ADHD: children as young as 5 on medication
In the US, around 2.4% of preschool children (under 6 years old) are diagnosed with attention deficit/hyperactivity disorder (ADHD). The standard treatment is behavioural modification, followed by medication with stimulants (methylphenidate) or, in around 25% of cases, α-2 adrenergic agonists (guanfacine or clonidine), for which there’s not much evidence of efficacy or safety.

This retrospective review of health records of 497 children with a median age of just 5 years found improvement in 66% of those receiving α-2 adrenergic agonists versus 78% of those taking stimulants and flagged up differences in adverse effect profiles. Daytime sleepiness was a more common side effect of α-2 adrenergic agonists (38% v 3%), whereas appetite suppression was a more common reported effect of stimulants (38% v 7%). Alarmingly, over a third of the children were put straight on to medication with no record of a behavioural intervention.

Access to a liver transplant
Most people who need a liver transplant die before they get one. The main reason is a lack of donor organs, but delays in referral are also to blame according to this large US cohort study of 34,494 veterans with cirrhosis. Only 1.6% of the cohort received a transplant within three years; 95% were never referred, and 40% weren’t put on the waiting list despite being eligible.

Inequity of access occurred primarily at the initial referral stage. Those with comorbidities, aged over 70 years, on lower income, African-American, or with alcohol related liver damage were less likely to be referred. The study was observational, so causality can’t be demonstrated and there may have been other factors affecting clinicians’ decisions. Tracking the whole process would be a good start in addressing these grim statistics.

Aspirin: less is more
What’s the best dose of aspirin to reduce the risk of death, myocardial infarction, and stroke in people with known cardiovascular disease, while keeping the risk of major bleeds to a minimum?

This pragmatic trial found that a higher dose of 325 mg aspirin was no better or safer than 81 mg, and patients were more likely to continue taking the lower dose. In both groups, death or hospitalisation for stroke or myocardial infarction occurred in around 7%, and major bleeds in a reassuringly low 0.6% of patients.

Results could have been skewed by the open label design, which meant that patients often switched doses—usually from 325 mg to 81 mg—and many patients had already been taking 81 mg aspirin before the study. But generally the lower dose seems to be as effective and safe as the higher dose, as well as being more acceptable to patients.

Kangaroo style parenting
Should human mothers behave more like kangaroos? “Kangaroo mother care” is the delightful name for keeping newborn infants in continuous contact with the mother’s chest and exclusively breastfeeding the baby. Apparently, it’s one of the most effective ways of preventing death in low birthweight infants.

WHO currently recommends short bursts of kangaroo mothering once the baby’s condition is stable. But this large study across several low resource hospitals found that starting continuous kangaroo mother care immediately after birth in low birthweight infants (1.0 kg to 1.799 kg) improved neonatal mortality by 25% compared with waiting for stabilisation (28 day mortality 12% v 16%) and reduced sepsis and hypothermia. There’s no way of knowing whether the benefit was due to the simple presence of the mother or whether having the baby clamped to her chest for a minimum 17 hours a day made a difference. The study may not be widely generalisable, as around 20% of the low birthweight babies couldn’t be enrolled because either the baby or mother was too unwell.

New radiotracer improves prostate cancer outcome
In this open label, phase II/III trial, men who had recurrent or persistent prostate cancer despite a radical prostatectomy, showed a 12% improvement in event free survival at three years when advanced molecular imaging using a new PET radiotracer, 18F-fluciclovine, was used to guide decisions about final radiotherapy treatment compared with standard imaging. There was no significant increase in toxicity. Randomised trials of imaging tests with endpoints of primary cancer control are few and far between. Most focus on diagnostics and decision making. Longer follow-up would be useful to see whether the survival advantage is maintained.
Virtual and in-person cardiac rehabilitation

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What you need to know

- Most eligible patients with coronary heart disease and heart failure do not participate in cardiac rehabilitation. Covid-19 has exacerbated this, with a substantial drop in the number of patients participating
- Home and telehealth based interventions are increasingly being used as alternatives to traditional centre based rehabilitation programmes
- Outcomes for patients participating in home based rehabilitation compare favourably with centre based programmes in terms of hospitalisations, quality of life, and cost
- Telehealth based interventions are promising, but some patients may find these interventions challenging
- Novel ways of delivering rehabilitation have been employed during the covid-19 pandemic, including hybrid models that are likely to be offered as alternatives to centre based rehabilitation in future, enabling greater patient choice and greater uptake of cardiac rehabilitation

