Interim results for sotrovimab in covid
Covid-19 has killed nearly five million people worldwide and is still raging. The quest for treatments continues, especially for older populations and those with underlying health conditions. In this phase III trial, high risk patients (those with at least one risk factor for disease progression such as being older than 55 years, diabetes, obesity) with mild to moderate covid, who received a single infusion of the monoclonal antibody sotrovimab, were less likely to be hospitalised for any reason or die within a month compared with those who received placebo (3/291 (1%) v 21/292 (7%). There was no significant difference in adverse events (17% v 19%).

The numbers are too small to make any great claims; only three people were admitted to hospital in the sotrovimab group, and uncommon adverse events may not have shown up. In theory, sotrovimab should be safe because it’s made from an antibody from a patient who with SARS-C0V-1 and targets an antigen on the virus (not the human host).

Covid immunity waning in Israel
This study from Israel found evidence of waning immunity among vaccinated adults who had received two doses of the Pfizer covid-19 vaccine. The national database showed that people who had had the second dose when their age group was first eligible were more likely to have covid in the study period (11-21 July 2021) than those who had had the second dose two months later (rate ratio of around 1.6 for all age groups over 16). The rate ratio for severe disease was 1.8 in the over 60s, 2.2 in 40-59 year olds, and too small to calculate in the 16-39 year olds.

Cases of covid-19 in Israel had all but disappeared in May, only to resurge by July as the dominant alpha variant was replaced by delta (98% of cases). It’s likely vaccine efficacy wanes over time and is less effective against the delta variant, but this study couldn’t distinguish between the two factors. Either way, these results led to a decision to offer a booster to anyone who had a second jab more than five months earlier.

A third covid jab provides an effective boost
Over 700 000 Israeli citizens with a median age of 52 years who were eligible for a booster dose of the Pfizer vaccine more than five months after their second dose were matched with a control group. One week after the booster, vaccine effectiveness was estimated to be 93% for admission to hospital (231 events for those who had received just two doses versus 29 events among those who had received three doses), 92% for severe disease (157 v 17 events), and 81% for covid-19 related deaths (44 v 7 events). This study was observational, so the possibility of unmeasured confounding factors exists, and the possible harms of a third dose (such as myocarditis) weren’t explored.

An editorial discusses the dangers of global vaccine shortages, which could leave under-vaccinated countries susceptible to covid-19 and create the conditions for new variants that may come back to haunt the thrice vaccinated.

The pitfalls of surrogate measures
This important meta-analysis of 144 randomised clinical trials and over a million participants found that, just because treatments reduced the incidence of non-fatal myocardial infarction, they can’t be assumed to have reduced all cause or cardiovascular mortality. Specifically, non-fatal myocardial infarction was not a surrogate for all cause mortality in primary, secondary, mixed primary and secondary prevention, or revascularisation trials. The study highlights the danger of inferring too much from surrogate endpoints. It’s possible that, over time, improved diagnosis and prevention treatments meant many non-fatal myocardial infarctions were no longer associated with increased mortality, but even studies from before 2000 (when high sensitivity troponin assays were introduced) failed to show a correlation between the effects of treatment on non-fatal myocardial infarction and reductions in all cause and cardiovascular mortality.

Plasma jabs for ankle osteoarthritis don’t work
Ultrasound guided platelet rich plasma (PRP) injections—using a patient’s own platelets—into the ankle joint didn’t improve ankle symptoms and function in patients with ankle osteoarthritis over 26 weeks compared with placebo, according to this small Dutch trial. Ankle osteoarthritis may only affect 3.4% of the adult population, but it’s more common than hip and knee osteoarthritis among younger people, and there’s no effective, non-surgical treatment.

Adverse effects were more common in the PRP group than the placebo group, who had an ultrasound guided intra-articular saline injection (13 v 8 events). Other PRP products may work better, although it’s hard to see why they would, and there was no information about other therapies that patients may have had (such as physiotherapy).

