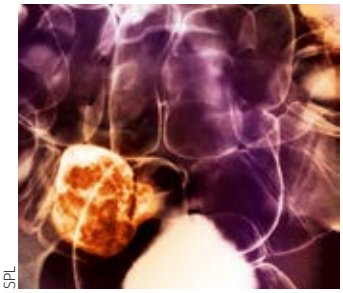
education

THE ART OF MEDICINE

A fateful omission


SPL

It was one of my first days at Stanford. Last night's admissions were discussed—most were elderly patients with multimorbidities.

One patient stood out however. I remember him as though it was yesterday. He was a fit 60 year old who had fainted in the shower. He was severely anaemic and was diagnosed as having caecal carcinoma, which had metastasised to the liver.

I kept thinking of him afterwards. I found it particularly shocking that we couldn't save him even though we could have detected this disease and prevented his death if simple guidelines had been followed.

This patient helped add a new focus to my daily practice and teaching. A study I did of GPs found that, although they endorsed screening for colorectal cancer, they were uncertain what constituted proper screening. Indeed, most colon cancers were diagnosed only once they became symptomatic, usually after they had metastasised.

I realised that similar fateful omissions apply to other effective primary preventive measures, including immunisation and early detection of osteoporosis, atrial fibrillation, and atherosclerosis in people at risk.

I started asking about patients' "prevention status" at each encounter, believing this would do more good than waiting for patients to become ill.

I kept instructing my juniors until "prevention" was covered in every patient's notes, ensuring that appropriate advice was provided.

All this was too late for that particular patient, but at the meagre cost of three minutes it remains one of the most powerful interventions that physicians can adopt.

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We welcome contributions to this column. Please email samuel.parker@bmj.com.

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CLINICAL UPDATES

American Heart Association issues statement on cardiac arrest in pregnancy

Cardiac arrests are fortunately rare in pregnancy. But should cardiopulmonary resuscitation be performed differently on pregnant women? The American Heart Association's recent scientific statement on cardiac arrest in pregnancy recommends using the most current recommendations for performing chest compressions in non-pregnant adults. Previously there had been debate about moving the hand position further up the sternum. The statement also provides an early warning score chart to predict when a pregnant patient might have a cardiac arrest.

www.ncbi.nlm.nih.gov/pubmed/26443610

NICE approves tolvaptan for autosomal dominant polycystic kidney disease (ADPKD) in adults

Tolvaptan is a selective vasopressin antagonist that reduces cell proliferation, cyst formation, and fluid excretion. This in turn reduces kidney growth and protects renal function. It has been approved by the National Institute for Health and Care Excellence for treatment of ADPKD in patients who have chronic kidney disease stage 2 or 3 at the start of treatment and evidence of rapidly progressing disease.

www.nice.org.uk/guidance/ta358

Atopic dermatitis guidelines: how to prevent flares

Atopic dermatitis can affect people of any age and disease flares cause considerable distress. Use of topical corticosteroids or topical calcineurin inhibitors is recommended after disease has stabilised to reduce disease flares. Educational programmes are advocated as an adjunct to conventional treatment. Guidelines advise asking about environmental and food allergies, which are common in these patients.

www.guideline.gov/content.aspx?id=49257#Section420

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FAST FACT—BELL'S PALSY

About one in 60 people will have Bell's palsy in their lifetime.[1] Because Bell's palsy is a diagnosis of exclusion, all patients need a full neurological examination to identify alternative causes. Pronator drift has a high sensitivity for predicting an upper motor neurone disease process (such as stroke).[2] A positive pronator drift result means a patient does not have Bell's palsy.

PRACTICE POINTER

Explaining laboratory test results to patients: what the clinician needs to know

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Better understanding by patients of why tests are performed and what the results mean increases satisfaction with care.[1-4] Patients increasingly have direct access to their test results through online portals. Although patients may discuss test results with family and friends or seek information on the internet,[5] the responsibility for explaining test results lies with clinicians. Discussions must take into account the patient's literacy and numeracy level, and clinicians should explain clearly what the results mean and how they influence treatment choices.

Why are tests performed?

It is crucial to understand why a test was done to understand the meaning of its result. The following are common reasons for testing:

- Diagnosis: to confirm (or exclude) a specific diagnosis when suggestive symptoms or signs are present—for example, measurement of glycated haemoglobin in a patient with thirst and suspected type 2 diabetes
- Monitoring: to monitor response to treatment (for example, prostate specific antigen in prostate cancer) or disease progression (estimated glomerular filtration rate in chronic kidney disease)
- Risk stratification: to help assess disease risk and the need for preventive therapy—for example, lipid measurement to help quantify cardiovascular disease risk
- Screening: undertaken in asymptomatic people to assess the risk of occult disease and the need for further confirmatory tests—for example, colorectal cancer screening by faecal occult blood testing or neonatal screening for inborn errors of metabolism.

Reference intervals

"My sodium level is slightly low at around 131 mmol/L: is there something wrong?"

Although most healthy people have a sodium value between 133 mmol/L and 146 mmol/L, one in every 40 healthy people will have a reading just below this range. Because you are otherwise well and the level has not changed, it is unlikely to be important.

A reference interval usually includes 95% of the test results obtained from a presumed healthy population (fig 1A).[6] For many tests the reference distribution is "normal" or has a Gaussian distribution around the population mean; for other tests it may be skewed to the right or to the left around a population median.[6] Quoted reference intervals may not take into account important factors such as the influence of sex, age, and ethnicity. By definition 2.5% of healthy people (one in 40) will have results just outside either end of the reference interval. The chance of a test result in a healthy person falling outside the reference interval is 5% when a single test is performed but increases to 64% when 20 tests (such as a full blood count, urea and electrolytes, and liver function tests) are performed. This may lead to unnecessary further investigation and overtesting; follow-up of such minor abnormalities in an otherwise well patient may not be indicated. It is useful for patients to know that reference intervals have limitations, and that if many tests are performed it is not surprising that the occasional result falls slightly outside the reference interval.

