risk patients with mild hypertension.

The findings suggest that overall cardiovascular risk may be more important than raised blood pressure alone and consideration of wider risk factors may be needed instead of treating isolated mildly raised blood pressure.

As such, it does support the current NICE approach, which suggests looking for non-pharmacological treatments such as lifestyle changes first in mild hypertension.

The study supports the NICE approach, such as lifestyle changes



SPOT DIAGNOSIS

Just a cutaneous (keratotic) horn?

A 70 year old woman attended a dermatologist with a lesion on the dorsum of her right hand (right). It had appeared over eight weeks and was painless but unsightly. She reported good health and no history of warts. Fifteen years ago, she had lymphoma treated by chemotherapy; her last treatment (biological therapy) had finished seven years ago and she had been well since. She had holidayed in Australia for three months at a time over the last three years and more recently had driven frequently from northern England to the south coast while a close relative was ill. She said she was careful to use sunscreen.

The lesion had a red, firm base 2 × 1 cm and 3 mm with a cutaneous horn protruding another 5 mm.

She had cryocautery twice by her general practitioner which did not alter the lesion and so chose to attend a private dermatologist. The lesion was excised.

What is the most likely diagnosis?

Submitted by Jane Wilcock and Yvonne Savage

Patient consent obtained.

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If you would like to write a Case Review or Spot Diagnosis for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

answers

For extra material, including patient outcome, go to bmj.com/endgames

SPOT DIAGNOSIS **Just a cutaneous (keratotic) horn?**

Invasive squamous cell cancer masquerading as a keratotic horn. A keratotic horn is derived from the superficial keratinocyte layer of the skin.

Differential diagnoses include seborrhoeic keratosis (seborrhoeic wart); human papilloma virus (HPV) wart and keratoacanthoma (benign); actinic keratosis, which is pre-malignant; Bowen's disease, which is a non-invasive squamous cell cancer; and invasive squamous cell cancer.

In this case, the speed of growth made a keratoacanthoma a possibility. However, the patient also had several risk factors for squamous cell cancer: age, sun exposure, past lymphoma, past chemotherapy, and no history of warts. Other invasive features of squamous cell cancer relevant to this case include the lesion's arrival over eight weeks and its wide, thick, red base with a diameter larger than the height of the horn. About 35% of keratotic horns are invasive squamous cell cancers.

Invasive squamous cell cancer is a non-melanotic skin malignancy with a good prognosis but may metastasise to the lymph nodes. One study reported a micro-metastasis rate of 3.4% at sentinel lymph node excision.

LEARNING POINTS

- Consider squamous cell cancer in cutaneous keratotic horn.
- Most squamous cell cancers do not present as cutaneous keratotic horns, but rates of squamous cell cancer in the base of horns range from 41 to 77%.[3]
- Refer patients with risk factors and features suggestive of invasive squamous cell cancer to dermatology departments.

PATIENT OUTCOME

Histology of the excised lesion confirmed invasive squamous cell cancer. Cancerous cells were evident in the deep margin, therefore the patient underwent further surgery. Second operative histology revealed no residual squamous cell cancer present.

CPD READING
0.5 HOURS

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LEARNING MODULE

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