Plasma jabs for ankle osteoarthritis don’t work

Ann Robinson is an NHS GP and health writer and broadcaster.
GUIDELINES

Routine antenatal care for women and their babies: summary of NICE guidance

Shalmali Deshpande,1 Maija Kallioinen,1 Kate Harding,2 on behalf of the Guideline Committee

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

Around 660 000 women give birth in England and Wales each year. Antenatal care provides women (and their partners) with support and information about pregnancy, birth, and the postnatal period, and assesses their risk of complications. Even in fit and healthy women, concerns and complications can still arise, and good quality antenatal care can enable women to identify and manage potential problems, to reduce the chance of poor outcomes for both the woman and the baby, and to enhance the woman’s (and her partner’s) experience of pregnancy and childbirth.

This new guideline from the National Institute for Health and Care Excellence (NICE)1 replaces the previous version of the NICE guideline on antenatal care published in 2008. This article summarises recommendations from the guideline. We use the terms “woman” or “mother” throughout, but the guidance should be taken to include people who do not identify as women but who are pregnant.

WHAT YOU NEED TO KNOW

- Refer women who are 13+ weeks pregnant with unexplained vaginal bleeding to secondary care for review
- Advise women to avoid going to sleep on their back after 28 weeks of pregnancy and to consider using (for example) pillows to maintain their position while sleeping
- Rates of maternal mortality and stillbirth are highest among women and babies from deprived areas, and higher among black, mixed ethnicit y, and Asian women and babies compared with those who are white
- Routine ultrasound scanning is not recommended in low risk singleton pregnancies during the third trimester

WHAT IS NEW IN THIS GUIDANCE

Pregnant women are enabled to start their antenatal care through various routes, which should improve timely access to antenatal care for women in various situations
Partner involvement in antenatal care is highlighted
Physiotherapy services are recommended to provide exercise advice and/or a lumbopelvic belt for pelvic girdle pain
Different pharmacological options for management of mild to moderate nausea and vomiting are summarised

Recommendations

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

Organisation and delivery of antenatal care

Starting antenatal care

Practice varies regarding when women access antenatal care, and disadvantaged groups such as ethnic minorities and socially excluded women may present late to antenatal care services owing to access barriers. The new recommendations should reduce these barriers by providing opportunities for timely access to antenatal care through multiple routes.

- Ensure that antenatal care can be started in a variety of straightforward ways, depending on women’s needs and circumstances, for example, by self-referral, referral by a GP, midwife, or another healthcare professional, or through a school nurse, community centre, or refugee hostel.
- At the point of antenatal care referral:
  - Offer an easy-to-complete referral form
  - Include information about modifiable factors that may affect the pregnancy, including stopping smoking, avoiding alcohol, taking supplements, and eating healthily (see also recommendation 1.3.9 and the NICE guidelines on maternal and child nutrition, vitamin D, and smoking: stopping in pregnancy and after childbirth2 3)
  - Ensure that the information is available in different languages or formats such as digital, printed, braille, or Easy Read.
• The referral form for women to start antenatal care should
  - Enable healthcare professionals to identify women with
    - specific health and social care needs
    - risk factors, including those that can potentially be addressed before the booking appointment, for example, smoking
  - Include contact details for the woman’s GP.

Monitoring fetal growth and wellbeing
Although some women may request routine ultrasound scans in late pregnancy (from 28 weeks), available evidence does not show benefit from routine ultrasound in late pregnancy for uncomplicated singleton pregnancies. Third trimester ultrasound should be offered when a clinical indication arises.

• Do not routinely offer ultrasound scans after 28 weeks for uncomplicated singleton pregnancies.

Sleep position
Evidence suggests that, after 28 weeks of pregnancy, women who fall asleep in a supine position (on their backs) have an increased associated risk of stillbirth and having a baby born small for gestational age. The risk is uncertain because of the small evidence base and design of the studies, which makes it difficult to assume that supine sleep position caused the adverse outcomes. Information about this association should be given to pregnant women.

• Explain to the woman that there may be a link between going to sleep on her back and stillbirth in late pregnancy (after 28 weeks).
• Advise women to avoid going to sleep on their back after 28 weeks of pregnancy and to consider using (for example) pillows to maintain their position while sleeping.

