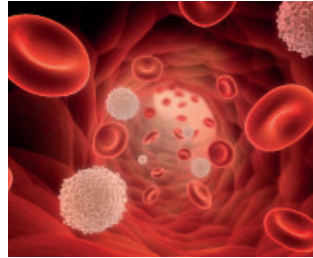


education

FROM THE JOURNALS Edited highlights of weekly research reviews on <https://bit.ly/2PLtl8>

Clots with the AstraZeneca vaccine

On the one hand, this clot news is an open-shut case because the benefits of the vaccine so gigantically outweigh the risks. On the other hand, there is more to this than a PR war about vaccine uptake. What is the mechanism



of thrombosis and thrombocytopenia? These reports from Germany, Austria, and Norway conclude that the thrombotic events represent immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against platelet factor as a result of the ChAdOx1 nCov-19 vaccine. The syndrome was reported to be similar to heparin induced thrombocytopenia, but the patients had never received heparin to explain this.

This syndrome has been triggered non-pharmacologically before—for example, after viral or bacterial infection or knee replacement surgery. The onset was 5-16 days after vaccination. Understandably, people who have had the vaccine will be worried about this, but they shouldn't because the rates are so low. If you're wondering why clots form when there are fewer platelets, it's because the platelet factor 4-antibody immune complexes activate platelets to produce platelet derived microparticles that promote excess thrombin generation.

• *N Engl J Med* doi:10.1056/NEJMoa2104840

• *N Engl J Med* doi:10.1056/NEJMoa2104882

Covid-19: previous infection and future protection

I am proud that I am personally contributing as a participant in this study. But more than that, I'm proud that the SIREN investigators designed a study to properly answer important questions about covid-19 by prospective paired antibody and PCR testing. Everyone hopes that previous infection will protect against future infection.

Intensive follow-up of a prospective cohort can give us a lot more information about this question than a case-control approach. It's a wonderful testament to the UK research scene. Study participants with a previous SARS-CoV-2 infection had an 84% lower risk of infection. The authors conclude: "previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals." Unfortunately, these data cover June to December 2020. Now that we have variants, does previous infection still protect you? Lucky for us, the SIREN study continues, so we'll be able to find out.

• *Lancet* doi:10.1016/S0140-6736(21)00675-9

Walking for peripheral artery disease

People with peripheral artery disease are more likely to walk at a comfortable pace than at speed, but McDermott and colleagues found that low intensity exercise (which did not induce ischaemic leg symptoms) did not carry the benefits of high intensity exercise (which caused ischaemic leg symptoms). A year after randomisation, the 6-minute walk distance was improved in the high intensity group, but not in the low intensity and non-exercise groups.

The exercise groups weren't just given advice to go exercise and sent on their way. They wore accelerometers recording the amount and intensity of exercise. A coach reviewed this data and telephoned them weekly to help them to adhere to the prescribed exercise. Interestingly, the patient-reported outcome (walking impairment questionnaire) did not show the same pattern of benefit; patients reported both exercise groups were better than non-exercise. Interestingly, patients in both exercise groups reported similar benefits compared with the non-exercise group, but the patients were not blinded to study arm. Overall it seems worth pushing through the pain and it appeared safe.

• *JAMA* doi:10.1001/jama.2021.2536

Diagnostic reasoning

Are we good at diagnostic reasoning? It's a large portion of our jobs, so one would hope so. The US practitioners who answered this survey about scenarios relating to common conditions, such as pneumonia and breast cancer, overestimated the probability of disease both before and after testing. "Correct" answers to the scenarios were based on expert review of scientific evidence.



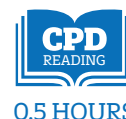
I'm going to be generous and infer that this overestimation stems from a sincere desire to offer patients answers and solutions rather than from an educational deficit. Practitioners are aware of pretest probability and how to interpret positive and negative results, but they just don't seem to use this knowledge in everyday practice. This almost certainly leads to overdiagnosis. This reflects a culture of both over-testing and over-reliance on test results, which is driven by patients and clinicians in a vicious cycle. The authors state: "Medical decisions, like other human decisions, may not be rational and are prone to errors associated with poor knowledge of the base rate of disease or other errors associated with probability."

• *JAMA Intern Med* doi:10.1001/jamainternmed.2021.0269

Alex Nowbar, clinical research fellow, Imperial College London

Uncomplicated urinary tract infection in women

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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.

A 32 year old woman presents with suspected urinary tract infection (UTI). She is passing urine more frequently and has suprapubic pain and dysuria. After two days, her symptoms have not improved.

This article outlines how to identify uncomplicated UTI in adult non-pregnant women (18-65 years old) and discuss options with women to help them make an informed decision about its management.



