Association of HRT and breast cancer

This long term follow-up of two placebo controlled, randomised studies involving over 27 000 women, found that women who had undergone a hysterectomy and took oestrogen alone (conjugated equine estrogen (CEE)) had a slightly lower risk of breast cancer than those who took placebo (annualised incidence 0.3% vs 0.37%). The same possible advantage didn’t hold for women who had not undergone hysterectomy who had to take a progestogen (medroxyprogesterone acetate) in addition to CEE. They had a significantly higher risk of breast cancer compared with placebo (0.45% vs 0.36%) though no increased risk of dying from breast cancer. There are lots of gaps in the data: the findings aren’t applicable to other doses and types of HRT, and information about breast cancer recurrence wasn’t available. In a broadly reassuring landscape of HRT and breast cancer data, every woman must surely be encouraged and helped to decide for herself.

Hydroxychloroquine, with or without azithromycin, doesn’t help against covid-19

This Brazilian randomised controlled trial of hospitalised, non-ventilated covid-19 patients with mild to moderate disease found no significant difference in clinical status (on a seven point scale ranging from good health to death) after 15 days between those treated with standard care alone, those given hydroxychloroquine, and those given hydroxychloroquine and azithromycin. Hydroxychloroquine caused more QT prolongation and abnormal liver enzymes than the control group, and there were more reports of adverse effects in the hydroxychloroquine and azithromycin group (39.3%) or hydroxychloroquine alone (33.7%) than in the controls (22.6%). However, this study wasn’t blinded, the design cannot rule out substantial benefit or harm of the drugs, there were deviations from the protocol, some of the patients had already been prescribed the drugs in the past, and some patients were enrolled on the trial up to 14 days after the onset of symptoms, by which time the drugs may have had less impact.

No bones about it: hip fractures are falling

This huge cohort study from the Framingham Heart Study (over 105 000 person years followed up over 40 years) found that people born more recently have fewer hip fractures for a given age. Falls in smoking and heavy drinking as well as improved detection and treatment of osteoporosis were all associated with the observed fall of 4.4% per year from 1970 to 2010. Other risk factors such as underweight, obesity, and early menopause didn’t change much over the 40 year period. There was a lack of data on bone mineral density data and medications across the study period. Despite the caveats, public health measures aimed at smoking cessation and limiting heavy drinking seem to be paying dividends in terms of bone health.

Obesity and covid-19—a complex picture

Obesity is bad for you, especially if you get covid-19. But this retrospective cohort study of 2466 patients from New York City found that the situation is complex. Over a median of seven days in hospital, 25% of the patients died, 22% were intubated, and 2% remained in hospital. In patients under 65 years old, being obese increased the risk of intubation or death, but in those over 65, it didn’t. There are lots of reasons why that might be so: age trumps obesity as a risk factor, and older people who are obese may be less frail than their skinnier peers. Surprisingly, body mass index wasn’t associated with admission levels of biomarkers of inflammation, cardiac injury, or fibrinolysis. The study is limited as data on body mass index were missing in 28% of patients.

Herd immunity in Geneva

Herd immunity seems to be disappointingly low in Geneva, Switzerland, despite high prevalence of covid-19, according to this population based study that tested randomly selected participants over the age of 5 years for SARS-CoV-2 IgG antibodies on a weekly basis to estimate seroprevalence in the Geneva population. There were 5000 reported clinical cases over 2.5 months in a population of 500 000 (1%) and an estimated 11.6 infections in the community for every reported confirmed case. The seroprevalence of antibodies was estimated as rising from 4.8% in the first week to 10.8% by the fifth week. Participants aged 20-49 years were most likely to be seropositive, and those under 9 or over 65 years were significantly less likely to be seropositive. Assuming that having antibodies confers immunity, these findings don’t provide much reassurance for authorities hoping to ease restrictions on the basis of widespread immunity.
Primary care assessment and management of common physical symptoms in pregnancy

Meena Bhatia, 1 Kamal R Mahtani, 2 Ruby Rochman, 3 Sally L Collins 1,4

A wide range of physical symptoms commonly occur during pregnancy, and it can be challenging to
- Assess whether the symptom is pregnancy related—is it gastroenteritis or hyperemesis gravidarum? Is it asthma or restricted lung volume? Is it abruption or appendicitis?
- Decide whether the pregnancy changes your management—what medications are safe? When is specialist assessment needed?