Cardiac rehabilitation before the pandemic

Historically, rates of referral to cardiac rehabilitation were suboptimal in the US15-19 and UK (<15% for heart failure).20 Uptake was also poor, with only 68 074 (50%) of the 135 861 patients with coronary heart disease in England, Wales, and Northern Ireland accepting an offer of cardiac rehabilitation in the 12 months before the pandemic.21

Most patients referred for rehabilitation after a cardiac event were offered supervised, group based classes, which ranged in frequency, intensity, duration of exercise, and self-help guidance.4 21 Cardiac rehabilitation was usually delivered in hospital outpatient departments or community centres, or (in some parts of Europe) as inpatient services.4 Collectively, these modes of delivery are termed “centre based cardiac rehabilitation.” Despite compelling evidence for clinical and cost effectiveness, participation in centre based programmes remained suboptimal, with overall participation rates <20% in the US22 and similar rates after a diagnosis of heart failure in Europe.23 Poor participation predominated in certain groups: women, older people, ethnic minorities, and those living in rural communities or who are socioeconomically deprived.4-26

Consequently, calls were made for alternatives to centre based cardiac rehabilitation.25 26 Suggested interventions included rehabilitation at home facilitated by healthcare professionals and supported by telehealth technologies, to improve uptake.26 27 Hybrid models involving a combination of home and centre based rehabilitation have been evaluated28 9 but not implemented widely.29 Tele-rehabilitation—“rehabilitation from a distance by using one or several devices monitoring and communicating patient specific information to the caregivers,”29 which often involves telephones, videoconferencing, and mobile apps (telehealth)30—is increasingly used, often as an adjunct to home based rehabilitation.

Box 3 (bmj.com) summarises key national and international recommendations on cardiac rehabilitation. Box 4 (bmj.com) discusses ways to improve delivery of cardiac rehabilitation for patients, including under-represented populations.

Before the covid-19 pandemic, 100 000 people were admitted to hospital with heart attacks and approximately 200 000 were diagnosed with heart failure annually in the UK.1 An estimated 7.4 million people in the UK live with cardiovascular diseases, and this is likely to increase with improved survival following coronary heart disease and an ageing population.1

A 2020 European position paper, in keeping with other national and international guidelines,2 3 stated that “comprehensive cardiac rehabilitation has been recognised as the most cost effective intervention to ensure favourable outcomes across a wide spectrum of cardiovascular disease.”4 Benefits include improvements in morbidity, hospital admissions, physical activity, exercise capacity, psychological wellbeing, and health related quality of life.3 4 11 Patient groups set to benefit are categorised, by evidence level, in box 1. To achieve these benefits, it is recommended that all core components of cardiac rehabilitation (box 2, see bmj.com) are included in a comprehensive programme.4 Guidelines from the UK also advocate long term strategies to promote secondary prevention in primary care and service evaluation through audit.

Even before the covid-19 pandemic, most patients in high and low to middle income countries were not offered cardiac rehabilitation14 15 and uptake was low. Lockdown measures owing to covid-19 have exacerbated this problem.15 16 Provision and use of cardiovascular healthcare have decreased worldwide, with substantial numbers of patients in Europe and North America unable to access routine hospital care.15 16
Cardiac rehabilitation during the pandemic

The number of patients with heart failure in the UK participating in rehabilitation decreased from 4969 (~10% of eligible patients) before the pandemic (May 2019-January 2020) to 1474 (~5% of eligible patients) during the first wave (February-August 2020). Covid-19 has therefore led to further calls for alternatives to traditional centre based cardiac rehabilitation programmes, with an emphasis on home based and digital technologies to provide virtual access.\textsuperscript{15, 16}

Indeed, although overall uptake of cardiac rehabilitation has decreased, the proportion of patients receiving home based rehabilitation in the UK has increased more than threefold since the pandemic—from 22.2% to 72.6%\textsuperscript{12}—as more services began to offer home based and remote delivery.\textsuperscript{17}

The rapid adoption of technology in response to suspension of centre based rehabilitation in the pandemic was also reported in an international survey of 330 cardiac rehabilitation healthcare professionals.\textsuperscript{14}

Use of tele-rehabilitation can provide “a safe solution for patients, family, and staff in the midst of covid-19.”\textsuperscript{30}

How can exercise capacity be assessed remotely during the pandemic?

Baseline assessment of exercise capacity is core to the effective and safe delivery of exercise interventions.\textsuperscript{2} In the UK, the incremental shuttle walk test, step test, and six minute walk test are part of routine practice.\textsuperscript{2} In response to covid-19, most cardiac rehabilitation programmes have adjusted assessments to include greater use of submaximal step tests, two and three minute walk tests, and other more subjective approaches, including physical activity questionnaires (eg, the Duke Activity Status index), fitness apps, and observation of patients carrying out activities such as chair based exercise or using hallways and stairs at home.