For many tests the reference interval depends on the analytical method used so only the reference interval provided by the testing laboratory should be used, not those used by other laboratories or from internet sources or comparisons with friends and family. Although initiatives are under way to harmonise reference intervals between laboratories in the United Kingdom, differences still exist for some commonly requested tests (sometimes for good scientific reasons).[7]

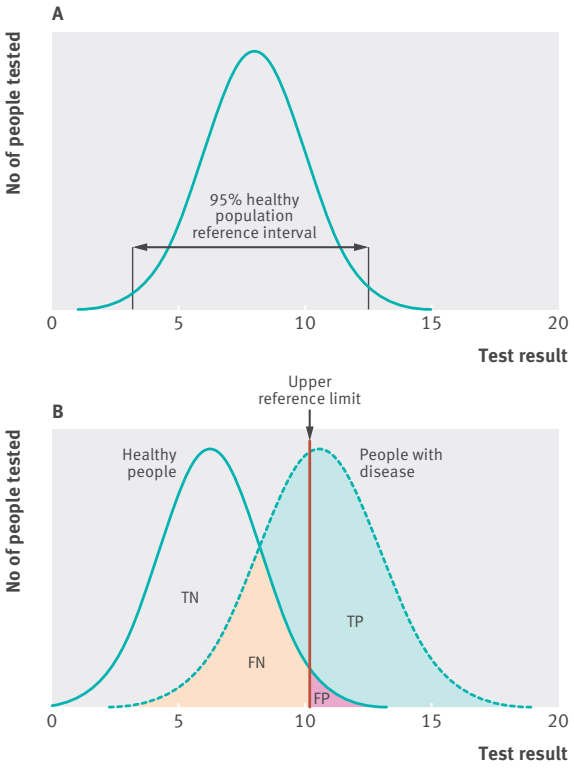

Fig 1 | (A) Distribution of test results in a healthy population with a 95% reference interval. (B) Distribution of test results in a healthy population and a population with disease illustrating a large overlap. Using a cut off (in this case the upper limit of the healthy population reference interval) the following may be defined: true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN)

The predictive value of tests

"My coeliac disease blood test result is negative: does this mean I have nothing to worry about?"

The negative test result makes coeliac disease unlikely but does not completely rule it out. However, because of your symptoms, I would like to discuss with the gastroenterology specialist whether further investigation for coeliac disease is needed.

Because test results in health and disease usually overlap (fig 1B), the results of an individual test may not always differentiate healthy people from those with disease. The positive predictive value (PPV) of a test is the probability that a patient with a positive test result has the disease, whereas the negative predictive value (NPV) is the probability that a patient with a negative test result does not have the disease. There is always a trade off between PPV and NPV, which will change with the particular cut off used to differentiate between the healthy and disease groups. A cut off chosen to maximise PPV will increase the number of false negatives; a cut off chosen to maximise NPV will do so at the cost of more false positives. No tests have both 100% sensitivity and 100% specificity. All test results must be interpreted in the context of the patient's clinical features, and if the index of suspicion is high further investigation may be warranted even if the test result is negative.

Furthermore, the performance of the test depends on the prevalence of the disease in the population tested: for a given cut off, as disease prevalence falls the PPV will also fall (the number of false positives will increase). Tests that perform well in a specialist hospital setting where the prevalence of a particular disease is high may be less useful in primary care where disease prevalence may be lower:

Faecal elastase is commonly measured to assess exocrine pancreatic function; it has a reported sensitivity and specificity of 75% and 95%, respectively. In a hospital patient cohort in which the prevalence of chronic pancreatitis was 8.5%, a positive test result had a predictive value for exocrine pancreatic insufficiency of 58%.[8] However, the prevalence of exocrine pancreatic insufficiency is much lower in primary care. If the test is applied to a population with a disease prevalence of 0.1% the positive predictive value falls to 1.2%.

Monitoring and variability in test results

My cholesterol was 5.7 mmol/L. I improved my diet but now it has gone up to 6.1 mmol/L: why?'

Cholesterol levels vary from day to day depending on such factors as body rhythms, fluid intake, and season of the year. A small change in cholesterol like this is probably due to this natural variation rather than a true rise in value.

All numerical test results vary over time even without a change in the patient's clinical status.[9] This variability comprises three elements:

- Pre-analytical variability: for example, time of sampling, fasting and hydration status, exercise, delay in sample centrifugation

WHAT YOU NEED TO KNOW

- Minor test abnormalities in well people may have no clinical relevance. By definition, 5% of healthy people will have test results that fall just outside the 95% healthy population reference interval
- Consider the possibility of false positives and negatives: the predictive value of tests varies with different disease prevalence in different settings; if the index of suspicion is high, further tests may be warranted even if the result is negative
- Outside of formal screening programmes, speculative screening tests in well asymptomatic people have little value and may result in overinvestigation and unnecessary treatment

TEK IMAGE/SPL

- Analytical variability: which arises from random error (imprecision) in measurement in the laboratory
- Biological variability: random fluctuation around a homeostatic set point. For tests that are affected by cyclical rhythms, such as gonadotrophins and sex hormones in women and testosterone in men, this may be great. However, even more stable tests fluctuate—for example, about 6% variation for total cholesterol and 5% for creatinine.

All these factors can combine to produce relatively large day to day variability in test results.[9 10] This is an important consideration when test results are used to monitor disease progression or response to treatment.

Taking into account these three components of variability, for a cholesterol level of 6.1 mmol/L, the "true" result is likely to be within the range 5.4-6.8 mmol/L, and for a level of 5.7 mmol/L it is likely to be within the range 5.0-6.4 mmol/L. Because of the overlap between these two ranges, the difference in the results may simply reflect expected variability rather than any increase in cholesterol concentration.[10]

Tests for risk stratification

"My cholesterol is high so why am I not being offered treatment?"

Only people at higher risk of heart disease benefit from cholesterol lowering tablets. Although your cholesterol level is increased, we calculated that your risk of heart disease over the next 10 years is low because you are otherwise healthy, don't smoke, and have normal blood pressure. The benefit from a cholesterol lowering tablet at this stage is likely to be low and such tablets may also have side effects.