In this article we discuss the primary care assessment and management of headache, breathlessness, nausea and vomiting, urinary symptoms, and abdominal pain—common presentations in primary care that can have more serious underlying causes; and we highlight red flags that suggest when specialist referral might be warranted. We refer to the most up-to-date evidence on vital signs.

What are the reference ranges for maternal vital signs during pregnancy?

Evidence from a five year, three centre, prospective longitudinal cohort study of 1041 pregnant women in the UK 1 offers reference ranges for maternal vital signs during pregnancy (figs 1-5). These are relevant predominantly with hypertension or stroke.

Approximately two thirds of headaches in pregnancy are common in pregnancy. 4,5

How might women with headache present?

Around one in three pregnant women experiences headache. 2,3 This may be continuation of an underlying headache, a new headache syndrome unrelated to pregnancy, or a headache specific to pregnancy. Migraine, tension headaches, and to a lesser extent cluster headaches are common in pregnancy. 4,5

A 2017 systematic review of observational studies suggested that most women continue to experience headaches similar to those they experienced when not pregnant, or that some find that symptoms improve in pregnancy. 6,7 Improvement might occur if non-pregnant headaches are triggered by fluctuating oestrogen levels (eg, with migraines) because during pregnancy oestrogen levels are high and stable. Relapse of improved migraine symptoms might occur in the first month post partum. 8

Approximately two thirds of headaches in pregnancy have no underlying pathology and usually occur in the first trimester. 7,8 However, increased coagulability in pregnancy can increase the risk of underlying pathology, including stroke and cerebral venous thrombosis, at any gestation.

Headache can also be a sign of pre-eclampsia, a major cause of maternal and fetal mortality. 9

Reversible cerebral vasoconstriction syndrome occurs most commonly in the postpartum period. It presents as a severe sudden onset headache and it may be associated with hypertension or stroke.

How do you assess headache?

Undertake neurological history and examination as you would with non-pregnant patients. 10

Identify whether it is a primary headache (eg, tension headache, cluster headache, migraine) or secondary to a serious pathology (eg, pre-eclampsia, cerebral venous thrombosis). 11

Assess vital signs (figs 1-5). 1

Assess for cerebral venous thrombosis and ischaemic stroke: 12
- Ask about associated visual disturbances, swelling (most commonly of the hands, feet, or face), right upper quadrant or epigastric abdominal pain, and nausea and vomiting 12
- Look for peripheral and facial oedema, proteinuria on dipstick, and blood pressure increases >140/90 mm Hg on at least two occasions.

Assess for cerebral venous thrombosis and ischaemic stroke: 12
- Ask about associated cognitive disturbance, seizure, family history, previous venous thromboembolism, reduced mobility, thrombophilia, and/or obesity.
• Prescribing non-steroidal anti-inflammatory (NSAID) medication—avoid NSAIDs completely in the third trimester as they are associated with premature closure of the fetal ductus arteriosus. 16

Refer to obstetric physicians or neurologists for review and consideration of second line medications if:

• The pregnancy is high risk or complex (eg, pre-existing or newly diagnosed medical condition, age under 20 or over 40, overweight/obese, carrying more than one fetus) 17

• Headaches are severe or persistent despite first line medication.