Several publications from North America and Europe discuss how to adapt and use different baseline fitness tests to assess the relative risk of exercise.\textsuperscript{14-16} Risk assessment to determine whether patients have a fitness level below five metabolic equivalents and a proportional response (eg, heart rate and rating of exertion) to exercise is a key focus\textsuperscript{13-15} (box 5).

### Box 1 | Patient groups who benefit from cardiac rehabilitation\textsuperscript{4}

**High level evidence**
- Post-acute coronary syndrome (ACS), post-primary coronary angioplasty, and coronary artery surgery:
  - Patients with ACS (class 1, level A)\textsuperscript{12, 13}
  - Including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina (class 1, level B)\textsuperscript{12, 13}
  - All patients undergoing reperfusion (eg, coronary artery bypass graft, primary percutaneous coronary intervention, and percutaneous coronary intervention (class 1, level A1 2)
- Chronic heart failure:
  - Patients with newly diagnosed chronic heart failure and chronic heart failure with a step change in clinical presentation (class 1, level A)\textsuperscript{12, 13}

**Limited evidence**
- Patients with heart transplant and ventricular assist devices
- Post-valve heart surgery (open and percutaneous)
- Adults and adolescents with congenital heart disease
- Atrial fibrillation
- Unlike other international guidelines, evidence informing guidance from the National Institute for Health and Care Excellence is assessed based on Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) criteria—the class/level approach is not used and therefore not referenced above

### Box 5 | Practical tips for remote/virtual delivery of cardiac rehabilitation\textsuperscript{15}

- **Make it easy**
  - Use tip sheets to help staff adjust to delivering care virtually
  - Avoid becoming overwhelmed by the multitude of available resources by finding a single, comprehensive, verified online resource for patients and staff
- **Don’t wait**
  - Encourage patients to attend at minimum intake assessments to discuss the merits of virtual cardiac rehabilitation
  - Follow a shared decision making process for enrolment in virtual rehabilitation, to ensure patients understand potential risks and benefits of participating virtually versus choosing to delay care
- **Focus on core components**
  - Consider lifestyle risk management, psychosocial support, medical advice, education
  - Provide simple exercise prescriptions aimed at encouraging low-to-moderate physical activity
- **Obtain patient metrics**
  - Examples include a self-administered six minute walk test for exercise capacity, using patients’ personal scales and blood pressure cuffs
- **Offer group sessions**
  - Reduce “labour intensive” one-to-one sessions when possible by providing group tele-/video-conferencing for educational sessions and patient support
- **Evaluate**
  - Formalise an evaluation process to assess the merits and efficacy of virtual care
- **Invest in access**
  - For rural and/or under-resourced areas, consider purchasing tablets, smartphones, or other electronic options for loan to participants to enhance a one-to-one personal experience

*Moulson et al suggest that it is possible to complete assessment of the core components digitally/virtually, including an exercise test, albeit with the limitations.\textsuperscript{11}

**How patients were involved in the creation of this article**

Chris Edgeler (“A carer’s story” bmj.com) was a patient of coauthor HD, having been admitted to hospital with a heart attack in 2012. Chris and his wife Cindy reviewed a draft version of the article.

We also received feedback from patients supported by the Wirral Community Cardiology Service, who have been delivering REACH-HF since 2019. Our patient coauthor KP has been a member of the REACH-HF study group for several years, having had a heart attack in 2008.

Our patient advisers acknowledged the usefulness of the digital approach to cardiac rehabilitation, but they also highlighted the need for a more hybrid approach so that rehabilitation is as accessible as possible. The final manuscript was modified to reflect the patients’ views.
How do home and centre based cardiac rehabilitation programmes compare?

In the UK, the Heart Manual—acknowledged as the “most extensively studied self-management programme”—has been used by the NHS for more than 10 years. Box 6 lists advantages and disadvantages of home based cardiac rehabilitation.

The standards and core components (box 2, see bmj.com) used in many home based cardiac rehabilitation studies are comparable with those in studies of centre based interventions. Cochrane reviews in coronary heart disease and heart failure consistently report statistically significant reductions in hospital admissions with centre and home based cardiac rehabilitation compared with usual care. Studies that directly or indirectly compared home and centre based cardiac rehabilitation found no statistically significant difference in 12 month mortality between the two approaches. A systematic review of 31 randomised controlled trials reported that home based and hybrid cardiac rehabilitation models can improve exercise capacity and are potential alternatives to centre based programmes.