Testing can be used for risk stratification and making decisions about preventive treatment. A good example is cardiovascular risk prediction where serum cholesterol on its own is a relatively poor predictor of risk. However, combined with other information such as age, sex, comorbidities, and family history in a risk calculator such as QRISK2 (www.Qrisk.org) it provides a more robust measure of absolute cardiovascular risk that can help to decide whether to offer lipid lowering therapy.[11] Two patients may therefore have the same cholesterol concentration but different cardiovascular risk, with one being offered lipid lowering therapy and the other not. Representation of risk by pictographs is well understood by patients (fig 2).[12]

"Can I get some cancer blood tests done as part of my health check?"

You have no features that make me worried about cancer. Cancer blood tests are not useful here as they are not very good at picking up cancer; they also give a lot of false positive readings that need further complex tests to sort out and can sometimes lead to unnecessary treatment and anxiety. They are mainly used for following up patients with known cancer. A better approach for picking up cancer is to come back to see me promptly if you have any worrying symptoms.

Screening tests

Screening tests assess the risk of disease in asymptomatic people, with subsequent tests needed to confirm the presence of disease. Examples include neonatal screening for inborn errors of metabolism and faecal occult blood testing in colorectal cancer screening programmes. The premise is that early detection of disease in asymptomatic people improves outcomes and that false positive results do not create a burden. This is not always the case, and the limitations of screening tests need to be carefully explained. For example, although some tumour markers have a role in monitoring known cancer, they have limited value as a screening test in apparently healthy people.[13] They generally lack sufficient sensitivity (will miss some tumours) and specificity (will give false positive results). The lack of specificity may lead to inappropriate further investigation and possibly unnecessary treatment (because the natural course of some cancers is poorly understood).

However the use of tumour markers in patients with symptoms of disease may be more useful—for example, CA-125 measurement combined with ultrasound can help make a diagnosis in women with symptoms suggestive of ovarian cancer.[14]

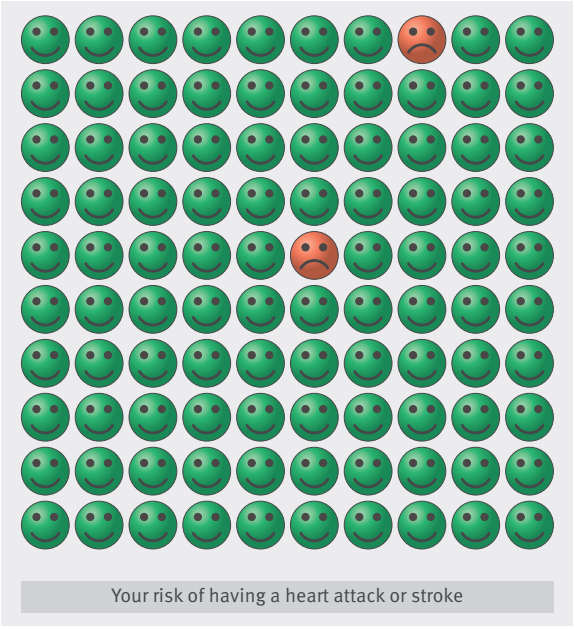

Fig 2 | Pictographs of the risk of having a heart attack or stroke within the next 10 years

Conclusion

It is important to explain test results and put them in the context of the patient's overall condition. A better understanding of test results may improve patient satisfaction with their care.

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HOW PATIENTS CONTRIBUTED TO THIS ARTICLE

The concept for this article came from discussions between the authors and many patients in outpatient clinics and other settings on how best to communicate laboratory test results. The specific vignettes were discussed with individual patients.

CLINICAL REVIEW

Nausea and vomiting in palliative care

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This is an edited version of the clinical review. The full version is on thebmj.com.

CPD/CME
1 CREDIT

HOW PATIENTS WERE INVOLVED IN THIS CLINICAL REVIEW

A patient perspective is included in this review

What is the likely cause?

It is important to determine the cause of nausea and vomiting to identify potentially reversible causes and to inform antiemetic strategy. In advanced cancer, six broad causes of nausea and vomiting have been identified (table 1). Gastric stasis and chemical disturbance are the most common.[1 2] However, the aetiology is often multifactorial.

How to identify the cause?

Table 1 includes the symptoms that might point to the underlying cause of the nausea and vomiting. The abdomen should be examined for signs of intestinal obstruction and also for hepatomegaly and ascites, which may suggest gastric stasis. The presence of a "succession splash" (heard through auscultation of upper abdomen while patient is rocked from side to side at the hips) is indicative of gastric outlet obstruction. Rectal examination should be performed if faecal impaction is suspected; however, in patients with possible neutropenia this should be avoided. A thorough neurological examination should be conducted to elicit signs of raised intracranial pressure or focal neurology suggestive of meningeal metastases or a base of skull tumour.

What investigations are appropriate?

It is important to communicate openly and honestly with the patient to understand their goals and to reach a shared consensus. All patients should have blood sugar measured and urine analysis to exclude infection. Specific blood tests and imaging are recommended in some cases to rule out underlying treatable causes (see table 1). Available treatments for reversible causes are listed in table 2.

WHAT YOU NEED TO KNOW

- Nausea and vomiting in advanced disease is often multifactorial. Common causes include gastric stasis, chemical disturbances, intestinal obstruction, and raised intracranial pressure
- It can cause serious physical complications, including nutritional deficiency, electrolyte disturbance, dehydration, and aspiration pneumonia
- Knowledge of the emetogenic pathway and antiemetic actions can help select an antiemetic that targets the underlying cause
- Check renal function, electrolytes, and calcium level when appropriate
- Give antiemetics orally unless the patient is vomiting or has suspected malabsorption or gastric stasis
- When symptoms persist, prescribe a regular antiemetic with another antiemetic to be taken as required
- Consider parenteral fluid replacement after an individual assessment of benefits and risk

Parenteral hydration in nausea and vomiting

The GMC recommends that clinically assisted hydration should be offered intravenously or subcutaneously if there is overall benefit.[4] Patients requiring parenteral hydration should be admitted, and clinicians should be vigilant to the signs of fluid overload as terminally ill patients require lower volumes for hydration.[5]

Which antiemetic should I prescribe?

Figure 1 shows the emetogenic pathway, including the receptors activated at different points, the underlying causes, and the antiemetics most effective in different circumstances. Details of the antiemetics used as first line and second line treatment on this basis are outlined in table 3, together with the common routes of administration and doses. The evidence base and side effect profiles of commonly used antiemetics are outlined in table 4 (see thebmj.com).