Box 1 lists red flag signs and symptoms associated with headache in pregnancy that warrant urgent/same day opinion from secondary care teams (general medicine, neurology, and/or obstetrician, dependent on local referral pathways). 17

How do you manage headache?
Initially treat benign headache as you would in non-pregnant patients:
• Encourage good sleep, adequate hydration, and avoidance of potential precipitants
• Consider paracetamol and anti-emetics if conservative measures are ineffective.
• Request specialist advice before
• Prescribing sumatriptan for migraine

CONSIDERATIONS FOR COVID-19
This article was commissioned and peer reviewed before the COVID-19 pandemic. For further guidance on the management of symptoms related to COVID-19 in pregnancy, please see guidance from the Royal College of Obstetricians and Gynaecologists: Coronavirus (COVID-19) infection in pregnancy [https://www.rcog.org.uk/coronavirus-pregnancy](https://www.rcog.org.uk/coronavirus-pregnancy)
Box 1 | Headache red flags: request same day/urgent specialist opinion for these headache red flags

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked change in pain</td>
<td>Focal neurological signs (table 1)</td>
</tr>
<tr>
<td>Headache pattern</td>
<td>Signs of meningism (neck stiffness and photophobia)</td>
</tr>
<tr>
<td>Sudden onset at peak of pain</td>
<td>Diplopia or papilloedema</td>
</tr>
<tr>
<td>Described as the “worst ever” headache</td>
<td>Reduced Glasgow coma score (GCS)</td>
</tr>
<tr>
<td>Pain takes longer to resolve than usual or persists for longer than 48 hours</td>
<td>Petechial rash</td>
</tr>
<tr>
<td>Focal neurological symptoms</td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>Fever (fig 5)</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Visual changes</td>
<td></td>
</tr>
<tr>
<td>Associated loss of consciousness</td>
<td></td>
</tr>
<tr>
<td>Headache persists</td>
<td></td>
</tr>
<tr>
<td>despite first line treatments</td>
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</table>

How might women with breathlessness present?

A small observational study of 62 women found that more than 75% with uncomplicated pregnancy reported some degree of breathlessness to an obstetrician in their final trimester but breathlessness can start at any gestation. In most cases, breathlessness is physiological. The combination of increased progesterone causing the respiratory drive to be increased and oxygen requirements increasing as pregnancy advances can cause physiological hyperventilation which some women experience as breathlessness. Typically, this physiological breathlessness is present at rest, may improve on mild activity, and is not associated with any oxygen desaturation. Women describe it as “air hunger” and it may interrupt their normal speech pattern—eg, they pause to take a breath during a sentence without appearing breathless to others. However, breathlessness can also be a symptom of underlying pathology.

- The relative risk of venous thromboembolism is higher during pregnancy and the postnatal period, particularly in the first six postpartum weeks.
- Varicella zoster pneumonitis and flu have higher morbidity and mortality in pregnancy, and can cause fetal varicella syndrome and varicella of the newborn.
- A systematic review and meta-analysis showed that for one third of pregnant women asthma gets better, for one third it deteriorates, and for one third it stays the same. In a large population based study in Sweden, uncontrolled asthma was associated with preterm birth, low birth weight, gestational diabetes, infant hypoglycaemia, and pre-eclampsia.
- Anaemia, community acquired pneumonia, and heart failure from peripartum cardiomyopathy can also cause breathlessness in pregnancy.

How do you assess breathlessness?

Assess vital signs at rest and on exertion (figs 1-5).

- Look for features of embolic phenomena: sudden onset dyspnoea, pleuritic chest pain, and haemoptysis. The Wells score is not currently validated for use in pregnancy.
- Look for features of varicella zoster pneumonitis (vesicular rash), flu, or community acquired pneumonia—fever, cough, tachy�noea—and consider sepsis if bacterial infection is suspected.

Look for exacerbations in asthma—increased wheeze, cough, chest tightness; measure peak flow and consider other lung function tests.

Look for signs of heart failure, which might suggest peripartum cardiomyopathy. Consider a full blood count for suspected anaemia, or measure C reactive protein and full blood count for suspected respiratory tract infection.

Table 2 (bmj.com) summarises the features of the common and serious causes of breathlessness in pregnancy.

How do you manage breathlessness?

If the woman’s symptoms of breathlessness are mild and vital signs are within normal ranges (figs 1-5), explain that symptoms are most likely due to expected pregnancy changes, and ask her to return if symptoms persist or worsen.