A meta-analysis of individual participant data and the updated Cochrane review showed that participation in home or centre based cardiac rehabilitation after heart failure resulted in a clinically meaningful improvement in health related quality of life, determined using the Minnesota Living with Heart Failure questionnaire score (7.1 (95% CI -3.7 to -10.5)), compared with no rehabilitation.

Improvements in modifiable cardiovascular risk factors with cardiac rehabilitation are documented in a US scientific statement. Differential effects on weight, blood pressure, lipids, and tobacco use were similar in the eight home versus centre based cardiac rehabilitation trials that were included (figure). Adherence to home based cardiac rehabilitation is comparable with that in centre based programmes; however, considerable variation is seen in reporting of adherence, and the US scientific statement noted limited ability to pool data to compare home and centre based programmes. A Cochrane review concluded that clinical benefits with centre and home based cardiac rehabilitation in patients with heart failure, myocardial infarction, and coronary revascularisation are similar and with equivalent costs.

Competing interests: See bmj.com.
Cite this as: BMJ 2021;373:n1270
Find the full version with references at http://dx.doi.org/10.1136/bmj.n1270

Box 6 Adantages and disadvantages of home based versus centre based cardiac rehabilitation

<table>
<thead>
<tr>
<th>Potential advantages</th>
<th>Potential disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Reduced enrolment delays</td>
<td>Lack of reimbursement*</td>
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<tr>
<td>Expanded capacity/access</td>
<td>Less intensive exercise training</td>
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<tr>
<td>Individually tailored programmes</td>
<td>Less social support</td>
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<tr>
<td>Flexible, convenient scheduling</td>
<td>Less patient accountability</td>
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<tr>
<td>Minimal travel/transportation barriers</td>
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<td>Greater privacy while receiving cardiac rehabilitation</td>
<td>Less face-to-face monitoring</td>
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<tr>
<td>Integration with regular home routine</td>
<td>Safety concerns for high risk patients</td>
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*Lack of reimbursement is an issue in some countries; however, the Centers for Medicare and Medicaid Services in the US introduced reimbursements for virtual cardiac rehabilitation in 2020.

EDUCATION INTO PRACTICE

• How well do you know the local pathways to refer patients for home based cardiac rehabilitation after a heart attack or new diagnosis of heart failure?
• In patients with a new diagnosis of heart failure, how many have been referred to and participated in a cardiac rehabilitation programme in the past 12 months?
Congenital cytomegalovirus infection

Megan H Pesch, Katie Kuboushek, Michael M McKee, Marc C Thorne, Jason B Weinberg

Congenital cytomegalovirus (cCMV) infection is a common congenital infection, affecting one in every 100-200 live births globally. Long term neurodevelopmental sequelae occur in a quarter of children affected. This article provides a clinical update of the literature on the prevention, diagnosis, treatment, and anticipatory management of infants and children with cCMV. Recommendations from the 2015 European Society of Paediatric Infectious Diseases (ESPID) Expert Consensus Group (largely based on expert opinion) are presented along with more recent literature relevant to the general practitioner.

What is congenital cytomegalovirus infection?

Cytomegalovirus (CMV) can cause self-limited generalised symptoms such as fatigue and lymphadenopathy in most healthy individuals, including pregnant people. CMV infection occurs when CMV transplacentally infects a developing fetus. The virus can cause damage to the placenta, and replicate in fetal central nervous system (CNS) cells, which may result in disrupted fetal development, miscarriage, or intrauterine fetal demise. Neonates with cCMV may experience a wide range of signs, symptoms, and long term sequelae (fig 1, bmj.com), although most experience no recognisable signs or symptoms.

Neonates born with visible signs or CNS involvement, commonly referred to as asymptomatic, make up 10% of cCMV cases and are at increased risk for long term neurodevelopmental sequelae. Neonates born without visible signs of infection or CNS involvement, referred to as asymptomatic, make up 90% of cases.

Approximately 15% of asymptomatic neonates develop isolated sensorineural hearing loss (SNHL), which may progress. Recent research has found an increased prevalence of cCMV in children with autism spectrum disorder, suggesting a possible association, although this remains an area of continued research.

What you need to know

- Congenital cytomegalovirus (cCMV) is common, occurring in one in every 100-200 live births
- The mainstay of prevention is prenatal education about behaviour change to reduce contact with saliva and urine of young children who may be shedding CMV
- cCMV most often presents with no visible signs at birth, yet infected infants are at increased risk for sensorineural hearing loss in childhood
- cCMV can be diagnosed shortly after birth using polymerase chain reaction to detect viral DNA in urine or saliva, or later in life by testing residual newborn dried blood spot (Guthrie card)
- All children with cCMV require close monitoring of their hearing and development

Who is at risk of having an infant with cCMV?