LEWIS HOUGHTON/SPL

What you should cover

Acute UTIs are common community infections. They affect most women at least once in their life and are far less prevalent among men.¹⁻³ Women with an acute UTI present with diverse symptoms that can be burdensome and adversely affect their quality of life.^{4,5}

History

Take a history to differentiate between an uncomplicated UTI and other causes of urinary symptoms. Recurrent UTI (≥ 3 UTIs within a year), asymptomatic bacteriuria, and infection associated with an indwelling urinary catheter each require a different approach, not covered here. Diagnostic studies support the diagnostic value of commonly recognised symptoms such as dysuria, haematuria, nocturia, urgency, and frequency, as well as those that reduce the probability that a patient has a UTI (vaginal discharge or irritation).^{6,7} In particular, the presence of two or three of the key symptoms (haematuria or cloudy urine, dysuria, and new nocturia) are indicative of a UTI.^{6,8,9} However, no individual or combination of symptoms can be fully diagnostic for a UTI. Check for red flags suggestive of acute pyelonephritis or sepsis (box 1), which would require immediate management or referral to hospital.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We discussed the article with two women who have had uncomplicated urinary tract infections; they emphasised the importance of information about whether alternatives to antibiotics work, about safety-netting information (box 2), and the provision of written information.

WHAT YOU NEED TO KNOW

- In about a third of women with an uncomplicated urinary tract infection, the infection may resolve by about 7-10 days without the need for antibiotics
- The option of "wait and see" (which typically involves providing a delayed prescription) can be discussed as part of a shared decision making process within the consultation
- Although the risk from delaying antibiotics is low, consider pyelonephritis or sepsis in patients who are systemically unwell and have high fever, rigors, nausea/vomiting, flank pain, low blood pressure, high heart rate, high respiratory rate, not passing urine for 12-18 hours, and behaviour change

Box 1 | Red flags for acute pyelonephritis and sepsis

ACUTE PYELONEPHRITIS^{10,11}

- Flank pain (on the back, at or below level of ribcage)
- Rigors or fever $>37.9^{\circ}\text{C}$
- Nausea or vomiting
- New or different myalgia, flu-like illness

SEPSIS¹²

- ≥ 21 breaths/min
- Heart rate ≥ 91 beats/min
- Systolic blood pressure 91-100 mm Hg or <90 mm Hg (that is, >40 mm Hg below normal)
- Not passed urine in the past 12-18 hours or more
- Behaviour changes (acute deterioration, altered behaviour or mental state)

Consider other causes—These include vaginal infections (such as *Trichomonas*, *Candida albicans*, *Gardnerella*), vaginitis (after sexual intercourse, irritants, pelvic inflammatory disease) and vulvovaginal atrophy.

Ask about:

- Recent sexual activity (UTIs are common among sexually active women¹⁰)
- Previous UTI (most women with a UTI report a history of UTI during the 12 months before the current episode¹³)
- Use of spermicidal agents or a diaphragm (spermicidal agents affect the vaginal flora, and the diaphragm increase the levels of introital and periurethral colonisation with bacteria¹⁴)
- Current pregnancy (UTIs are common during pregnancy)
- Diabetes (UTIs are more common in patients with type 2 diabetes¹⁰).

Is examination necessary?

In most non-pregnant women with UTIs, clinical examination is not required, and the consultation can be safely conducted remotely. However, if the patient is systemically unwell and presents with any red flag symptom, arrange a physical examination. Assess her temperature, blood pressure, heart rate, and respiratory rate for signs of systemic illness or sepsis and palpate the abdomen and the back for flank or suprapubic tenderness.

What investigations might be needed?

Urine dipstick tests are the most commonly used point of care test in primary care.¹⁵ For the laboratory diagnosis of UTI, dipstick results can modestly improve diagnostic precision, but cannot definitively rule out a UTI (table). Where symptoms are highly suggestive of a UTI, a urine dipstick is usually not needed.

Investigations for uncomplicated UTI in 18-65 year old non-pregnant women ¹⁵					
No of suggestive symptoms present*	Urine dipstick score			Possibility of UTI	Further testing
	Nitrite	Leucocyte	RBC		
2 or 3	May not be needed [‡]			Highly likely	Urine culture typically not needed
1	+	–	+	Likely ^{†15}	Send urine for culture [‡]
	+	+	–		
	+	–	–	Likely [§]	
	–	+	+		
	–	+	–	Equally likely to other diagnosis	
	–	–	–		
	–	–	–	Less likely [¶]	No indication for urine culture

Urine dipstick cut-off score is based on the sum of nitrite=2, leucocyte=1.5, red blood cells (RBC)=1.

*Suggestive symptoms: dysuria, new nocturia, cloudy urine/haematuria

†Positive predictive value of 92% (95% CI 86% to 96%).

‡Growth cut-off thresholds used to define a UTI can vary.

§Positive predictive value of 81% (95% CI= 77% to 84%).

¶Negative predictive value 76% (95% CI 66 to 84%).

What you should do

Constructing a shared decision making conversation

There are typically two main options that are reasonable to consider: immediate antibiotics or a “wait and see” approach. To enable the patient to make an informed decision, the clinician needs to explain both options, with the benefits and harms of each, and discuss the patient’s preferences. Box 2 suggests an approach to this.

What is the natural course of a UTI?

There is uncertainty around the natural course of uncomplicated UTI, with few studies examining this.

In a systematic review of the placebo-controlled arms of three randomised trials (346 placebo group participants), some women seemed to improve or become symptom-free spontaneously, with most improvement occurring in the first nine days.¹⁷ When asked at seven days, the percentage of participants who reported being symptom-free was 37% in one study and 28% in another. One study asked women again at nine days and six weeks, with 42% and 36% respectively reporting being symptom-free. In 39% of the women, symptoms either failed to improve by six weeks or became worse. The rate of serious complications was low, with progression to pyelonephritis reported in only one placebo participant each in two of the trials.