Interventions for common problems during pregnancy

Nausea and vomiting of pregnancy
Up to 80% of pregnant women experience nausea and vomiting symptoms to a varying degree.

Antiemetics. Take into account her preferences and her experience with treatments in previous pregnancies.

- Reassure women that mild to moderate nausea and vomiting are common in pregnancy, and are likely to resolve before 16 to 20 weeks.
- Recognise that by the time women seek advice from healthcare professionals about nausea and vomiting in pregnancy, they may have already tried a number of different interventions.
- For pregnant women with mild to moderate nausea and vomiting who prefer a non-pharmacological option, suggest that they try ginger.
- When considering pharmacological treatments for nausea and vomiting in pregnancy, discuss with the woman the advantages and disadvantages of different antiemetics. Take into account her preferences and her experience with treatments in previous pregnancies.
The main challenge to implementation of this guidance is that service organisation for providing antenatal care is variable.

Implementation

The main challenge to implementation of this guidance is that service organisation for providing care is variable: changes to practice will depend on the availability of services within a particular local area. For example, physiotherapy services for pregnant women with pelvic girdle pain may be limited in some areas.

For pregnant women with nausea and vomiting who choose a pharmacological treatment, offer an antiemetic.

For pregnant women with moderate to severe nausea and vomiting:
- Consider intravenous fluids, ideally on an outpatient basis.
- Consider acupuncture as an adjunct treatment.
- Consider inpatient care if vomiting is severe and not responding to primary care or outpatient management. This will include women with hyperemesis gravidarum.

Heartburn

Many women experience heartburn during pregnancy—it can be uncomfortable and can negatively affect women’s experience of pregnancy and their quality of life. A NICE guideline on gastro-oesophageal reflux and dyspepsia in adults gives guidance on dietary and lifestyle modifications. Some evidence suggests that antacid or alginate can be effective in the management of heartburn during pregnancy.

Pelvic girdle pain

Approximately one in five women experience pain in the pelvic girdle region during pregnancy. Pelvic girdle pain can make daily activities during pregnancy difficult for women and may have an effect on pain intensity felt during labour or birth. Evidence suggests that exercise advice and/or a non-rigid lumbopelvic belt from physiotherapy services may reduce pain intensity and pelvic related functional disability, and is likely to be cost effective.

- For women with pregnancy related pelvic girdle pain, consider referral to physiotherapy services for:
  - Exercise advice and/or
  - A non-rigid lumbopelvic belt.

Unexplained vaginal bleeding after 13 weeks’ gestation

- Refer women who are 13+ weeks pregnant with unexplained vaginal bleeding to secondary care for review.
- Offer anti-D immunoglobulin to women who present with vaginal bleeding after 13 weeks of pregnancy if they are:
  - Rhesus D-negative and
  - At risk of isoimmunisation.
- Consider discussing the increased risk of preterm birth with women who have unexplained vaginal bleeding.

FURTHER INFORMATION ON THE GUIDANCE

Throughout the development of this guideline, the committee has considered how antenatal care could be made accessible, fair, and high quality for all women, regardless of their background or situation. We have also published a guideline on postnatal care, which covers the topics of emotional attachment and baby feeding.

Methods

This guidance was developed by the National Guideline Alliance in accordance with NICE guideline methodology (https://www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A Guideline Committee (GC) was established by the National Guideline Alliance, which incorporated healthcare and allied healthcare professionals (two obstetricians, two midwives with an interest in antenatal care, one consultant midwife with an interest in antenatal care, one academic midwife, one public health practitioner, and one sonographer, with co-opted members including one general practitioner, one lay member, and one obstetric physician) and two lay members.

The guideline is available at: https://www.nice.org.uk/guidance/ng201

The committee identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or, when evidence was not found, based on their experience and opinion using informal consensus methods.