All people of childbearing age are at risk of contracting CMV and transmitting the virus to a fetus when pregnant. Primary infections occur when CMV is contracted for the first time just before or during pregnancy, posing a 30-35% risk of fetal transmission. Non-primary infections occur when the childbearing parent has pre-existing CMV immunity but is exposed to a different strain, or has a reactivation of a latent infection. The risk for fetal transmission is lower (~1%) with non-primary infections. Primary infections (versus non-primary) and those that occur earlier (versus later) in gestation are associated with poorer fetal outcomes.

CMV is transmitted through bodily fluids, most commonly through the saliva or urine of young children. Children who attend nursery or daycare may shed high levels of the CMV in their saliva or urine for weeks to months after acute symptoms resolve. Pregnant people in contact with young children (eg, parents, nursery teachers, paediatric healthcare providers) are at heightened risk of having pregnancies complicated by cCMV.

How is it prevented, diagnosed, and managed during pregnancy?

While the focus of this clinical update is diagnosis and management of cCMV in the newborn, general practitioners should also know about the prevention, diagnosis, and management of cCMV in pregnancy. General practitioners can play an important role in counselling for prenatal cCMV risk reduction, which includes basic hygiene and behavioural change practices to avoid contact with potentially infectious bodily fluids (box). An expert review of CMV in pregnancy recommended counselling and subsequent behaviour changes beginning in the weeks before conception. Prenatal CMV antibody screening can be performed in individuals with symptoms; routine screening remains controversial. A congenital infection may be suspected based on fetal imaging findings (eg, intrauterine growth restriction, intracrani al calcifications) or maternal seroconversion.

5 June 2021 [the bmj]
Refer cases of suspected cCMV infection in utero to a specialist in maternal fetal medicine. A prenatal diagnosis of cCMV can be made by polymerase chain reaction (PCR) detection of virus in amniotic fluid obtained via amniocentesis. Surveillance by ultrasound may help to identify potential cCMV related sequelae in the fetus; fetal brain abnormalities are associated with adverse outcomes, although studies have been limited by loss to follow-up and terminations of pregnancy.

No licensed treatments exist to prevent vertical transmission or fetal disease, although valaciclovir has shown promise. Individuals who have previously had a child with cCMV are not at an increased risk in subsequent pregnancies.

Two articles provide further discussion of perinatal cCMV prevention, management, and recommended counselling practice.

### Advice on ways to reduce the risk of CMV in pregnancy
- Avoid contact with children’s saliva—young children, especially those at daycare or nursery, commonly shed CMV in their bodily fluids. Avoid kissing on the lips; offer a cheek or forehead instead.
- Avoid sharing food or utensils—including straws, utensils, or cups, especially with young children. Avoid sharing food with young children.
- Wash hands after nappy/diaper changes and wiping a child’s nose—washing hands thoroughly for at least 20 seconds or using hand sanitiser can reduce CMV transmission.
- Avoid putting pacifiers in your mouth—avoid “cleaning” a child’s pacifier in your mouth if it falls on the floor.

### How Patients Were Involved in the Creation of This Article
Megan Pesch is the mother of a young daughter with congenital CMV. She contributed in drafting and revising this manuscript and recommended emphasising the importance of prenatal education around cCMV prevention in this article.

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**Possible Visible Signs at Birth**
- Hypotonia/lethargy
  - Originating from intracranial abnormalities
- Seizures
  - Originating from intracranial abnormalities
- Feeding difficulties
  - Due to hypotonia and/or difficulty coordinating suck-swallow sequence
- Microcephaly
  - Head circumference >2 standard deviations below the mean for gestational age
- Hepatosplenomegaly
  - Secondary to viral hepatitis and intrahepatic cholestasis
- Small for gestational age
  - Birth weight-for-gestational age >2 standard deviations below the mean
- Petechial rash
  - A generalised rash which can last up to several weeks

**Potential Invisible Findings at Birth and Later Sequelae**
- Vision loss
- Chorioretinitis
  - Inflammatory process that may lead to scarring
- Hearing loss
  - Sensorineural hearing loss, unilateral or bilateral, can fluctuate in infancy
- Intracranial abnormalities
  - May be visible on imaging (e.g., calcifications, white matter lesions, cortical migration defects) or may be suspected due to clinical signs
- Intracranial abnormalities
- Vision loss
- Late onset hearing loss
  - Progressive or rapid onset, may occur through adolescence
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**POSSIBLE VISIBLE SIGNS AT BIRTH**