Which route of administration?

Oral

Antiemetics should be prescribed orally if there is no vomiting, malabsorption, or severe gastric stasis. For persistent symptoms, an antiemetic should be prescribed regularly with a second line antiemetic prescribed on an "as required" basis.

Parenteral

Parenteral administration of antiemetics is recommended if there is vomiting, malabsorption, or severe gastric stasis. If intravenous access is already established, this route can be used to provide a continuous infusion, with additional doses given by direct intravenous injection. If intravenous access is not in situ, the subcutaneous route is favoured as it is least invasive. Syringe drivers can provide a continuous subcutaneous infusion over 24 hours. Up to three drugs are commonly combined within a syringe driver, including opioids for pain. Syringe drivers should not be reserved for end of life care and can also be used to manage mucositis and bowel obstruction. The appropriate diluent (water or normal saline) and compatibility of agents within the infusion should be checked before administration—specialist help should be sought if there is any uncertainty. Syringe driver prescriptions should be reviewed daily, and sites of infusion on the skin inspected closely for evidence of erythema or tenderness, which should prompt relocation. Extra doses can be given by direct subcutaneous injection or via a second indwelling subcutaneous line. Intramuscular administration should be avoided as this is painful and can cause haematomas in patients with bleeding tendencies. Box 2 lists alternatives to parenteral or oral administration.

How to titrate antiemetics

Figure 2 (see thebmj.com) provides a guide to titrating antiemetics. Using a similar approach, in a before-after

Just relax and concentrate on your breathing

Olivia Fulton questions the value of telling people to focus on breathing during an asthma attack.

WHAT YOU NEED TO KNOW

- Avoid saying "just concentrate on your breathing; don't talk." Although this statement is meant to reassure, it can have the opposite effect, with patients focusing on their inability to breathe and becoming even more frightened
- Ask patients what position they find most comfortable
- Take time to ask patients about their usual treatment and whether they have a care plan. Offer a pen and paper if talking is too difficult

"Just relax and concentrate on your breathing" is a comment heard by most patients attending an emergency department with an exacerbation of acute asthma. It's meant to reassure, but it has exactly the opposite effect.

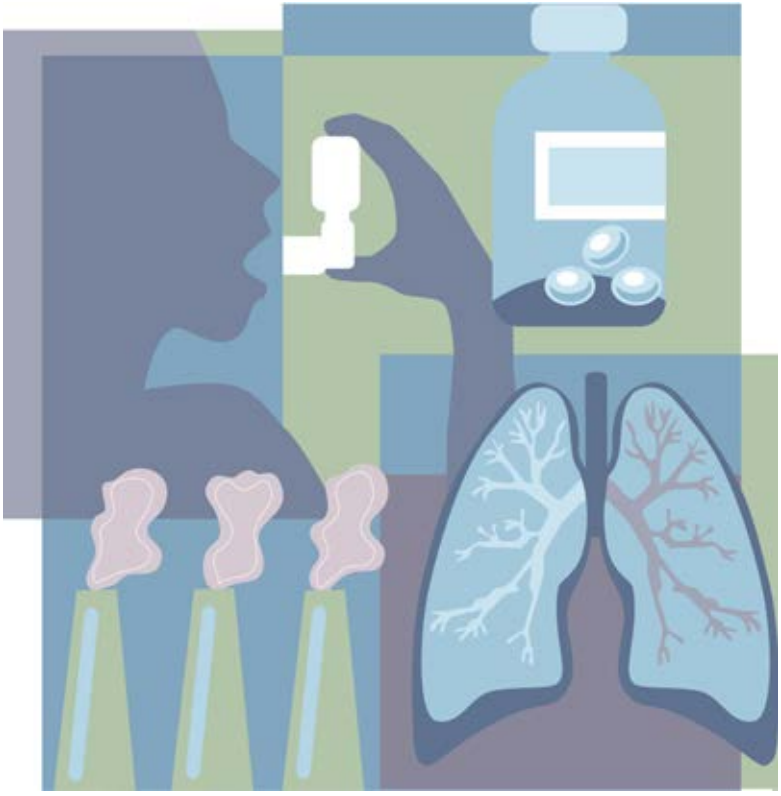
I have severe asthma and often have to attend my local emergency department with acute attacks. These attacks leave me struggling to breathe; sitting up is difficult and speaking almost impossible. Doctors' and nurses' initial instinct is to offer support, and because of how I look their advice is to sit back, relax, and don't talk.

I always try to talk, however, and other people with asthma tell me that they do too. Concentrating on breathing induces panic because you can't do it and fear about what will happen if this is not resolved. Talking makes you concentrate on something else. Your speech may not be great, and speaking will look like a huge effort, but the effort of talking takes away the fear of not being able to breathe. This can help people having an asthma attack from falling into a vicious cycle where over-focusing on breathing ends up making them hyperventilate.

Ask what works

In the initial stages of an attack, when I'm in the emergency department, the doctors need to know everything about me as a patient. Patients with long term conditions, especially those with severe and uncontrolled asthma, often have a lot of useful information about what works and what doesn't. I often overhear doctors speculating about the best course of treatment. I sit there willing them to ask me about my asthma and treatment but know they don't want to force me to talk, as from the outside it appears so difficult.

Even if it takes 5-10 minutes to complete a sentence, having someone take the time to listen is almost as much a relief as intravenous magnesium or aminophylline might be. You are reassured that the important people know the information they need to know.



VISUAL MOZART/IMAGEZOO/CORBIS

Concentrating on your breathing induces panic because you can't do it and fear about what will happen if this is not resolved. Talking makes you concentrate on something else

CPD/CME

Link to this article online for CPD/CME credits

Offer pen and paper

Ask us if we have a care plan or what our usual treatment would be. Offer a pen and paper if talking is too difficult. Patients are far more interested in the care they receive, and feel more confident, when doctors and nurses take the time to include them in decisions.

When struggling to breathe different patients adopt different positions. I like to sit as upright as possible or lean over, bracing myself with my arms on my knees. As a doctor you want to help patients into the best position for them but you also need to examine them. "Lie back and relax" is what comes to mind, but this often makes people who have difficulty breathing feel the weight of their chest even more. Asking patients to find a comfortable position themselves will mean they are not fighting with you to get out of a position they don't want to be in. This may seem very trivial but a comfortable patient is easier to manage than an uncomfortable one.