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

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

Future research

The GC prioritised the following research recommendations:

- What is the clinical and cost effectiveness of hospitalisation compared with outpatient management for pregnant women with unexplained vaginal bleeding?
- What is the clinical and cost effectiveness of medication for women with nausea and vomiting in pregnancy?
- What is the clinical and cost effectiveness of different models of antenatal care with varying numbers and times of appointment, and should different models be used for groups at risk of worse outcomes?
- What is the clinical and cost effectiveness of routine ultrasound from 36+0 weeks compared with selective ultrasound in identifying breech presentation?
- What is the clinical and cost effectiveness of corticosteroids for women with severe nausea and vomiting in pregnancy?
NIHR Alerts aim to help busy health and care professionals put research into practice

Helen Saul,1 Cat Chatfield2

Unprecedented extra demands on healthcare staff during the covid-19 pandemic have made it more difficult than ever for professionals to keep up to date with research. This time of major upheaval has underlined the need for health and social care to be the best and most efficient possible. To ensure that changes represent progress, they need to be based on sound research.

With this in mind, The BMJ is restarting its partnership with the National Institute for Health Research (NIHR). The NIHR is one of the UK’s largest funders of health and care research. It is funded by the Department of Health and Social Care and provides infrastructure support and research grants for clinical, social care, public health, and global health research. For this research to have an impact, it must reach those best placed to act on it, and in an accessible and useful format.

The NIHR Centre for Engagement and Dissemination (CED) was set up in April 2020 as a step towards meeting this need. The centre brings together and builds on the work of the previous NIHR Dissemination Centre and NIHR Involve (supporting wider patient and public engagement in research).

Hundreds of NIHR funded research papers are published every month; frontline health and care professionals cannot possibly read them all. The CED filters the research, selecting studies with novel findings and implications for practice. Plain language summaries of these studies, NIHR Alerts, are published on the NIHR Evidence website.

Accessible research summaries
Readers of The BMJ say they would like to see the most important findings presented in an easily accessible form. In an ongoing partnership, a selection of NIHR Alerts—those most relevant to busy clinicians—will be republished regularly in The BMJ.

The selection process is rigorous. The published literature is screened every month for NIHR funded research. An initial in-house screen at CED selects original research based on patients or service users (not laboratory based studies). The aim is to find papers based on sound science, with a novel finding, which can be implemented. Or indeed, interventions which should not be used. Some of the messages are a clear “do not do,” based on firm evidence.

Reviewers are selected from a pool of professionals, patients, and members of the public. They fill in a brief questionnaire giving their views on the paper and what importance they attach to it. Papers are then discussed by the CED editorial board, which has expertise across health and social care sectors and includes two members of the public. Once selected, the NIHR Alerts are written, assessed for readability by a public reviewer, and posted on the NIHR Evidence website. Those most relevant to The BMJ’s readership will be highlighted in these pages.

As the collaboration between The BMJ and NIHR restarts, we hope you will find the NIHR Alerts interesting and relevant to your practice. As ever, we welcome your feedback.

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.n2526

NIHR Alerts are summaries of NIHR-funded research with novel findings and implications for practice. They are intended for health and care professionals, commissioners, researchers and members of the public.

To read the full NIHR Alert, go to https://bit.ly/3meFA7E

NIHR Central Commissioning Facility

1NIHR Central Commissioning Facility

2The BMJ

Correspondence to: helen.saul@nihr.ac.uk; cchatfield@bmj.com

The impact of chronic kidney disease Stages 3-5 on pregnancy outcomes
Wiles K, Webster P, Seed PT, et al
Nephrol Dial Transplant 2020;gfaa247

0.5 HOURS

Women with kidney disease can be given a personal risk assessment for pregnancy

The study

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Women with kidney disease can be given a personal risk assessment for pregnancy
What did this study do?

The researchers looked at the records of 159 women, who had 178 pregnancies between 2003 and 2017. The women had been treated in six specialist units in the UK. Women on dialysis at the start of the pregnancy were not included.

The researchers considered how well the babies were at birth, factors that predicted the babies' health, and what happened to the women's kidney function during and after their pregnancies.