**Hypotonia/lethargy**
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**POTENTIAL INVISIBLE FINDINGS AT BIRTH AND LATER SEQUELAE**

**Vision loss**
- Chorioretinitis
  - Inflammatory process that may lead to scarring

**Hearing loss**
- Sensorineural hearing loss, unilateral or bilateral, can fluctuate in infancy

**Intracranial abnormalities**
- May be visible on imaging (e.g., calcifications, white matter lesions, cortical migration defects) or may be suspected due to clinical signs

**Thrombocytopenia**
- Due to decreased platelet production from bone marrow involvement

**Elevated transaminases**
- Due to hepatitis

**Intracranial abnormalities**
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**Fig 2 | Potential clinically visible and invisible signs and sequelae of cCMV at birth and later in life**
How does neonatal cCMV infection present?

At birth, roughly 90% of neonates with cCMV have no overt signs of infection.\(^2\)\(^9\) Of the 10% who are symptomatic, most have a combination of one or more findings.\(^9\) Classical signs of cCMV in neonates include small for gestational age, microcephaly, jaundice, hepatosplenomegaly, petechial rash, seizures, or intracranial abnormalities (eg, calcifications). Sensorineural hearing loss (unilateral or bilateral) is also common (fig 2). Neonates with no overt symptoms may be diagnosed through systematic neonatal screening or retrospectively after sensorineural hearing loss is diagnosed later in childhood. A differential diagnosis for infants presenting with signs concerning for cCMV is shown in box 2 (bmj.com).

How is cCMV infection diagnosed in the neonate or child?

cCMV may be diagnosed by urine or saliva PCR in the first 21 days of life. After that time it becomes difficult to distinguish congenital infection from postnatal infection.\(^2\)\(^9\) When based on clinical suspicion alone, 90% of symptomatic cases go undiagnosed at birth.\(^20\) Implementation of systematic neonatal cCMV screening, either universal or targeted to infants with hearing loss, increases diagnosis of both symptomatic and asymptomatic cases.\(^21\) Incidental findings or delayed onset symptoms may also lead to a diagnosis later in infancy or childhood.

Infants and children older than 21 days

Clinical suspicion for cCMV may be raised by a delayed onset or recognition of symptoms, particularly SNHL. CMV PCR can be performed on...
a stored residual dried blood spot left over from newborn screening. The sensitivity of this approach is low (30-85%); a negative result cannot definitively rule out cCMV.22 If no dried blood spot is available, a definitive diagnosis of cCMV cannot be made.

No consensus recommendations exist for the presumptive diagnosis of cCMV. A definitive diagnosis of cCMV in an otherwise asymptomatic infant allows for close monitoring of hearing and development, and early intervention should concerns arise. However, close monitoring can still be implemented if only a presumptive diagnosis can be made.

If definitive diagnosis of cCMV cannot be made, additional testing may lend support for or against a presumptive diagnosis. While the ESPID guidelines do not address how to rule out cCMV in children older than 21 days,2 we find the following tests and parameters useful in our own clinical practice based on existing literature.27

First, evaluate for findings consistent with cCMV through cranial imaging, eye examination, and/or laboratory studies. Second, rule out other possible contributors to the clinical presentation (eg, genetic causes of hearing loss). Third, test for previous exposure to CMV by measuring CMV IgG. A positive result cannot differentiate between congenital and postnatal disease, but a negative result substantially diminishes the likelihood of cCMV. For children <18 months, a positive urine or saliva CMV PCR confirms previous exposure to the virus (we caution against using IgG in this age group because of the potential for persistence of maternal antibodies in the infant). For children older than 18 months, a positive CMV IgG suggests previous exposure to the virus. Shedding of CMV in urine and saliva of a child with cCMV may not persist indefinitely, making those tests less reliable in older children.27

How is congenital CMV infection managed?

ESPID recommendations for the initial evaluation, scheduled monitoring, and ongoing surveillance of an infant with cCMV are summarised in fig 3.2 Additional recommendations based on more recent studies and the authors’ expert opinion are presented in table 1 (bmj.com).