- If she has signs of asthma
  - Manage them as you would in non-pregnant patients and escalate treatment based on symptom frequency.
  - Consider same day/urgent referral to secondary care for women with exacerbation of asthma in pregnancy.
  - Provide sufficient inhalers to manage symptoms, even if asthma has improved in pregnancy.

Safety of inhaled and oral steroids is a common concern during pregnancy. Guidelines from the Scottish Intercollegiate Guidelines Network (SIGN) and the British Thoracic Society (BTS) suggest that evidence is sufficient to support the use of inhaled corticosteroids as normal during pregnancy. For oral steroids, these guidelines recommend use as normal for severe asthma, with explanation that the benefits outweigh the risks.

Offer flu vaccination at all gestations in line with national recommendations. Arrange same day hospital assessment if you suspect flu infection or symptoms suggestive of varicella associated pneumonia (urgent referral if there is haemodynamic instability)—and take appropriate measures to avoid exposing other pregnant women to chickenpox.

Speak to the obstetrics and infectious disease teams regarding the correct location and referral pathway.

Box 2 lists red flag signs and symptoms associated with breathlessness in pregnancy that warrant urgent/same day opinion from secondary care teams.
How might women with nausea and/or vomiting present?

Nausea and vomiting are the most commonly reported symptoms in pregnancy, affecting almost 80% of pregnant women. Symptoms typically start at 6-7 weeks’ gestation and usually resolve by 16 weeks. They are a common reason for hospital admission.

Guidelines from the Royal College of Obstetricians and Gynaecologists (RCOG) define hyperemesis gravidarum as protracted nausea and/or vomiting, with a triad of more than 5% pre-pregnancy weight loss, dehydration, and electrolyte imbalance. Ketonuria in the absence of other symptoms is considered a feature that guides referral or treatment of hyperemesis gravidarum.

More serious obstetric conditions may initially present with non-specific symptoms of nausea and vomiting, usually at more advanced gestation:
- Acute fatty liver disease of pregnancy is rare but potentially fatal (typically presents after 30 weeks)
- Pre-eclampsia occasionally presents with nausea and vomiting (typically presents after 20 weeks)
- Nausea and vomiting might also be caused by antibiotics, iron supplements, viral gastroenteritis, and surgical causes of abdominal pain.

How do you assess nausea and vomiting?

Assess vital signs (figs 1-5).
- Ask about associated symptoms, such as diarrhoea and abdominal pain, and about recent food and drug ingestion.

Determine hydration status:
- Ask about symptom improvement with hydration
- Assess fluid balance
- Look for signs of dehydration on examination and urine dipstick.

Use clinical judgment to decide whether vomiting can be considered as “protracted” (the National Institute for Health and Care Excellence (NICE) does not offer parameters for “protracted vomiting” in its definition of hyperemesis gravidarum).

Measure whether there has been weight loss of >5% of the pre-pregnant weight.

RCOG guidelines recommend assessing symptom severity using a Pregnancy-Unique Quantification of Emesis (PUQE) score (fig 6, bmj.com).

Arrange laboratory investigations to check for electrolyte imbalance, thyroid dysfunction, or inflammatory marker derangement.

Assess for acute fatty liver disease of pregnancy:
- Ask about right upper quadrant pain, generalised malaise, polydypsia, polyuria
- Look for signs of encephalopathy.

Assess for pre-eclampsia as above (under headache).

Table 3 (bmj.com) summarises the features and causes of nausea and/or vomiting in pregnancy.

How do you manage nausea and vomiting?

A systematic review of 67 randomised clinical trials and 11 non-randomised studies showed that mild symptoms can be managed effectively in the community using ginger (fresh or ginger-containing food items: teas, tinctures, or tablets), vitamin B<sub>6</sub>, and/or acupuncture.

If vomiting is related to antibiotic, iron, or other medication intake, consider changing preparations if symptoms persist. If symptoms are not well controlled, or if a woman is finding the symptoms very challenging, consider the following safe and effective anti-emetics: promethazine, cyclizine, or prochlorperazine. If symptoms persist and clinical judgment dictates that a secondary care referral is not needed, consider trying chlorpromazine, metoclopramide, ondansetron, or domperidone.