The key findings were:

Babies' health at birth
- Almost all pregnancies (98%) that had lasted at least 20 weeks resulted in a baby
- Most (99 of 178) babies were born before 37 weeks (preterm) and 47 were born before 34 weeks (very preterm)
- Fifty eight babies needed special care in a neonatal unit.

Signs in the mother that predict risks to babies
- Long term high blood pressure before pregnancy increased the risk of very preterm birth. This affected most of the women, and one in three with high blood pressure had very preterm babies
- Proteinuria was linked to low birth weight
- Creatinine levels that dropped by 10% or less indicated that a woman's kidneys were not adapting to pregnancy and were not removing this waste product. This affected more than half the women (86 of 162) and they had double the risk of a very preterm delivery

Mothers' long term health
- More advanced kidney disease increased the risk of preterm birth. But high blood pressure and proteinuria increased the risks more.
- One year after childbirth, nine women had started renal replacement therapy (dialysis or transplant), and another 19 women needed this within two years
- The decline in kidney function varied by the stage of kidney disease. Women with the least advanced disease (stage 3a) lost kidney function equivalent to 1.7 years of kidney disease. Those with more advanced disease (stage 4 and 5) lost the equivalent of 4.9 years
- On average, women were likely to need dialysis or a transplant 2.5 years earlier than if they had not been pregnant
- High blood pressure also predicted loss of kidney function
- The 43 women who had previously had a kidney transplant were no more likely to have preterm births or a big decline in kidney function than women who had not had a transplant. Factors like high blood pressure were more important.

Why was this study needed?

Pregnancy is known to put additional strain on the kidneys of women with advanced chronic kidney disease (CKD) (stages 3-5). Small historical studies have shown that women with CKD before pregnancy are at higher risk of having preterm and low birthweight babies. These babies are at increased risk of having health and development problems.

Around 1 in 750 pregnancies involves a woman with advanced disease. Obesity and diabetes increase the risk of CKD, and as these conditions become more common, the number of women with disease having babies is likely to increase. These women will need reliable information about their chances of having problems, to enable them to plan their care.

To date, little reliable information has been available to guide women considering having a baby. Most historical studies did not take the severity of CKD into account, and larger studies were needed to predict which women are at higher risk of problems, and which factors can best assess a woman's risk.

A new study—the largest to date—aimed to give estimates of how much a woman's kidney disease is likely to progress during pregnancy.

What did it find?

The researchers looked at the records of 159 women, who had 178 pregnancies between 2003 and 2017. The women had been treated in six specialist units in the UK. Women on dialysis at the start of the pregnancy were not included.

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Why is this important?

This is the largest and most reliable study to date into the outcomes for mothers and babies in advanced CKD. Converting the decline in kidney function during pregnancy into its equivalent when not pregnant is a new approach. It gives women and their doctors a clear indication of the effect of pregnancy on kidney function.

It will enable doctors to have informed conversations with women with CKD who are considering pregnancy, or are already pregnant. They will be able to discuss the likely risks for the individual woman, monitor women better during pregnancy, and plan for the care of the woman and baby.

What's next?

The researchers are already using the results in their clinical practice when counselling women.

It would be useful to look at the same outcomes for women with less advanced kidney disease. Trials on interventions—for example, on whether treatment to lower blood pressure before or during pregnancy would improve outcomes—would also be helpful. However, it is difficult to carry out such trials in pregnant women.

Longer term studies to look at the health of the babies would also be useful. The study was not able to find out, for example, what happened to very preterm or low birthweight babies.
A man in his 50s presented with a two week history of a large ecchymosis on his left ankle and foot, and a two month history of petechial rash on his lower limbs (figure). He had no history of recent trauma, fevers, night sweats, weight loss, or upper respiratory symptoms, and did not report any bleeding from other sites. His diet largely consisted of ready meals and he had not consumed fresh fruit or vegetables for more than a year.

He said that he had not used alcohol or injected drugs in the past six months; however, he had a history of excess alcohol intake (>70 units weekly) and injecting drug use.

Other history included HIV (controlled with antiretrovirals) and hepatitis C (for which he underwent curative treatment three years earlier).

He did not take any drugs that might cause spontaneous bruising.