Another estimate of the mean duration of UTI symptoms is provided by an observational study of women with suspected uncomplicated UTI.¹⁸ In the 511 women who had seen a clinician for their symptoms and rated the initial problem as moderately bad or worse, the mean reported symptom duration was 3.8 days. However, most of the study participants took antibiotics. For the 17 participants (approximately 3%) who did not take antibiotics, their reported mean symptom duration was 4.9 days. In a related five-arm randomised trial, a similar duration of moderately bad or worse symptoms was reported: 3.5 days in the immediate antibiotic group and 4.8 days in the delayed (by 48 hours) prescription group.¹⁹

What difference do antibiotics make?

Surprisingly, we could not find a synthesis of antibiotic versus placebo randomised controlled trials for uncomplicated UTI in women under 65 years old, and therefore no quantification of the effect, perhaps because antibiotic treatment is the traditional management of uncomplicated UTI. The extent to which antibiotics reduce recovery time, reduce the risk of progression to pyelonephritis, and reduce the risk of recurrence is unknown and not presented in evidence based clinical practice guidelines.

Harms are also hard to quantify; for the antibiotics most commonly prescribed for UTI (such as nitrofurantoin, trimethoprim), we could not find synthesised evidence of their harms. For other antibiotics commonly prescribed in primary care, often reported adverse effects include diarrhoea, rash, and nausea.^{20 21} Candidiasis is also possible from antibiotic use. Another harm of antibiotic use is the contribution to antibiotic resistance. This is already particularly a problem for trimethoprim, with existing resistance rates of at least 30% of *Escherichia coli* isolates to trimethoprim.²² Patients with antibiotic resistant *E coli* UTI are more like to experience clinical response failure.²³

Box 2 | Elements of a shared decision making conversation

A shared decision making discussion following the diagnosis of an uncomplicated UTI typically involves the following (although it may not be a simple linear process as presented here).

Explain that there is choice about the next steps and a decision to be made—Invite the patient to partner with you in the decision making to the extent that she desires, and reassure any patient who feels overwhelmed or uncertain about her involvement

Elicit the patient's expectations about management of the condition—This can include past treatments and experiences, along with fears and concerns (including symptom severity and how it may affect daily tasks); this allows for detecting and discussing misperceptions where necessary, either now or later in the process

Explain the options:

- Wait and see (this may involve providing a delayed prescription for antibiotics and clear information about to when to use it)
- Start taking antibiotics immediately

Discuss the options' benefits and harms (including their likely probability or size):

- Describe the natural course of an uncomplicated UTI and explain that, for some women, it will resolve within about a week without taking antibiotics. Also explain that there is uncertainty about exact timeframes and whether the patient will be one of the women who gets better without antibiotics (if not, antibiotics may need to be started later)
- Explain that taking antibiotics will probably shorten the duration of symptoms, but this carries the risk of side effects and of antibiotic resistance
- Regardless of which option is chosen, provide advice on symptom management (such as paracetamol or ibuprofen)

Weighing up—Provide the opportunity for the patient to weigh up the benefits and harms of the options and consider them in the context of her preferences, values, and circumstances

Check the patient's decision making readiness—Explore if the patient has any questions, is ready to make a decision, or needs further information, time, or the involvement of other people

Safety-netting—Provide safety-netting information about when to start taking antibiotics (if delayed prescription) or reconsult:

- Nausea or vomiting
- Rigors
- Shivering, chills, and muscle pain
- Feeling confused or very drowsy
- Not passing urine all day
- Blood in the urine
- Temperature above 38°C
- Kidney pain in the back or under the ribs
- Worsening UTI symptoms
- If taking antibiotics, no improvement in UTI symptoms after 48 hours

Written information—Provide written patient information leaflet with summary information¹⁶

Despite being unable to quantify how much difference antibiotics make to UTI symptom duration, they are effective in treating the infection. Refer to the current National Institute for Health and Care Excellence (NICE) guideline for information on which antibiotic to use (guided by local antibiotic resistance patterns, where possible), and recommended dose and duration.²⁴

Offering a delayed prescription

The option of a delayed prescription will be acceptable to many patients. In a cohort study in Amsterdam, 37% of women who were asked by their general practitioner to delay antibiotic treatment were willing to do so (however no further details about how this option was presented to patients are provided in the study).²⁵ When a delayed antibiotic prescription is chosen, NICE recommend advising patients to start taking them if symptoms do not begin to improve within two days (or sooner if symptoms worsen).²⁴ However, there is no evidence provided in support of this timeframe, and it is unclear whether the two day limit is from the start of symptoms or from first consultation. The findings from the systematic review that estimated the natural course of uncomplicated UTI¹⁷ suggest that a two day timeframe may be too short, with few participants likely to have improved by then, although about a third may have improved by 7–10 days. There seems to be considerable uncertainty and variability in the time for spontaneous recovery; so when “wait and see” (delayed prescribing) is discussed with the patient as an option, this should include careful description of when to reconsult or start antibiotics (box 2).