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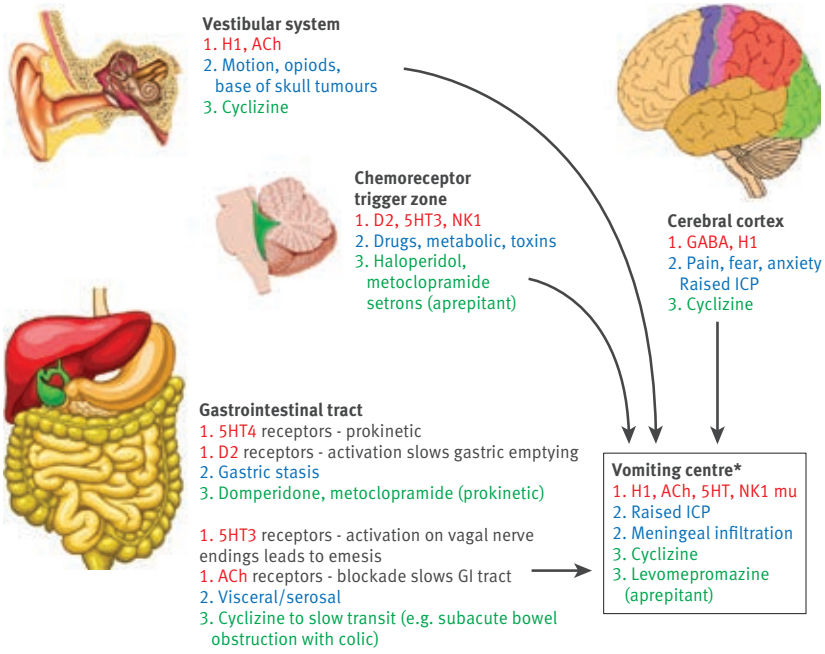
Table 1 | Causes of nausea and vomiting, key clinical features, and investigations (adapted from Stephenson and Davies[1])

Cause and triggers	Key features	Investigations
Chemical		
Drugs—opioids*, digoxin, antibiotics, antifungals, iron, SSRIs, NSAIDs, dopamine agonists, chemotherapy Metabolic—renal failure, liver failure, hypercalcaemia, hyponatraemia, ketoacidosis, toxins—ischaemic bowel, tumour products, infection	Co-existent delirium may suggest metabolic cause (can also be a consequence of metabolic derangements secondary to vomiting) Polyuria and polydipsia can accompany nausea and vomiting caused by hypercalcaemia and hyperglycaemia	Review drug sheet Blood sugar to exclude hyperglycaemia (all patients) Urine analysis to exclude infection (all patients) Urea and electrolytes (hyponatraemia, hypokalaemia, uraemia) Calcium and liver function (all patients who consent and for whom treatment to reverse derangements would be appropriate) Uraemia and hypercalcaemia can mimic the dying phase but may also reflect irreversible progression into the dying phase
Impaired gastric emptying		
Drugs—opioids, tricyclics, phenothiazines, anticholinergics, tumour ascites, hepatomegaly, autonomic dysfunction, tumour infiltration	Early satiety, reflux, hiccups	Consider abdominal ultrasound scan or CT to investigate physical causes
Visceral or serosal		
Bowel obstruction, severe constipation or faecal impaction Liver capsule stretch, ureteric distension, mesenteric metastases, difficult expectoration or pharyngeal stimulation	Vomiting undigested food hours after ingestion suggests gastric outlet obstruction Abdominal pain and change in bowel habit suggest intestinal obstruction Progression of vomiting from stomach contents to bile to faeculent material indicates intestinal obstruction	Abdominal x ray and/or CT if bowel obstruction is suspected (either gastric outlet, small or large bowel) Contrast studies may be done (such as barium meal) Suspected gastric outlet or intestinal obstruction requires inpatient admission at presentation (if in line with preferences) until symptoms have been managed Early discussion with oncologists, surgeons, and palliative care specialists is advised in all cases of suspected bowel obstruction
Cranial		
Raised intracranial pressure—tumour, bleed, infarction, meningeal infiltration, radiotherapy	Headache (especially in morning) suggests raised intracranial pressure Personality change, visual changes, depressed consciousness can occur with raised intracranial pressure	CT or MRI of head should be done if new features of raised intracranial pressure or focal neurology. MRI is preferred in cases of suspected meningeal disease Discussion with patient's oncologist or palliative care specialists is advised
Vestibular		
Drugs—opioids, motion sickness, base of skull tumour	Less common cause of nausea and vomiting Symptoms are movement related (this is not pathognomic and can occur with gastric stasis)	CT or MRI should be done if base of skull tumour is suspected Discussion with patient's oncologist or palliative medicine specialists is advised
Cortical		
Anxiety, pain	Anticipatory nausea Psychological or physical distress	In depth psychosocial assessment

SSRI=selective serotonin reuptake inhibitor, NSAID=non-steroidal anti-inflammatory drug, CT=computed tomography, MRI=magnetic resonance imaging.
*If the dose of opioid is stable, it is unlikely to be the cause of nausea and vomiting.



H1 = histamine type 1 receptor, ACh = acetylcholine receptor, 5HT4 = serotonin type 4 receptor, 5HT3 = serotonin type 3 receptor, D2 = dopamine type 2 receptor, mu = μ-opioid receptor, NK1 = neurokinin 1 receptor, ICP = intracranial pressure
* Vomiting centre in humans is a collection of nuclei within brainstem. It receives inputs from cerebral areas, gastrointestinal tract via vagal afferents, area postrema or chemoreceptor trigger zone, and vestibular system. Antiemetics mediate their clinical effect by acting as antagonists at different receptors in this pathway
This schematic aetiological approach is likely a simplification; it is more probable that emetic triggers act at multiple points within pathway and receptors are more widely distributed than depicted
1. Red = receptors; 2. Blue = causes; 3. Green = suggested treatment to target cause

Fig 1 | The emetogenic pathway. Adapted from Gordon et al,[6] Glare et al,[7] Harris[8]