The patient was underweight (body mass index 17.4) and had poor dentition, with several teeth missing. He had full range of movement in his legs, and no effusion of the left ankle joint.

The table shows the results of relevant investigations.

**What is the most likely diagnosis?**

Submitted by Melanie Etti and Gurjinder Sandhu

Patient consent obtained.

Cite this as: BMJ 2021;375:n2511

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**What is the most likely diagnosis?**

Vitamin C deficiency (scurvy) caused by poor dietary intake of foods rich in vitamin C. Vitamin C (ascorbic acid) cannot be stored in tissues, thus signs and symptoms of deficiency can occur within one to three months of poor dietary intake. Perifollicular haemorrhages surrounding prominent hyperkeratotic follicles and corkscrew hairs are pathognomonic of scurvy.

Anaemia is present in up to 75% of cases because vitamin C facilitates the reduction of dietary iron from the ferric form (Fe³⁺) to the ferrous form (Fe²⁺), which is important for iron absorption. Other clinical signs include gingival inflammation and bleeding, splinter haemorrhages, delayed wound healing, and joint swelling.

Diagnosis can be established with a detailed dietary history, confirming the patient’s diet over the past one to three months. A detailed dietary history covering at least one month should be taken.

When patients present with unexplained subcutaneous haemorrhage, consider vitamin C deficiency as a differential diagnosis. Similarly, perifollicular haemorrhages are often seen in scurvy.

**Patient outcome**

**LEARNING OUTCOME**

What is the most likely diagnosis?

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

Endgames

**SPOT DIAGNOSIS**

Lower limb ecchymosis in a man with a history of alcohol misuse

Large ecchymosis over patient’s left ankle and foot, with hyperkeratosis of skin overlying dorsal and lateral aspects of the foot. Multiple perifollicular haemorrhages on medial aspect of patient’s right lower leg

**Results of relevant investigations**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>114 g/L</td>
<td>130-170 g/L</td>
</tr>
<tr>
<td>Mean corpuscular volume, white cell count, platelet count</td>
<td>Within normal ranges</td>
<td>–</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm in first hour)</td>
<td>101</td>
<td>1-20</td>
</tr>
<tr>
<td>Prothrombin time, activated partial thromboplastin time (with kaolin)</td>
<td>Within normal ranges</td>
<td>–</td>
</tr>
<tr>
<td>CD4+ cells</td>
<td>272×10⁶/L</td>
<td>560-1460</td>
</tr>
<tr>
<td>Urea</td>
<td>7.5 mmol/L</td>
<td>2.5-7.8</td>
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<tr>
<td>Creatinine</td>
<td>148 mmol/L</td>
<td>62-106</td>
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<tr>
<td>Liver enzymes, serum calcium, lactate dehydrogenase, vitamin B₁₂, serum folate</td>
<td>Within normal ranges</td>
<td>–</td>
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<tr>
<td>Vasculitis screen</td>
<td>Negative</td>
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<tr>
<td>Urine protein:creatinine ratio</td>
<td>16.5 mg/mmol</td>
<td>&lt;50 mg/mmol</td>
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<tr>
<td>Cryoglobulins</td>
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<td>–</td>
</tr>
<tr>
<td>Complement C3 and C4</td>
<td>Within normal ranges</td>
<td>–</td>
</tr>
<tr>
<td>Immunoglobulins G, A, and M</td>
<td>Within normal ranges</td>
<td>–</td>
</tr>
<tr>
<td>HIV RNA</td>
<td>&lt;50 copies/mL</td>
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<tr>
<td>Hepatitis C viral load</td>
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<td>–</td>
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<tr>
<td>Computed tomography of neck, abdomen, and pelvis</td>
<td>No lymphadenopathy seen</td>
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</tr>
<tr>
<td>Urine dipstick</td>
<td>Trace proteinuria, no haematuria</td>
<td>–</td>
</tr>
</tbody>
</table>

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Articles with a “learning module” logo have a linked BMJ Learning module at http://learning.bmj.com.
**Multiple myeloma with conjunctival involvement**

This is amyloid light chain (AL) amyloidosis on the conjunctiva of a man in his 40s who subsequently received a diagnosis of multiple myeloma. He presented to the nephrology department with severe bilateral oedema of the legs and was found to have nephrotic syndrome. He had also noticed bilateral subconjunctival haemorrhages associated with a yellowish deposit of the conjunctiva. Conjunctival biopsy was performed. Congo red staining of the biopsy samples showed apple-green birefringence, and antibody based typing showed light chain amyloid.