If one medication is not controlling symptoms effectively, consider changing the medication or building up to dual/triple anti-emetic therapy. A combination of up to three of these anti-emetics can be used safely if they provide symptomatic relief.

Treatment progress may be tracked with RCOG PUQE scores (fig 6, see bmj.com).

If the PUQE score is less than 13 and primary care measures are unsuccessful, RCOG green-top guidelines advise ambulatory day care management and inpatient management if one or more of the following applies:
- Unable to keep down oral anti-emetics
- Ketonuria (1+ ketones on urine dipstick) and/or weight loss (greater than 5% of pre-pregnant body weight). However, a systematic review and meta-analysis did not find support for the use of ketonuria as a feature that guides referral or treatment of hyperemesis gravidarum.
- Suspected comorbidity (eg, urinary tract infection and unable to keep down oral antibiotics).

Box 3 | Nausea/vomiting red flags: request urgent/same specialist opinion if patients present with these nausea and/or vomiting red flags

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to tolerate oral intake despite anti-emetics, with associated weight loss or signs of severe dehydration</td>
<td>Severe dehydration (decreased urine output, dizziness, increased thirst, dry mouth)</td>
</tr>
<tr>
<td>Confirmed or suspected comorbidity (eg, urinary tract infection, diabetes)</td>
<td>Haemodynamic instability (figs 1-5)</td>
</tr>
<tr>
<td>Severe headache</td>
<td>Biochemical abnormality</td>
</tr>
<tr>
<td>Severe abdominal pain, especially epigastric or right upper quadrant pain</td>
<td></td>
</tr>
</tbody>
</table>

Box 4 | Urinary symptom red flags: request same day/urgent specialist opinion if patients present with these urinary symptom red flags

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe abdominal pain/ loin pain</td>
<td>Severe dehydration</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Fever (fig 5)</td>
</tr>
<tr>
<td>Frank haematuria</td>
<td>Tachycardia (fig 2)</td>
</tr>
<tr>
<td>Rigid/tender uterus</td>
<td>Hypotension (fig 1)</td>
</tr>
<tr>
<td>Uterine irritability or contractions</td>
<td>Suspected of pyelonephritis</td>
</tr>
<tr>
<td>Rigors</td>
<td></td>
</tr>
<tr>
<td>Unwell pregnant woman with urinary tract infection and medical comorbidity</td>
<td></td>
</tr>
</tbody>
</table>

How might urinary symptoms present?

Urinary symptoms are very common in pregnancy.

One observational study of 256 pregnant women found that 91% experienced increased frequency. Another observational study of 100 pregnant women found that 72% experienced increased frequency, 63% experienced urgency, and 75% nocturia.

With advancing gestation, the plasma volume increases and the pressure effect of the uterus on the bladder may cause increased frequency of micturition and nocturia.

Urinary tract infections may present as asymptomatic bacteruria, acute cystitis, or pyelonephritis.

Pyelonephritis is more common during pregnancy because of physiological dilatation of the upper renal tract, and it is associated with increased risk of preterm labour and low birthweight infant. It is one of the main reasons for urine screening tests in pregnancy, and the reason urinary tract infections in pregnancy are treated so aggressively.

Polyuria may be a sign of acute fatty liver disease of pregnancy, and reduced urine output can be a sign of sepsis or acute kidney injury in pregnancy.
How do you assess urinary symptoms?
- Ask about dysuria, frequency, and nocturia and haematuria in anyone who is unwell or describes a change of urinary habit and perform a urine dipstick test.
- Consider pyelonephritis if there is associated fever and lumbar and/or flank pain.
- Internationally, guidelines vary on how often to perform urinalysis. However, consider performing urinalysis at all antenatal visits to GPs, midwives, and obstetricians because asymptomatic bacteriuria is also an important cause of preterm labour that requires immediate treatment in the community.

Table 4 (bmj.com) summarises features and causes of urinary symptoms in pregnancy.

How do you manage urinary symptoms?
If patients have lower urinary tract infection symptoms, start empirical antibiotics regardless of the urine dipstick result. Concerns about resistance can be reduced by avoiding empirical treatment with broad spectrum antibiotics.