Other treatments

There is little evidence to support the use of various over-the-counter medications that patients will often have tried before a consultation or concurrently with antibiotics. A 2016 Cochrane review of urinary alkalisers found no randomised trials.²⁶ There are no randomised trials of cranberry products for the treatment of uncomplicated UTI,^{27 28} and a Cochrane review found they did not prevent recurrent urinary tract infections in women any more than placebo or no treatment (risk ratio 0.86, 95% CI 0.71 to 1.04).²⁹

A systematic review of the effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) compared with antibiotics for uncomplicated UTI found five randomised trials.³⁰ For the outcome of symptom resolution, three trials found that NSAIDs were inferior to antibiotics, but two trials (smaller, with higher or unclear risk of bias) found no significant difference between the arms. In the groups that received NSAIDs, the percentage of women with symptom resolution by day 3 or 4 ranged from 39% to 58%. In two of the three trials that reported pyelonephritis, rates were slightly higher in the NSAID group.

Competing interests: TCH and CDM have received funding from the Australian National Health and Medical Research Council for research on reducing antibiotic resistance for acute infections and for shared decision making, and from the Australian Commission on Safety and Quality in Health Care for the development of shared decision making resources. MB has no competing interests to declare.

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EDUCATION INTO PRACTICE

- How do you invite patients to share in decision making about management of an uncomplicated UTI, including a discussion about their expectations?
- How can you facilitate a balanced discussion about the benefits and harms of using antibiotics immediately or adopting a “wait and see” approach?

10-MINUTE CONSULTATION

Otitis externa

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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.

A 57 year old man presents to his general practitioner with a 3 day history of severe right sided ear pain, reduced hearing, and discharge. He is a self-employed car mechanic with a small business, and has been absent from work for the past two days because of the pain and subsequent lack of sleep. He has hypertension and type 2 diabetes.

Otitis externa is an infection of the skin of the outer ear canal which typically presents with severe otalgia with or without ear discharge and reduced hearing. It is a common condition with an annual incidence of 1% that affects 10% of the population during their lifetime.^{1,2} In 98% of cases the cause is bacterial, with *Pseudomonas aeruginosa* and *Staphylococcus aureus* the most common pathogens.³ Otitis externa often causes severe pain and can have a major impact on quality of life, disturbing sleep, and the ability to work or exercise.

HOW THIS ARTICLE WAS CREATED

We discussed with our GP coauthor the common problems GPs face when assessing patients with otitis externa and what information would be most beneficial to include in the article. We carried out a literature search on 18 March 2020 with the search terms "otitis externa", "otalgia", "management of otitis externa", and "risk factors for otitis externa". We used these sources to explore the condition in depth looking at epidemiology, diagnosis, and management to compile a comprehensive approach for the management of otitis externa in primary care.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We discussed this article with a patient who had recently received a diagnosis and had been treated for otitis externa. She highlighted the need for appropriate and prompt treatment to avoid prolonged symptoms.

WHAT YOU NEED TO KNOW

- Acute uncomplicated otitis externa can be managed effectively with topical treatments, for up to 14 days if required
- Clues for malignant otitis externa include fever, disproportionate pain, or a poor response to first line treatment, particularly in people with diabetes or immunocompromise
- Consider cholesteatoma in patients with recurrent discharge



0.5 HOURS



See <http://learning.bmj.com> for linked learning module

What you should cover

As with any primary care consultation, take a focused history to narrow down the differential diagnosis (table) and explore the patient's ideas and concerns. Ask specifically about risk factors and clinical features for malignant otitis externa (box). This extension of the infection into the temporal bone can be easily missed and is a serious complication requiring long term intravenous antibiotic treatment. If not treated it may lead to sepsis and intracranial complications.

Malignant otitis externa

Malignant otitis externa is a rare but serious extension of otitis externa, whereby infection spreads to surrounding structures leading to osteomyelitis of the temporal bone. Soft tissue, cartilage, and bone are all affected as osteomyelitis spreads along the skull base.⁴

Risk factors

- Diabetes—up to 90% of patients with malignant otitis externa have diabetes^{5,6}
- Older age
- Immunocompromise

Differentiating otitis externa from malignant otitis externa

- Clinically, differentiating malignant otitis externa from otitis externa is challenging and may not be always possible on the initial assessment in primary care. Have a high index of suspicion in patients with risk factors, in particular diabetes, who have otitis externa that is not responding to initial treatment
- Granulation tissue or exposed bone in the floor of the osseocartilaginous junction, if seen, is pathognomonic of malignant otitis externa
- One clear difference that would point towards malignant otitis externa is cranial nerve involvement, typically facial nerve palsy⁶
- Disproportionate pain with fever may indicate malignant otitis externa; however, otitis externa is known to be extremely painful so this is a relatively soft differentiating sign and should be used alongside the full clinical picture. Associated vertigo and hearing loss may indicate malignant otitis externa
- If you suspect malignant otitis externa arrange an urgent (same day) ear, nose, and throat (ENT) review. A computed tomography imaging scan is typically required to confirm the diagnosis.⁵