Table 2 | Reversible causes of nausea and vomiting with an outline of appropriate treatment

Cause	Treatment
Hyperglycaemia	Intravenous fluids, insulin
Hypercalcaemia	Intravenous fluids, bisphosphonate infusion
Hyponatraemia	Depends on cause: discuss with endocrinologist
Constipation	Rectal suppository (such as glycerin and bisacodyl) or enema
Cerebral metastases	Dexamethasone trial: improvement in 48 hours in 70% of patients Consider radiotherapy: liaise with oncologist[3]
Symptomatic ascites	Therapeutic paracentesis
Medications	Review and discontinue if possible

uncontrolled study of patients in a hospice, resolution of nausea occurred in 82% of patients and resolution of vomiting in 84% of patients.[2] The median time to complete resolution of symptoms was two days. In a second similarly designed study, vomiting was controlled in 89% and nausea only in 56% of patients at one week, although almost all patients reported an improvement in nausea.[1]

During titration, antiemetics with similar receptor profiles (such as metoclopramide and domperidone) should not be combined. Combinations with competing mechanisms of action (for example, prokinetics such as metoclopramide and anticholinergics such as cyclizine) should also be avoided. Agents with activity at multiple receptors, such as levomepromazine or olanzapine, have

Table 3 | Recommended antiemetics in palliative care (from Stephenson and Davies,[1] Andrews and Sanger,[9] and Davis.[10] Recommended drug doses from Stephenson and Davies,[1] Glare et al,[7] and Harris[8])

Cause	First line	Second line	Third line
Chemical	Haloperidol: 0.5-1.5 mg oral or subcutaneous 3 times daily *or* 1.5-5 mg/24 hours CSCI	Levomepromazine: 3.125-6.25 mg oral or subcutaneous 3 times daily *or* 6.25-25 mg/24 hours CSCI	5-HT_3 antagonists (such as ondansetron: 4-8 mg 1 or 2 times daily *or* 16-24 mg/24 hours CSCI)
Visceral or serosal	Cyclizine: 50 mg oral or subcutaneous 3 times daily *or* 150 mg/24 hours CSCI	Levomepromazine: 3.125-6.25 mg oral or subcutaneous 3 times daily *or* 6.25-25 mg/24 hours CSCI	—
Gastric stasis	Domperidone 10 mg oral 4 times daily before meals	Metoclopramide: 10 mg oral 3 or 4 times daily before meals *or* 30 mg CSCI	—
Cranial	Cyclizine: 50 mg oral or subcutaneous 3 times daily *or* 150 mg/24 hours CSCI (Add dexamethasone 8-16 mg oral or subcutaneous 1 times daily if raised ICP)	Haloperidol: 0.5-1.5 mg oral or subcutaneous 3 times daily *or* 1.5-5 mg/24 hours CSCI	Levomepromazine: 3.125-6.25 mg oral or subcutaneous 3 times daily *or* 6.25-25 mg/24 hours CSCI (Reduction in seizure threshold with all antipsychotics)
Vestibular	Cyclizine: 50 mg oral or subcutaneous 3 times daily *or* 150 mg/24 hours CSCI	Levomepromazine: 3.125-6.25 mg oral or subcutaneous 3 times daily *or* 6.25-25 mg/24 hours CSCI	Hyoscine hydrobromide 1 mg/72 hours topical *or* Prochlorperazine 5-10 mg oral 3 times daily
Cortical	Lorazepam 0.5-1 mg sublingual 4 times daily as needed	Levomepromazine: 3.125-6.25 mg oral or subcutaneous 3 times daily *or* 6.25-25 mg/24 hours CSCI	—

CSCI=continuous subcutaneous infusion (syringe driver). Other antiemetics in use include olanzapine and aprepitant (see thebmj.com).
For patients requiring haloperidol >3 mg in 24 hours via CSCI, levomepromazine >12.5 mg in 24 hours, >2 doses of 0.5 mg lorazepam in 24 hours, nausea and vomiting refractory to the above measures, or any concerns, contact specialist palliative care early for advice.

a broader side effect profile, but they can be effective as second line agents when more selective first line agents have failed.[33]

What is the role of dexamethasone?

Dexamethasone is used when there is evidence of raised intracranial pressure.[6] It can also be used in malignant bowel obstruction. Clinicians and patients should be vigilant to side effects, including myopathy, hyperglycaemia, mood changes, and changes in body image. To minimise side effects, the lowest effective dose should be used for the shortest time.

Managing nausea and vomiting in malignant bowel obstruction

Malignant bowel obstruction not amenable to surgical intervention is managed with the use of opioids and antiemetics, and sometimes also antisecretory agents, via a continuous subcutaneous infusion.

During titration antiemetics with similar receptor profiles should not be combined

A PATIENT'S PERSPECTIVE

Nausea has been one of the most disabling symptoms from diagnosis [leukaemia]. Originally this was from the chemotherapy. I was lucky to be treated in a unit where they used aprepitant and palonosetron with the chemotherapy, as these worked well for me.

As I've become less well with recurrent disease, I've had to have a lot of antifungals and antibiotics. These have made the nausea much worse. Cyclizine doesn't work for me and makes me feel spaced out. I've got a scopoderm patch on, which works OK, and omeprazole helps a bit with the reflux. I use levomepromazine as a top-up, and it works but gives me a horrible hangover feeling the next day. Complementary therapy helps [reiki and reflexology] for a few hours and makes me feel better overall. It's really important to me.

Recently I've had bowel obstruction; they don't really know why, there isn't a blockage. I know I can't have steroids, and I had such bad crampy pain on the metoclopramide when it first happened that I'm scared to try it again. I had to stop my palonosetron to try and help my bowel start working again. I didn't want a syringe driver as it's just another pump attached to me. I did have a [nasogastric] tube, which made me feel a bit better. Thankfully it's out now, and I seem to be doing a bit better again. Bowel obstruction is really horrible.