- Longer courses of antibiotic therapy offer better cure rates, reduce women’s risk of pyelonephritis, and reduce the risk of urinary tract infection inducing pre-term labour.
- NICE guidelines recommend seven day courses of antibiotics for urinary tract infection in pregnancy and nitrofurantoin as the first choice antibiotic (nitrofurantoin is to be avoided at term). If symptoms do not improve after 48 hours, or if nitrofurantoin is not suitable, NICE recommends amoxicillin (if culture results confirm susceptibility) or cefalexin, or to consult the microbiologist for a suitable antibiotic based on the culture results.
- Trimethoprim can be used; however, it is generally avoided during the first trimester because of the risk of neural tube defects in the fetus.
- Request an obstetrician’s opinion if symptoms fail to respond to treatment or if urinary tract infections are recurrent.
- Determine the level of urgency of referral on a case-by-case basis.
- No evidence supports cranberry juice as treatment for urinary tract infection in pregnancy.
- If you suspect pyelonephritis refer for same day/urgent intravenous antibiotics. Box 4 lists red flag urinary signs and symptoms in pregnancy that warrant same day/urgent opinion from secondary care teams.

Box 4: Abdominal pain: red flags

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal bleeding</td>
<td>Syncope</td>
</tr>
<tr>
<td>Constant or severe abdominal pain</td>
<td>Any sign of sepsis</td>
</tr>
<tr>
<td>Green or foul smelling discharge</td>
<td>Woody hard</td>
</tr>
<tr>
<td>Accompanying loss of fluid vaginally</td>
<td>tender</td>
</tr>
<tr>
<td>Prolonged moderate pain not settling with oral analgesia</td>
<td>Guarding and/or rebound tenderness</td>
</tr>
</tbody>
</table>

How might patients with abdominal pain present?
Abdominal pain is one of the most frequently reported symptoms in pregnancy. The differential is wide and includes pregnancy related causes and numerous non-obstetric intra or extra-abdominal causes.

Physiological and anatomical changes in pregnancy can make diagnosis challenging. For example, appendicitis may occur atypically in pregnancy, and in late pregnancy guarding from peritonitis may not occur, owing to loss of elasticity of the abdominal wall musculature. Additionally, physiological leucocytosis that typically occurs in pregnancy (6-16 × 10^9/L in the first and second trimesters, and 20-30 × 10^9/L in the third trimester) can complicate interpretation of white cell count. The displacement and potential compression of intra-abdominal organs by the gravid uterus during pregnancy can create anatomical distortion.

However, mild symptoms that self-resolve and have no associated features are generally less likely to be concerning and more in keeping with normal physiology. Round ligament pain is associated with the gravid uterus pulling on the round ligament with maternal movements—for example, turning in bed.

Acute pancreatitis in pregnancy is rare but most commonly occurs in the third trimester because of the presence of gallstones.

Placental abruption (where the placenta begins to detach from the uterine wall, reducing blood flow to the fetus) and uterine rupture are obstetric emergencies which have potentially fatal consequences for mother and fetus. Acute fatty liver of pregnancy, chorioamnionitis, and pre-eclampsia are not classed as obstetric emergencies, but they also have potentially fatal consequences for mother and fetus.

How do you assess abdominal pain?
Establish where the pain is, and its severity:
- Stitch-like pain radiating to the groin might suggest round ligament pain
- Severe unilateral pain could suggest torsion, haemorrhage, or rupture of an ovarian cyst; or in the first trimester it could suggest ectopic pregnancy or fibroid degeneration
- Intermittent, tightening pains could suggest labour, pre-term labour, or Braxton-Hicks contractions if they are short lived.

How do you manage abdominal pain?
- Manage mild or moderate pain with simple analgesia initially.
- Urgently refer any severe pain to the obstetric team for diagnosis. If a surgical cause is suspected, referral to the surgical team is made by the obstetric team after obstetric assessment.

Box 5 lists red flag signs and symptoms associated with abdominal pain in pregnancy that warrant same day/urgent opinion from secondary care teams.