Differential diagnosis ³						
	<i>Pain</i>	<i>Itch</i>	<i>Discharge</i>	<i>Fever</i>	<i>Duration</i>	<i>Other features</i>
<i>Acute otitis externa</i>	+++	++	+	Uncommon	<6 weeks	Severe pain is the hallmark of otitis externa, commonly associated with purulent discharge
<i>Chronic otitis externa</i>	+	++	+/-	Uncommon	>3 months, usually relapsing-remitting	May be associated with an underlying dermatological diagnosis
<i>Acute localised otitis externa (furuncle)</i>	+++	-	-	Uncommon	Hours or days	Severe localised pain. A small staphylococcal abscess of the hair follicle occurs in the hair-bearing outer part of the ear canal
<i>Malignant otitis externa</i>	++++	+/-	+	Fever should prompt suspicion of malignant otitis externa, particularly in at-risk patients (box)	Acute onset. Persistent and refractory to treatment	History of diabetes, older age, or immunocompromise
<i>Otitis media</i>	+++	-	+/-	May be present	Hours or days	Tympanic membrane is erythematous or bulging
<i>Wax</i>	+/-	+/-	+/-	Absent	Variable	
<i>Herpes zoster oticus (Ramsay-Hunt syndrome)</i>	+++	+/-	+/-	Uncommon	Hours or days	Vesicles may be present within the ear canal. Facial palsy
<i>Cholesteatoma</i>	+/-	+/-	++	Absent	Days to years	Persistent or recurrent otorrhoea. Deep retraction pocket in the tympanic membrane—most commonly pars flaccida. Previous ear surgery (for cholesteatoma or grommets), recurrent infections

Otitis externa often causes severe pain, disturbing sleep

Ear symptoms

- **Duration**—Symptoms of acute otitis externa typically last less than six weeks; chronic otitis externa lasts more than three months. Symptoms that last between six weeks and three months are defined as subacute otitis externa.
 - **Pain**—Pain is present in 70% of people with acute otitis externa;³ however, deep severe pain that is out of proportion to the general presentation of the patient should alert you to the possibility of malignant otitis externa.
 - **Itch**—Itch is present in 60% of acute otitis externa cases.³ It can be a symptom of the infection itself, or of an underlying dermatosis such as eczema or psoriasis.
 - **Discharge**—Bacterial infection is typically associated with scant white purulent discharge, which occasionally can be thick. Fungal discharge is typically described as fluffy white to off-white, but can also be black or grey, with or without fungal spores.⁷
 - **Hearing loss**—Loss of hearing typically presents only when discharge or swelling obscures the tympanic membrane and therefore improves with resolution of the infection. Hearing loss is present in around a third of cases of acute otitis externa at initial presentation.³
 - **Tinnitus**—Tinnitus is rarely seen in isolation with otitis externa, but a conductive hearing loss caused by ear canal oedema may worsen pre-existing tinnitus.
- Systemic symptoms such as fever, headaches, or loss of appetite are unusual in uncomplicated otitis externa and should rouse suspicion of malignant otitis externa or an alternative pathology.

Risk factors for otitis externa³

- **Water exposure**—This is typically from swimming, with fresh water posing highest risk, but organisms responsible for acute otitis externa are also often found in hot tubs and water sources that comply with water quality standards
- **Trauma**—Trauma to the ear canal can occur from cleaning, scratching, or instrumentation

- Use of hearing aids or ear plugs as these can introduce bacteria and cause trauma, and may cause the ear to sweat
- Dermatitis
- Diabetes, other causes of immunocompromise, or older age
- Previous ear surgery.

Examination

Examine both ears, starting with the unaffected or less affected ear.

Inspect the ear for erythema, swelling, or scarring. Erythema and swelling, primarily affecting the pinna but sparing the ear lobe, may indicate perichondritis: seek a same day ENT opinion as urgent intravenous antibiotics may be indicated to prevent sepsis and long term deformity from destruction of the cartilage. Simple pinna cellulitis will typically involve the ear lobe.

Worsening pain with traction of the pinna or when pressing the tragus is characteristic of otitis externa,⁸ but if the diagnosis is clear this test may not be necessary to your examination.

Examine the mastoid area for erythema, swelling, and tenderness. Tenderness over this area is common in otitis externa; however, if the patient has associated boggy/fluctuance, loss of the post-auricular sulcus, or protrusion of the pinna, this should raise suspicion of mastoiditis and we recommend a same day ENT review. Mastoiditis is rare, particularly in adults. It is a complication of otitis media rather than otitis externa as the mastoid is contiguous with the middle ear.

Otoscopy

Gently examine the external auditory canal and tympanic membrane. Otitis externa is indicated by inflammation and erythema of the ear canal. White debris, which can be thick, and commonly has an offensive odour, is often present in the canal (figure a, p78). The tympanic membrane may be difficult to see clearly because of swelling of the walls and debris within the canal.

If the patient reports systemic features or appears unwell, check their temperature, heart rate, and blood pressure. These observations will rarely be out of normal range in uncomplicated otitis externa.



(a) Otitis externa. White purulent debris can be seen at the external auditory meatus. (b) Otitis externa. The ear canal is narrowed, making it appear more slit-like, with white debris sitting on the canal wall

What you should do

Acute uncomplicated otitis externa

Topical antibiotics can be prescribed in preparations with or without corticosteroid. A Cochrane review in 2010 found topical antibiotics to be effective for uncomplicated acute otitis externa, with little to no difference between the efficacy of different topical treatments.^{9 10} Sprays are a good first choice, as they may be easier to use than drops and are often better tolerated.¹¹ Regardless of which topical agent is prescribed, 65–90% of patients improve clinically in 7–10 days.³ Some patients require a longer course of treatment, and those who still have symptoms after 7 days should continue the same treatment for up to 14 days. If not resolved after 14 days, then consider this as treatment failure.⁹ Acetic acid can be used as an alternative to topical antibiotics in mild cases of otitis externa.