Subsequent imaging showed AL amyloidosis involving the kidneys and heart, caused by underlying myeloma. Myeloma is a malignancy of plasma cells. In 10-30% of myeloma patients, light chain proteins misfold causing AL amyloidosis. Abnormal AL amyloid proteins can be deposited almost anywhere causing organ dysfunction.

If AL amyloidosis is diagnosed, investigate for any systemic involvement and search for underlying myeloma to avoid any treatment delays to ensure prompt treatment can be instigated.

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

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**Treating Lyme disease**

A half forgotten antimicrobial, hygromycin A, shows unexpectedly specific activity against *Borrelia burgdorferi*, the organism which causes Lyme disease. So far the benefits have been seen only in mice, where the antibiotic cleared *B burgdorferi* infections without harming the animals’ gut bacteria. If hygromycin A proves safe in humans, it may be possible to avoid the long courses of broad spectrum antibiotics currently used to treat Lyme disease (Cell doi:10.1016/j.cell.2021.09.011).

**Trust the public**

In Nature, a Danish psychologist argues that one of the most important lessons of the pandemic is that the public can be trusted with hard truths. He cites evidence that, after disasters, people react with solidarity, not panic. They become more willing to share resources with strangers, not less. When governments are open and truthful, vaccine acceptance is high and misinformation is less likely to gain traction (doi.org/10.1038/ doi: 10.1097/ JOM.00000000000002331).

**The health of Gulf war veterans**

Military personnel who saw active service during the Gulf war in 1991 subsequently reported poor health. However, despite the multiple symptoms, little evidence has been available to show an increase in any defined disease category. Continuing follow-up suggests that may be changing.

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**When governments are open and truthful, vaccine acceptance is high**

**Growth in adolescence and risk of breast and prostate cancer**

Two thousand Icelanders, born 1915 to 1935, were followed for 65 years. Breast cancer was twice as common in women who had been in the highest third of growth rates in adolescence compared with women in the lowest third. In men, by contrast, those with the highest growth rates in adolescence were least likely to develop advanced prostate cancer (Am J Epidemiol doi:10.1093/aje/kwab250).

**White coat hypertension**

Eighteen people with essential hypertension were monitored during blood pressure measurements both in the presence and in the absence of a doctor. Minerva wasn’t surprised to learn that, when a doctor was present, beat-to-beat finger blood pressures, heart rate, and microneurographic activity in skin sympathetic nerves were all higher (Hypertension doi:10.1161/ HYPERTENSIONAHA.121.17657). Still, it’s a reminder that, when making decisions about the treatment of hypertension, it’s important to take account of how and when blood pressure was measured.

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**Prophylactic aspirin for pregnant women with diabetes**

Prescribing aspirin to all pregnant women with diabetes failed to reduce the prevalence of pre-eclampsia, according to a study from Denmark. Before this policy was introduced, aspirin prophylaxis had been given only to women judged to be at high risk. The proportion of women who developed pre-eclampsia was around 12% both before and after the change (Diabetes Care doi:10.2337/dc21-1182).

**Preventing flu**

Last winter, when the world was trying to contain the spread of SARS-CoV-2, cases of flu almost disappeared. The predicted “twindemic,” a double whammy of flu and covid, never occurred. Measures such as mask wearing, distancing, remote learning, working from home, and limiting social gatherings prevented the spread of influenza viruses. Countries can’t go into lockdown each winter to prevent seasonal flu, but perhaps more modest precautions could make a substantial difference (www.thelancet.com/ health/archive/2021/10/flu-season-winter- america-choice/620373/).

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**MINERVA**

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