Statements of fitness in pregnancy
Consider issuing a fit note when there is a protracted period away from work or where symptoms potentially require modifications to be made to the work schedule or role.

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.m2248
Covid-19 communication aids

**What People May Ask...**

**Admitting**

“Does this mean I have COVID-19?”

**What You Can Say...**

“We will need to wait for your swab results, which will be back tomorrow. It’s normal to feel stressed while you wait. Do the things that help you stay balanced in the meantime.”

**Admitting**

“But how bad is this!”

**What You Can Say...**

“From the information that I have, it’s serious enough that you need to be in the hospital. We will know more in the next day, and we will update you as soon as we can.”

---

Extracted from the graphic medicine adaptation of a guide by VitalTalk, this graphic gives training to support conversations around serious illness.

The guide is a starting place for improving conversations with patients and families facing covid-19.

The original text is at www.vitaltalk.org/guides/covid-19-communication-skills/
Nathan A Gray, assistant professor, Duke University School of Medicine, Durham, North Carolina
Anthony L Back, co-founder VitalTalk, professor, University of Washington, Seattle

Cite this as: BMJ 2020;370:m2928
See bmj.com for the graphic in full

WHAT PEOPLE MAY ASK . . .

“Is my grandfather going to make it?”

WHAT YOU CAN SAY . . .

“I know this must be scary. Because of his frail condition, it’s quite possible that he could die from this illness. We are hoping for the best, but prepared to provide the best care we can for him no matter what.”

“How can you not let anyone visit?! I’m all alone here.”

“I can only imagine how hard it is not to have visitors. Right now, they will be in more danger if they come here. We can help you with phone or video messaging, although I know it’s not the same as having them here.”
CASE REVIEW
Ptosis that resolves with application of an ice pack

A man in his 50s presented with a one week history of left sided ptosis and difficulty swallowing. The ptosis was absent on waking, worsened during the day, and improved after rest. His medical history included hypertension. Apart from bilateral ptosis that was worse on the left (figure, a), clinical examination was unremarkable. Application of an ice pack to the left eye for five minutes led to improvement of the ptosis on that side (figure, b). The ptosis recurred 20-30 minutes after the ice pack was removed.

Within two weeks of the initial presentation, the patient started to experience difficulty chewing, dysphagia for food and saliva, dysarthria, fatigue, and generalised proximal weakness.

Anti-acetylcholine receptor (anti-AChR) autoantibody titre was noticeably increased, at $581 \times 10^{-10}$ mol/L (normal range $0-5 \times 10^{-10}$ mol/L).

Single fibre electromyography showed increased jitter of the left orbicularis oculi muscle, and repetitive nerve stimulation showed reduced compound muscle action potential of the nasalis muscle.

What is the most likely underlying diagnosis?

Submitted by Arup Chakraborty and John Jacob

Patient consent obtained.

Cite this as: BMJ 2020;369:m1147

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

PATIENT OUTCOME

The patient underwent computed tomography of the chest, which did not show a thymoma. He was successfully treated with pyridostigmine and prednisolone.

LEARNING POINTS

- Generalised weakness.
- Ocular manifestations.

**What is the most likely underlying diagnosis?**

**Generalised myasthenia gravis.**

Most patients have multifocal involvement, but the condition can present bilaterally.

Diagnosis is confirmed by raised anti-AChR antibodies as well as clinical manifestations, in 85% of cases. A 12% chance that the result will also be positive in patients with non-myasthenic disorders.

What are the key diagnostic features?

- Ptosis that is absent on waking, worsens as the day progresses, and improves with rest.
- Increased jitter on single fibre electromyography.
- Reduced compound muscle action potential on repetitive nerve stimulation.

What is the most likely underlying diagnosis?

**Generalised myasthenia gravis.**

Most patients have multifocal involvement, but the condition can present bilaterally.