Oral antibiotics are rarely indicated. Their use should be reserved for patients with poorly controlled diabetes mellitus, immunosuppression, or where the infection extends beyond the ear canal causing pinna cellulitis.¹² In these instances, topical treatment should still be used alongside oral antibiotics.

Minimise any aggravating factors—for example, advise patients to limit use of ear plugs or hearing aids if possible—and suggest that they keep the ear dry until the infection is resolved. This can be achieved by placing cotton wool soaked in petroleum jelly at the meatus, sitting in the conchal bowl, but not inserted into the canal. Advise patients with associated skin conditions to consider avoiding possible precipitating factors (eg, use of earphones, soaps, certain hair products) to apply an emollient regularly, and to use a topical steroid cream during acute flare ups. Offer analgesia according to the World Health Organization analgesic ladder.

Heavy discharge, canal stenosis, and swabs

Consider cleaning the external auditory canal (known as aural toilet) if heavy discharge is present, as discharge may impair topical treatment. This can be done using either dry swabbing or microsuction. We do not recommend ear syringing as this will likely be very painful for the patient. To perform dry swabbing use a Jobson Horne with cotton wool wrapped around

the tip (or a simple swab) to soak up the excessive discharge in the external auditory meatus under direct vision. Specific training is not required to perform dry swabbing, but remember that a clear view of the tip of the instrument or swab being used is important to ensure no damage to the tympanic membrane or middle ear structures. Note that without a microscope or endoscope you will not be cleaning very deep into the canal. Taking a swab for microscopy and culture is not necessary in patients with uncomplicated otitis externa.¹³ However, if treatment has not been effective after 14 days, taking a swab from the ear canal for culture can aid in targeting antimicrobial treatment.⁹

Follow-up and treatment failure

Follow-up is not required for most patients with uncomplicated acute otitis externa. Review patients who have

- ongoing symptoms despite treatment
- accompanying extra-auricular cellulitis
- diabetes, or who are immunocompromised
- associated wax impaction or a stenosed ear canal, or if you were not able to see the tympanic membrane clearly enough to rule out other causes of infection and discharge such as a cholesteatoma.

In the UK, most ENT departments run emergency clinics for patients with otitis externa and other ENT emergencies, such as recurrent epistaxis and foreign body in the ear. For patients with otitis externa we recommend referring to an ENT emergency clinic if

- the otitis externa does not respond to 14 days of topical antibiotics
- the ear canal is completely stenosed where drops cannot penetrate and wick insertion may be required
- when the canal is full of debris and aural toilet cannot be carried out in primary care.

Competing interests: None declared.

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EDUCATION INTO PRACTICE

- Which topical treatments are recommended for otitis externa in your local prescribing guidelines?
- How do you assess and document the risk of malignant otitis externa in patients presenting with ear pain and discharge?

CLINICAL OPINION

Polycystic ovary syndrome: why widening the diagnostic criteria may harm women

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The 2018 International Guidelines¹ for polycystic ovary syndrome (PCOS) were intended to standardise diagnosis and improve care, but they also endorsed the controversial Rotterdam diagnostic criteria. These include a larger pool of individuals than alternative definitions and turn many more women into PCOS patients. A growing body of research² shows that labelling some women with this condition can have harmful, lifelong consequences.

An increase in prevalence

The previous 1990 National Institutes of Health definition of PCOS required both (a) oligo-/anovulation (eg, irregular menstrual cycles) and (b) signs of hyperandrogenism (eg, excess hair growth, acne, or excess male hormones/androgens). The 2003 Rotterdam³ definition added a third criterion: (c) polycystic ovaries on ultrasound (enlarged ovaries with lots of small follicles), but required only two of the three criteria to meet the definition. This introduced four categories or subtypes that now fall within the scope of the PCOS label (a+b, b+c, a+c, and a+b+c) and dramatically increased prevalence (estimates doubling from 9% to 18%⁴ in Australian women aged 27–34). The 2018 guidelines¹ made several minor modifications to the Rotterdam criteria.

The ultrasound criteria have been tightened to reflect the greater sensitivity of modern imaging technology. Ultrasounds are also no longer recommended in adolescents because of the overlap with normal ovarian physiology. While these specific changes reduce the risk of overdiagnosis, the newly endorsed criteria still capture many women with few or mild symptoms. The

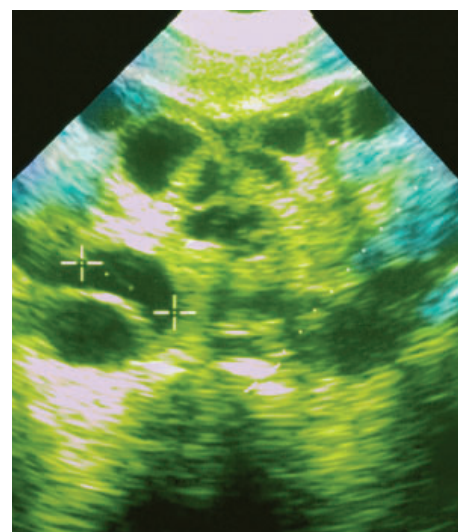
Consequences of PCOS are not the same for all women who are diagnosed

lowered score for hirsutism (excess hair growth) in the 2018 guidelines has also raised concerns⁵ about overdiagnosis.