Antiviral therapy
Treatment with a six month course of valganciclovir starting in the first month of life has been associated with improved hearing and developmental outcomes at 24 months.28 Owing to the risk of associated toxicities, particularly neutropenia, ESPID experts recommend valganciclovir treatment for infants with symptomatic disease (full consensus) and those with isolated sensorineural hearing loss (majority consensus), but not for asymptomatic infants.2 Infants should be monitored for toxicities by a paediatric infectious disease specialist throughout the treatment course.28

Hearing surveillance
Serial audiological evaluations—starting at baseline and continuing every 3-6 months until 3 years, and then annually until 6 years—are recommended by ESPID because of the high risk of hearing deterioration in this period.2229 Others recommend continuing routine audiological evaluations through adolescence.2 Hearing amplification and early access to oral or sign language can improve educational and communication outcomes in children with hearing loss.3031

Vision surveillance
Refer infants with cCMV for an ophthalmological evaluation at diagnosis followed by yearly surveillance until age 5 in those with symptomatic disease.2 Delayed onset chorioretinal sequelae are rare.32

Developmental surveillance
Children with cCMV, even those who are asymptomatic, may be at increased risk for neurodevelopmental sequelae; this remains an area of active research.33 In addition to routine developmental monitoring, general practitioners should keep a heightened suspicion for autism spectrum disorder, although evidence to support formal screening recommendations is lacking. Refer children who received antiviral treatment for formal neurodevelopmental assessments at ages 12 months and 24 months.2

What are the long term outcomes for children with cCMV infection?

The range of possible neurodevelopmental outcomes in children with cCMV is wide, and is associated with CNS involvement (fig 2).3

Cognitive
Cognitive outcomes are strongly tied to the presence of intracranial involvement,2 with just under half (43%) of those with such involvement having an intellectual disability. Asymptomatic children do not appear to have functional differences in cognitive or academic skills compared with controls, although this remains an area of active inquiry.3335

Gross motor
Intracranial abnormalities at birth (occurring in 5-9% of all cases) are associated with increased risk of major motor disability, including cerebral palsy.36 Vestibular, gaze, and balance disorders are also common.37 Consider referrals for vestibular testing, physical therapy, supportive bracing, or mobility assistance in those with gross motor delays.

Competing interests: MP is an unpaid board member of National CMV Foundation.

Cite this as: BMJ 2021;373:n1212

Find the full version with references at http://dx.doi.org/10.1136/bmj.n1212
CASE REVIEW Pain in right buttock after carbon monoxide poisoning

A woman in her 30s, eight weeks into her second pregnancy, was found disorientated at home. She had been lying on her right side in bed for about six hours in an airtight room with a coal stove that had nearly burnt out. On admission to the emergency department, she had a Glasgow coma scale score of 8 and her serum carboxyhaemoglobin level was 25%. Acute carbon monoxide poisoning was diagnosed. The patient was assessed by a gynaecologist on admission. No fetal heart beat was detected on ultrasonography.

Chest computed tomography was requested to rule out pneumothorax before hyperbaric oxygen therapy was initiated for carbon monoxide poisoning. After 10 hours of hyperbaric oxygen therapy the woman regained full consciousness, and she mentioned pain in her right buttock. Examination revealed mild swelling and tenderness over the area. She had reduced sensation over her right thigh, but nothing else was found on neurological examination. Her urine was dark.

The table shows the results of other relevant investigations.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine kinase (U/L)</td>
<td>14988</td>
<td>26-140</td>
</tr>
<tr>
<td>Serum myoglobin (ng/mL)</td>
<td>1177.0</td>
<td>14.3-65.8</td>
</tr>
<tr>
<td>Urine myoglobin</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Carbon dioxide combining power (mmol/L)</td>
<td>23.9</td>
<td>22-29</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>4.4</td>
<td>2.9-8.2</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>48.1</td>
<td>53-97</td>
</tr>
<tr>
<td>Uric acid (μmol/L)</td>
<td>118.3</td>
<td>155-357</td>
</tr>
</tbody>
</table>

The noticeably increased levels of creatinine, serum myoglobin, and creatine kinase indicate a diagnosis of rhabdomyolysis. The markedly increased serum and urinary myoglobin indicate a diagnosis of rhabdomyolysis. The dark urine was suggestive of myoglobinuria.

The patient was assessed by a gynaecologist on 5 June 2021.

1. What is the most likely cause of the buttock and thigh signs, and the dark urine?

Pain in right buttock after carbon monoxide poisoning

The fetal circulation system is also vulnerable to hypoxia, putting the fetus at risk of disability or death. Fetal heart beat was related to hypoxia from maternal carbon monoxide poisoning.

2. How would you manage this condition?

Consider fluid resuscitation and sodium bicarbonate for the rhabdomyolysis, although they might also be absent. Monitor for acute renal failure and refer to nephrology if biomarkers deteriorate.