Box 2 | Alternatives to oral, intravenous, or subcutaneous administration of antiemetics

- Ondansetron suppositories—16 mg per suppository, £14.39 per dose
- Granisetron transdermal patch—31 mg for 24 hours, £56.00 per patch
- Hyoscine hydrobromide transdermal post-auricular patch (Scopaderm) —1.5 mg for 72 hours, £2 per patch

Antiemetics

Metoclopramide can be used in early stage, partial obstruction because of its prokinetic effect. However, it should be avoided if there is complete obstruction or colic,[34] when cyclizine with or without haloperidol or levomepromazine is used.

Antisecretory agents

If large volume vomiting occurs despite the above measures, antisecretory drugs such as hyoscine butylbromide (an anticholinergic) or octreotide (a somatostatin analogue) or a combination can be used. Both have antispasmodic action if colic is problematic, with hysocine butylbromide more commonly used for this effect. A recent randomised trial failed to show benefit of octreotide given first line in addition to standard therapy (which included dexamethasone) on the primary outcome of vomit-free days.[35] However, there was a reduction in the number of vomiting episodes in patients receiving octreotide. The role of octreotide as second line therapy in patients who continue to vomit despite standard first line therapy requires further research.

Dexamethasone

Dexamethasone can be used in addition to antiemetics and antisecretory agents in malignant bowel obstruction. A systematic review of its use in malignant bowel obstruction in advanced gynaecological and gastrointestinal cancer failed to show a significant benefit, but its use in malignant bowel obstruction remains widespread.[36] A typical dose is 4-16 mg (subcutaneous or intravenous) daily. Response to treatment should be reviewed after five days.

Other interventions for refractory symptoms

About 10% of patients with malignant bowel obstruction continue to vomit despite palliative pharmacological management.[37] Some patients may therefore benefit from a wide bore 'Ryles' nasogastric tube to decompress the stomach and for ongoing drainage of gastric contents and any oral intake ingested for pleasure.[38] If a nasogastric tube is effective in helping relieve symptoms, venting gastrostomy insertion can provide a longer term option to allow for discharge home. A small retrospective case notes review showed that in six out of seven cases, venting gastrostomy relieved nausea and vomiting with only minor complications, with the same proportion achieving discharge home.[39]

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CASE REVIEW

Atypical psoriasis

A 34 year old woman presented with an extensive cutaneous eruption on the lower limbs and buttocks. She had had atopic dermatitis with recurrent flares until age 22. She currently had idiopathic hirsutism and chronic foot onychodystrophy. Results of fungal culture of the nails three years earlier were negative. She had no personal or family history of psoriasis and no pets. When the lesions first appeared on her knees six months earlier she had consulted her general practitioner. A diagnosis of psoriasis was suspected and daily topical calcipotriol and betamethasone (strength III—potent topical steroid) were prescribed. The treatment was continued even though the lesions worsened and extended to her thighs and buttocks, with intense pruritus and burning. Finally she consulted our dermatological emergency unit.

She had multiple, widespread, pruritic, mostly well demarcated, erythematous plaques on her knees (fig 1A), thighs, and buttocks. She had disfigurement of her big toe nails, with white-yellow coloration (xanthonychia), thickening of the nail plate (pachyonychia), and distal onycholysis (fig 1B). She was otherwise well with no systemic features such as fever.

1. What is your diagnosis and what history and clinical findings suggest this?
2. What is the best laboratory test to confirm the diagnosis?
3. How should the patient be treated?

Submitted by Saskia Ingen-Housz-Oro, Françoise Foulet, and Olivier Chosidow

Patient consent obtained.

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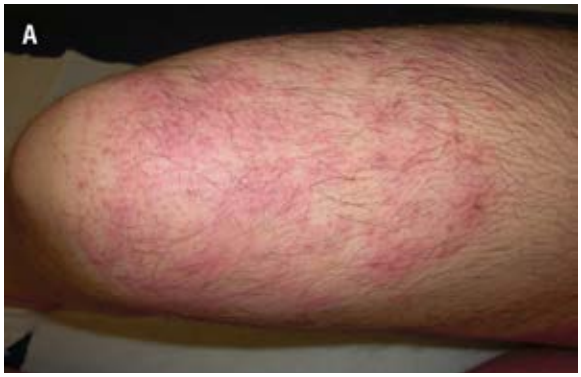

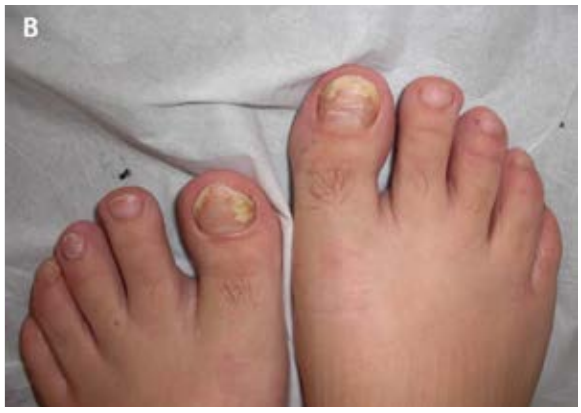

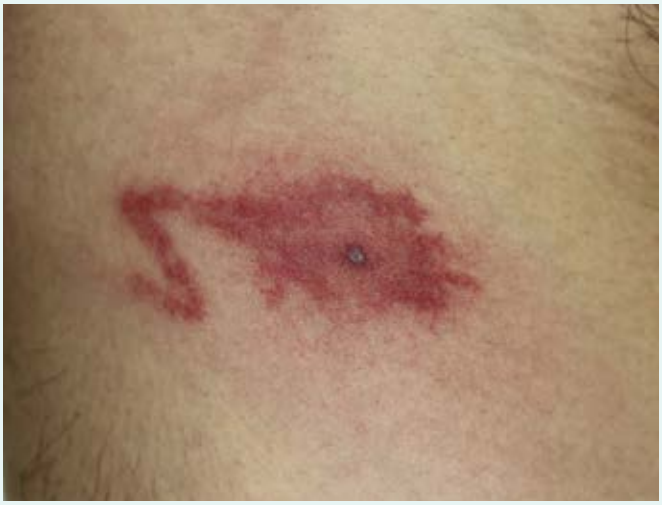

CASE SCENARIO

Creeping lymphangitis

A 35 year old man presented with a two day history of a tender rash on the right thigh. Examination showed serpiginous erythema extending from a vesiculopustule. *Staphylococcus aureus* was identified in a culture of the vesiculopustular fluid. The diagnosis of lymphangitis spreading from folliculitis was made. The patient was successfully treated with oral ampicillin.