Different disease subtypes

PCOS is associated with an increased risk⁶ of infertility and metabolic complications including insulin resistance, obesity, metabolic syndrome, and type 2 diabetes. However, the potential consequences are not the same for all women diagnosed. Cross sectional studies⁷ consistently show that the non-hyperandrogenic subtype (meeting criteria a+c) does not have the same increased risk of adverse metabolic complications found in the hyperandrogenic subtypes (a+b, b+c, a+b+c), indicating different clinical courses. Furthermore, features of this subtype⁸ overlap with hypothalamic amenorrhea (absence of menstruation triggered by stress, overexercising, or undereating), resulting in women being misdiagnosed with PCOS and not receiving care for their actual condition.

Given evidence of the disparate metabolic risk profiles between subtypes and the potential for overdiagnosis, why did the recent guidelines endorse the broader Rotterdam criteria? No rationale was provided. Probably it is driven by good intentions—trying to ensure nobody misses out on potentially beneficial care. However, we could find no acknowledgment in the 2018 guidelines of the evidence suggesting that the non-hyperandrogenic subtype has a lower risk metabolic profile. This leads women to believe their likelihood of future



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disease is higher than it actually is, causing undue distress and worry and potentially affecting insurance premiums. Furthermore, limited evidence⁹ has found that prevalence of all subtypes rapidly decreases after 25 years of age, suggesting symptoms might be transitory for some younger women.

Harms of overdiagnosis

Some may ask: *How is overdiagnosis of PCOS harmful?* The benefits of a timely PCOS diagnosis are well described. However, research¹⁰ now highlights several unintended harms, such as altered self-perceptions and longlasting worry about future health. Our qualitative study² showed fear of infertility can result in adverse psychological and behavioural consequences including anxiety, depression, lower self-worth, altered life and education goals, risk taking with contraception, and unintended pregnancies.

Others may ask: *But doesn't a diagnosis enable healthy lifestyle changes?* Multiple trials¹² in various conditions have shown that disclosure of risk status or a diagnosis¹³ do not improve health related behaviours. Similarly, in PCOS, our longitudinal analysis¹¹ found young women newly diagnosed with PCOS did not increase their physical activity or increase their vegetable intake.

Ascribing a diagnosis should improve patient centred outcomes, not merely categorise and label more individuals as abnormal. Stratifying subtypes into separate conditions may reduce the harms of trying to contain such a heterogeneous condition in one diagnostic label.

Competing interests: See bmj.com.

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CASE REVIEW Unilateral nipple rash in a man

A man in his 50s was referred to the breast surgery clinic with a one month history of an exudating, oedematous, itchy right nipple-areolar complex. He had experienced hay fever in the past but reported no recent contact with known irritants or allergens. He had not used topical steroids before presentation. On examination, both the right nipple and the areola were erythematous, thickened, and excoriated (figure). The left nipple was unaffected, and there were no palpable breast lumps or axillary lymphadenopathy bilaterally. Lesions were not present elsewhere. Mammography and ultrasonography showed only thickened right areolar skin. Right areolar punch biopsy revealed epidermal hyperplasia, hyperkeratosis/parakeratosis, and spongiosis with subepithelial inflammation.

1 What are the malignant differential diagnoses of nipple lesions?

2 What are the benign differential diagnoses of nipple lesions?

3 What is the diagnosis in this case?

Submitted by Hamid Abudhaise, Mohsin Dani, and Haresh Devalia

Patient consent obtained.

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Right nipple eczema, showing erythema, oedema, and excoriation of the nipple-areolar complex

CASE REVIEW Unilateral nipple rash in a man

1 What are the malignant differential diagnoses of nipple lesions?

• Paget's disease of the nipple (1.5% of breast cancers in male patients)—red flag signs are unilateral eczematous changes in the nipple that persist despite the use of topical steroid, nipple ulceration, palpable breast lump, discharge from the nipple including bleeding, and nipple pain or itching. In advanced cases, lesions can spread to the areola.

• Basal cell carcinoma of the nipple-areolar complex (uncommon)—affects men more often than women, possibly because of greater sun exposure in that area. It can present as a plaque, nodule, or papule. Red flags include unilateral, slow growing, and non-healing lesions; ulceration; and nipple erosion.

• Bowen's disease (squamous cell carcinoma in situ) of the nipple (rare)—presents as an eczematous lesion. Red flags include a unilateral, persistent lesion, and no response to topical steroids.

Breast cancer in male patients accounts for less than 1% of all breast cancers.

Histology is the ideal approach for diagnosis.

2 What are the benign differential diagnoses of nipple lesions?

• Dermatitis (breast eczema)—typically bilateral, although unilateral lesions might be seen in

that malignancy was unlikely.

and ultrasonography findings already suggested breast; in this case, however, the mammography (and excluding) malignant transformation in the

Histology is the ideal approach for diagnosing inflammation on histology.

hyperkeratosis/parakeratosis, and subepithelial confirmed by epidermal hyperplasia,

Adult atopic dermatitis (prevalence 2-10%)—

3 What is the diagnosis in this case?

biopsy might be needed for diagnosis.