3. What are the considerations for pregnant women with carbon monoxide poisoning and this diagnosis?

Monitor for compartment syndrome. Refer to radiology if compartment syndrome is suspected in those who are unable to communicate, are uncooperative, or are unconscious.

COLLABORATION

Submitted by Huijun Hu and Qiang Sun

Patient consent obtained.

Cite this as: BMJ 2021;373:n1233

You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.
of cardiovascular events were noted. However, no corresponding reductions in mortality or the incidence of kidney replacement therapy was reduced by around 20% in those who had transglutaminase titres above this level. Almost all patients with high titres had unequivocal histology of coeliac disease at biopsy (Gut doi:10.1136/gutjnl-2020-320913).

Eating fruit and vegetables may help to relieve stress
Eating a diet rich in fruit and vegetables is associated with lower stress, according to an Australian study. Among 9000 adults, levels of perceived stress were 10% less in those in the top quarter of the distribution of fruit and vegetable consumption than in those in the lowest quarter (Clin Nutr doi:10.1016/j.clnu.2021.03.043). The investigators speculate that fruit and vegetables contain nutrients that contribute to mental wellbeing. Or could it be that people under stress eat a poorer diet?

Flaws in producing evidence
An article in Nature argues that the pandemic has revealed flaws in the way the scientific world produces and evaluates evidence. More than 2900 clinical trials related to covid-19 have been registered, but most are too small or poorly designed to be of much use. Organisations worldwide have tried to synthesise the available evidence on drugs, masks, and other key issues, but can’t keep up with the outpouring of new research and often repeat others’ work (www.nature.com/articles/d41586-021-01246-x).

Cite this as: BMJ 2021;373:n1364

MINERVA

Refractory cheilitis and delayed growth in a child
These are the lips of a boy who presented with a two year history of angular stomatitis and chapping refractory to topical corticosteroid or emollient treatment.

His parents mentioned he was a picky eater and that growth was delayed (height and weight 5th centile for age). On examination, fissures and erythematous patches with oozing, yellowish crusts were present on both lips, and mildly eczematous changes were seen on the perianal skin.

Blood tests for suspected zinc deficiency showed plasma zinc levels of 10.27 μmol/L (normal range 13.77-18.36 μmol/L). After treatment with zinc gluconate (78 mg/day) for one month the chapping had resolved, and the boy subsequently gained height and weight.

Mild to moderate zinc deficiency affects at least one third of the global population. Although refractory cheilitis in children with delayed growth is a rare presentation, it warrants further investigation for zinc deficiency.

Slowing the progression of kidney disease
People with kidney disease have a better prognosis if they’re treated with drugs that inhibit the renin-angiotensin system than if they’re given calcium channel blockers, according to an analysis of a Swedish database (Am J Kidney Dis doi: 10.1053/j.ajkd.2020.10.006). The need for kidney replacement therapy was reduced by around 20% in those taking renin-angiotensin system inhibitors. However, no corresponding reductions in mortality or the incidence of cardiovascular events were noted.

Bariatric surgery 10 years on
Ten years after obesity surgery, 18 patients were interviewed about their experiences. Their accounts revealed two broad themes. One was optimistic and included thoughts about better health, a brighter future, and achieving weight regulation. The other was about continuing difficulties—with physical activity, helping their children avoid overweight and obesity, and self-criticism. Generally, participants expressed satisfaction with how their bariatric surgery had turned out (Surg Obesity Rel Dis doi: 10.1016/j.soard.2021.02.024).

AI sparks new dreams theory
Sigmund Freud thought that dreams represented the disguised fulfilment of a repressed wish. Other hypotheses about the function of dreams involve the consolidation of memories or the amelioration of the emotional consequences of unpleasant experiences. A new theory proposes that dreams are simply a random string of memories that helps the brain generate new ideas (Patterns doi:10.1016/j. pattern.2021.100244). The theory is inspired by studies in artificial intelligence in which randomised data assisted machines to learn and adapt.

Lying down and pseudo-anæmia
A supine posture redistributes plasma into the vascular space, leading to dilution of blood constituents. In an experimental study, 35 patients had blood taken for haemoglobin measurement after being recumbent for six hours and again after sitting upright for an hour (J Hosp Med doi:10.12788/jhm.3580). Ten of the 35 patients showed an increase in haemoglobin of 1.0 g/dL or more.

No need for a biopsy to confirm coeliac disease
Titres of IgA anti-transglutaminase greater than 10 times the upper limit of normal have such a high positive predictive value for coeliac disease that it’s unnecessary to confirm the diagnosis with a biopsy. That’s the conclusion from a study of 1417 patients, 431 of whom had transglutaminase titres above this