Learning points:

- Lymphangitis is a rare complication of bacterial infections and insect bites
- A recent study in the United States reported an incidence of 0.16 per 1000 person years
- It usually appears as a red straight streak, but serpiginous streaks can also be seen from the course of travel along the lymphatic vessels

Submitted by Shota Takashima and Mitsuhito Ota

Patient consent obtained.

Cite this as: *BMJ* 2015;351:h5416

We welcome contributions that would help doctors with postgraduate examinations. We also welcome submissions relevant to primary care. See thebmj.com/endgames

answers

CASE REVIEW

Atypical psoriasis

1 Tinea incognito, an atypical extensive dermatophytosis (tinea corporis) often seen with chronic use of topical steroids.
2 Direct microscopy and culture of skin mycology samples taken by scraping cutaneous lesions and toenails.
3 Terbinafine (250 mg/day) for four to six weeks for tinea corporis and three months for toenail onychomycosis, often combined with topical antifungal drugs (azoles) in the first few weeks.

A bulging in the back

A 33 year old woman presented with bulging in her lower neck. Magnetic resonance imaging showed a large cystic mass in the neck. She underwent fine needle aspiration (FNA). Protoscolices and hooklets were identified on cytological examination, confirming hydatid cyst. Excisional biopsy was uneventful. Echinococcosis is caused by infection with *Echinococcus granulosus* through consumption of contaminated food and can be diagnosed using ultrasonography, computed tomography, or magnetic resonance imaging. Treatments comprise surgery, injection of a scolicidal agent, and antihelmintic therapy. Hydatid cyst can be diagnosed by imaging or FNA.

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Patient consent obtained.

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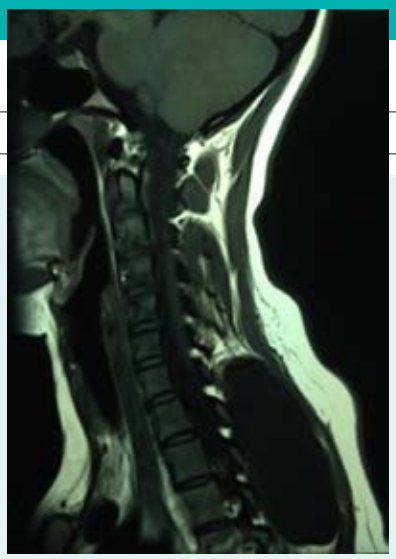

Thalidomide for nosebleeds

Although the terrible story of thalidomide, well told in Druin Burch's *Taking the Medicine*, has still not reached full resolution, the drug has a surprising variety of unexpected uses. It is now a familiar drug for multiple myeloma and has just undergone a phase II unblinded trial in people with hereditary haemorrhagic telangiectasia (*Lancet Haematol* 2015;2:e465-73, doi:10.1016/S2352-3026(15)00195-7). Low dose thalidomide showed benefit in all the 31 patients who had recurrent severe epistaxis, with a complete response in three.

Bad drugs for older patients

It is universally acknowledged that many older people take too many drugs, and that many are being harmed by taking the wrong drugs or the wrong combination of drugs. One metric for this is called the Beers criteria, endorsed by the American Geriatrics Society and recently applied to a sample of 13 900 patients aged 65 or over from the UK Clinical Practice Research Dataset (*BMC Geriatr* 2015;15:146, doi:10.1186/s12877-015-0143-8). Polypharmacy rates have risen sharply since 2003, but high risk medication prevalence has remained stable over a decade. A third of older people take high risk drugs, but only half of the total prevalence was long term. Non-steroidal anti-inflammatory drugs top the list.

Protective poo

Dutch researchers have recently uncovered the protective role of intestinal microbiota during pneumococcal pneumonia (*Gut* 2015, doi:10.1136/gutjnl-2015-309728). Admittedly this was in a faecal transplantation experiment in mice, but it does give Minerva new respect for the contents of the large bowel. The wonder of medical science lies in the constant discovery of how everything is connected to everything else.

Where brains light up

Having emerged fully grown from her father Zeus's forehead, Minerva observed the working of his brain at close quarters. Now mere mortals can do this using the Neurosynth site (www.neurosynth.org), a platform for large scale automated synthesis of functional magnetic resonance imaging (fMRI) data. It "takes thousands of published articles reporting the results of fMRI studies, chews on them for a bit, and then spits out images." This is data sharing on an epic scale, and fun to dabble in.

Placebo neuroscience

The latest phenomenon to be given the full neuroscientific work-up is the placebo response (*Neuroscience* 2015;307:171-90, doi:10.1016/j.neuroscience.2015.08.017). This review goes beyond mere neuroimaging to discuss the theory of expectancy learning mechanisms and even "a promising link between genetic variants in the dopamine, opioid, serotonin, and endocannabinoid pathways and placebo responsiveness." Not an article for those with a strong nocebo response to speculation.

Authors, check your Ps

Damned lies about statistics are to be found everywhere but are often simply due to errors of calculation. The inventors of a new P value checker that can automatically scan text looked at more than 258 000 P values reported in articles in eight major psychology journals from 1985 to 2015 (*Behav Res Methods* 2015, doi:10.3758/s13428-015-0664-2). About half the articles contained a P value error and 13% contained an error that changed their conclusion: non-significant results were reported as significant, or vice versa. The statcheck program is available on open source software (*Nature* 2015, doi:10.1038/nature.2015.18657) and its developers suggest that as well as being useful for journal editors, many reporting errors could be avoided if researchers used it to check their own papers.

Softly moaning flutes

The earliest known flutes date to 43 000 BC, long before the shepherds of antique poetry tootled them on every hill, and Greek ladies of pleasure used them for entertainment at the end of drinking parties. These ancient little pipes bear scant resemblance to the modern metal flute, played through a side hole and held in an awkward horizontal position. A survey of the literature (*Occup Med (Lond)* 2015, doi:10.1093/occmed/kqv162) estimated that 15-95% of flautists experienced musculoskeletal symptoms, depending on the populations and symptoms investigated. Minerva wonders if the same range of discomfort also applies to listeners.

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