Microscopy, culture of skin scrapings, or tissue immunocompromised individuals and lactating

flaky nipple-areolar complex; more common in Candidal infection—a sore, erythematous, or

a nipple nodule, or nipple induration and erosion.

usually affects middle aged women, and presents with unilateral serous or bloody nipple discharge,

benign growth of the nipple lactiferous ducts that Papillary adenoma of the nipple (uncommon)—a

surfaces of the limbs and the scalp.

• Psoriasis—psoriatic lesions might be present on other areas of the body—commonly the extensor

the nipple. History might include atopy or recent contact with known irritants or allergens.

eczema. Typically affects the areola but spares the absence of other lesions, such as flexural

PATIENT OUTCOME

Ecema of the nipple-areolar complex resolved completely after treatment with emollients and topical steroids. This was confirmed clinically during follow-up assessment.

basal cell carcinoma.

Bowen's disease, and disease of the nipple, common than Paget's

areolar complex is more common than Paget's

• Dermatitis of the nipple-areolar complex is more common than Paget's

histological evaluation, investigations, and assessment, radiological

surgeons for specialist areolar complex to breast

changes of the nipple-areolar complex to breast

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Moist lesion in the third webspace of the fingers

This is interdigital candidiasis in a patient in her 70s. Interdigital candidiasis, a form of candidal intertrigo, is caused by *Candida* infection and is associated with frequent exposure to water. It occurs in the webspaces between the fingers, most commonly the third web between the middle and ring fingers.

The patient gave a three month history of handwashing, about 40 times daily, after the onset of the covid-19 pandemic because she was worried about infection. She first noticed a tingling in the web between her second and third fingers and then went on to develop a moist, raw

and well demarcated lesion. On examination this was shiny and erythematous and ringed by a white collarette.

Interdigital candidiasis should be considered in patients presenting with this characteristic appearance in the finger webspaces who report a history of frequent handwashing or immunosuppression, or both.

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Patient consent obtained.

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Space travel

The cleverness of rocket scientists is legendary, but Minerva sometimes wonders if they've fully grasped



the physiological challenges of the prolonged weightlessness that interplanetary travel entails. Data from an astronaut who spent a year on the International Space Station show a gradual but progressive loss of left ventricular mass despite sustained periods of exercise (*Circulation* doi:10.1161/CIRCULATIONAHA.120.050418). The same thing occurred in an extreme long-distance swimmer—another activity that reduces gravitational loading.

Non-steroidal anti-inflammatory drugs in older people

Non-steroidal anti-inflammatory drugs inhibit cyclo-oxygenases and alter renal haemodynamics and salt and water excretion. However, a study from the US suggests that this rarely results in harm to the kidney (*J Am Ger Soc* doi:10.1111/jgs.16961). Among 3000 older adults, use of these drugs wasn't associated with markers of glomerular or tubular damage. Over 10 years of observation, decline in kidney function was no faster in those using non-steroidal anti-inflammatory drugs than in non-users.

Recreational drugs

People who use recreational drugs such as alcohol, tobacco, cocaine, amphetamine, and cannabis are more likely to develop atherosclerosis according to a database analysis of US veterans (*Heart* doi:10.1136/heartjnl-2020-318119). Risk was highest in people who had used several drugs. Those using four or more had nearly 10 times the rate of premature atherosclerotic disease than non-users. Amphetamine was especially dangerous.

Low dose aspirin

A few years ago, a trial of low dose aspirin in healthy older people found an unexpected increase in mortality in those taking daily aspirin, mainly owing to higher rates of cancer related death (*N Engl J Med* doi:10.1056/NEJMoa1803955). Another large trial in community dwelling people aged 70 or older reports something similar. Although no differences were noted between groups in incident cancers, those taking aspirin had a higher risk of cancer that had already metastasised by the time of diagnosis (*JNCI* doi:10.1093/jnci/djaa114).

Beta blockers

Although it's widely believed that β blockers cause depression and other psychiatric conditions, a systematic review raises doubts. An analysis of data from more than 50 000 people who took part in 285 randomised controlled trials showed that psychiatric

symptoms were common during β blocker therapy, with depression, insomnia, unusual dreams, sleep disturbance, and somnolence being most prevalent (*Hypertension* doi:10.1161/HYPERTENSIONAHA.120.16590). However, these symptoms were equally common in those treated with placebo or active comparator.

Vegetarian diet in pregnancy

A survey of 2000 pregnant women in the US found that roughly 6% defined themselves as vegetarian. Although their babies were more likely to be born small for gestational age, there was no accompanying increase in post-natal morbidity. A vegetarian diet was not associated with gestational diabetes, hypertensive disorders, or gestational anaemia (*Int J Epidemiol* doi:10.1093/ije/dyaa200).

Rhinitis and as needed nasal sprays

Regular use of an intranasal corticosteroid spray is an effective treatment for allergic rhinitis. But it looks as if giving patients a nasal spray and telling them to use it when they need it works just as well. In a 6 week trial, participants assigned to fluticasone nasal spray to be used as required reported similar improvements to those taking two sprays daily (*JACI* doi:10.1016/j.jaip.2020.09.057). Steroid exposure was lower in the as-required group.

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