Diagnosis is confirmed by raised anti-AChR antibodies as well as clinical manifestations, in 85% of cases. A 12% chance that the result will also be positive in patients with non-myasthenic disorders.
MINERVA

Taken by surprise

Despite widespread criticism of significance testing, doctors, scientists, and journal editors continue to use P values as a way of dichotomising studies into significant or non-significant, positive or negative. Two articles in the American Journal of Epidemiology explain why this is misleading and suggest that we should try using the S value instead. The S value measures the degree to which the observed data are surprising using a scale that is the equivalent to the number of consecutive coin flips all coming up heads (Am J Epidemiol doi:10.1093/aje/kwaa136; doi:10.1093/aje/kwaa137).

Sounds of sickness

Some coughs are characteristic of a particular infection—whooping cough or the seal-like bark of children with croup, for example—but most coughs don’t announce their cause so clearly. Paid volunteers were played audio clips of coughs or sneezes and asked if the sounds they heard were produced by someone with a communicable disease or by someone coughing or sneezing for another reason (Proc Royal Soc B doi:10.1098/rspb.2020.0944). The more disgusting the listeners perceived a sound to be, the more likely they were to say that it came from an infected person, but this bore no relation to whether the sound actually came from an infected person.

Preterm births during lockdown

Two reports, one from the Republic of Ireland, the other from Denmark, note that fewer very premature babies are being born during the coronavirus pandemic. Extremely premature births decreased by 90% during Denmark’s lockdown, compared with the rate in the preceding five years. In Ireland very low birthweight deliveries at the University Maternity Hospital in Limerick fell by 73% during January to April 2020 by comparison with the preceding 20 year timeframe (MedRxiv https://doi.org/10.1101/2020.06.03.20121442; https://doi.org/10.1101/2020.05.22.20109793).

Frailty

Cigarette smoking, physical activity, alcohol consumption, and dietary intake of fruit and vegetables were recorded in 6000 participants of the Whitehall II study at the age of 50. During 20 years’ follow-up the incidence of frailty in those with healthy behaviours in regard to these variables was about 70% lower than in those with unhealthy behaviours (PLoS Med doi:10.1371/journal.pmed.1003147). This may not seem surprising, but the investigators say that, unlike studies with shorter follow-up that have shown a similar association, their results can’t be explained by reverse causation.

Green spaces

The pandemic has drawn attention to the need for people living in towns and cities to have access to green space, fresh air, and recreational facilities. Improving and promoting parks and other urban green areas might save health services large amounts of money, especially in treating obesity related illnesses and in reducing mental illness. Few local authorities have the financial resources to pursue a programme of extending parks and recreational facilities, so why not redirect a small part of the health budget specifically for this purpose? (https://www.thetimes.co.uk/article/we-need-to-protect-the-green-space-in-our-troubled-urban-lives-qnf6nq6p2).

Statins on Twitter

A qualitative study of 12 000 tweets that mentioned statins found that more than half were jokes, advertisements, or financial reports. Among posts that were health related, most provided factual information, such as a link to a journal article (JAMA Netw Open doi:10.1001/jamanetworkopen.2020.8953). Some tweets gave the impression that people taking statins thought they could increase their intake of fat and calories with impunity. Others offered the opposing view that it was better to eat a healthier diet than take drugs. Minerva was doubtful whether anything useful could be concluded from these findings.

Vitamin D in diabetes

A systematic review of trials of vitamin D supplementation in the prevention of type 2 diabetes finds no benefit overall. However, slicing up the data reveals a different pattern. Trials testing moderate to high doses of vitamin D (>1000 IU/day), conducted among people with pre-diabetes, showed a small protective effect (JCEM doi:10.1210/clinem/dga335). By contrast, trials testing lower doses, conducted in general population samples, found no benefit.

Thrombectomy for stroke in older people

Outcomes after endovascular thrombectomy for acute ischaemic stroke are poorer in people over the age of 80 than in younger people, according to an analysis of registry data from the Netherlands. Three months after the procedure, half of the older adults had died (Neurology doi:10.1212/WNL.0000000000009764). This doesn’t necessarily mean that thrombectomy shouldn’t be considered in this age group. Among older adults who were functionally independent before the stroke, one in four achieved a good functional outcome after thrombectomy.

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