Stem cell transplants: why have outcomes improved?
This study found that a cohort of around 1100 patients who had allogeneic haematopoietic cell transplantation in 2013-17 fared significantly better than a similar cohort who had had a transplant 10 years earlier. Just over six months after the transplant (200 days), overall mortality had fallen (hazard ratio of 0.66) in the 2013-17 group. The fall in mortality was similar whether the donor was a sibling or unrelated, and in patients who underwent reduced intensity or total ablation of their bone marrow before the transplant. Complications also fell.

The results are cheering, although overall survival from stem cell transplantation remains around only 50% and disease relapse is still the main cause of death. The problem with a cohort study is that we don’t know why survival rates have improved; improved donor selection and transplant management are likely causes, but confounding factors such as transplanting less sick patients may also have contributed.

Low dose aspirin to prevent preterm delivery
Low dose aspirin (81 mg) given to nulliparous pregnant women from 6-13 weeks’ gestation until 36 weeks significantly reduced the risk of preterm birth, according to this trial in low and middle income countries. Preterm births (<37 weeks) occurred in 11.6% of women who took aspirin compared with 13.1% of those who took placebo. Aspirin cut the risk of perinatal mortality by 14% and early prematurity (<34 weeks) by 25%. The results of this large and well conducted study generally chime with previous studies. The “low cost and proven tolerability of aspirin in this population” suggests it can be safely adopted across a range of global sites, say the authors. The optimal dose and time to start aspirin are still not certain. And it’s not clear whether the findings translate to high income countries, where rates of prematurity and perinatal mortality are lower.

The new virus in town: how will it behave?
A cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China, just a month ago. With impressive speed, this report of the isolation and identification of a novel betacoronavirus (2019-nCoV) details the results of a race to trace and identify the likely organism in three original cases. 2019-nCoV is similar to some betacoronaviruses detected in bats, which may be the zoonotic source, possibly with an intermediate vector. It is also similar to, but distinct from, the two other novel coronaviruses that have emerged over the past 20 years, SARS-CoV (2003) and MERS-CoV (2012).

The authors admit their analysis implicates rather than proves the link between this virus and the Wuhan outbreak. A linked editorial comments that fear played a large part in the economic and social consequences of the SARS epidemic and that specific anti-coronavirus therapies are in development but not yet available. Strict infection control, prompt diagnosis, and quarantining helped to contain transmission of SARS and MERS and hopefully will help to contain this new virus.

Coronavirus: person to person spread confirmed
A key question is whether the 2019-nCoV can be transmitted from human to human. It would be reassuring if all the index cases had been infected after direct contact with animals. Unfortunately, this study of a family cluster of cases suggests that person to person transmission is already happening.

Five family members out of six who travelled to Wuhan had evidence of 2019-nCoV infection on their return to Shenzhen, which is more than 1000 km away. None had visited an animal market, but two of them had been in Wuhan hospital. Notably, an additional family member who didn’t travel with them was subsequently infected. All developed respiratory symptoms, fever, and/or diarrhoea.
What is the best method for managing early miscarriage?

Justin Chu, 1, 2 Pollyanna Hardy, 4 Leanne Beeson, 4 Arri Coomarasamy 3

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An early miscarriage is the loss of pregnancy at ≤13 weeks’ gestation. 1 It is a major life event and can have a potentially devastating psychological impact on the woman in addition to the physical effects such as bleeding and pain. 2 About one in four pregnancies, where a woman has missed a menstrual period and has a positive pregnancy test, ends in early miscarriage. 3 Nearly 125 000 early miscarriages occur annually in the UK, accounting for 50 000 hospital admissions. 4

Early miscarriage is usually diagnosed by pelvic ultrasound after a woman has experienced vaginal bleeding or abdominal pain. Women with a complete miscarriage, where expulsion of pregnancy tissue is complete, are managed conservatively without further intervention. Women with a missed or incomplete miscarriage (see box overleaf) may require further intervention.

Surgery under general anaesthesia used to be the standard treatment for miscarriage, 6 but a wider choice of management options is now available (figure). 3 Over the past two decades there has been a shift towards individualised care and shared decision making between clinician and patient. Up to 70% of women with miscarriage opted for expectant management, ie, waiting for spontaneous miscarriage, in a prospective cohort study (312 women). 7 Women may have preferences around how promptly they want the miscarriage managed, or they may have concerns about surgery and future fertility.

Uncertainty exists about the preferred option in a given situation and there is a lack of clarity about the most meaningful outcomes, particularly from a woman’s perspective.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE
At a large teaching hospital outpatient clinic, we asked 10 women who have had recurrent miscarriages what they felt were the biggest uncertainties surrounding how they had their miscarriages managed. Their answers revealed that patient choice regarding the management option selected for their miscarriages was what mattered most to these patients. As such, we ensured that patient choice was a central theme for this article.

WHAT YOU NEED TO KNOW
- Guidelines from the National Institute for Health and Care Excellence recommend expectant management, ie, waiting for spontaneous miscarriage, for 7–14 days after early miscarriage is diagnosed if there are no complications
- Medical management with misoprostol has comparable success rates to surgery but there is uncertainty about the appropriate dosing regimen, the route of administration, and the role of mifepristone
- Evidence is limited on outcomes such as women’s preferences, satisfaction, and subsequent fertility

Management options for miscarriage

Diagnosis of a miscarriage
- Missed miscarriage
- Incomplete miscarriage

Woman centred care

Expectant management
- Offered as first line management strategy
  - For 7–14 days as per NICE guidelines 1
  - Up to 8 weeks as per ACOG guidelines 14

Medical management
- Misoprostol alone (a prostaglandin analogue) administered vaginally, orally, sublingually or rectally, as a single dose or divided doses
  - Optional: Mifepristone (an anti-progesterone) given prior to misoprostol to potentiate its effects.

Surgical management
- Suction curettage under general anaesthesia
- Manual vacuum aspiration under local anaesthesia

Uncertainties surrounding:
- Regimen
- Dose
- Route of administration

Uncertainties surrounding:
- Duration of expectant management
- Best surgical option
- Best anaesthesia
Categories of early miscarriage

Missed miscarriage—pregnancy tissue is complete inside the uterus without fetal heart activity. The woman may have minimal symptoms.

Incomplete miscarriage—ultrasound imaging shows that some but not all of the pregnancy tissue has passed. Women have usually had pain and bleeding.

What is the evidence of uncertainty?

Risks and benefits of different options

We found three Cochrane reviews comparing two or more management approaches for early miscarriage. Overall, surgical management has higher rates of miscarriage resolution in comparison with medical and expectant management. The relative success rates, defined as complete miscarriage, are 58% with expectant management, 81% with medical management, and 96% with surgery, as per the most recent Cochrane review (24 studies, 5577 women). We found no important difference in subsequent fertility, women’s satisfaction, or psychological wellbeing with medical, surgical, or expectant management, although the evidence is limited and of very low quality. A network meta-analysis concluded that medical treatments for first trimester miscarriage have similar effectiveness to surgery in achieving complete evacuation of the uterus and severity of side effects (nausea, vomiting, and diarrhoea).

Systematic reviews and randomised controlled trials have focused on complete emptying of the uterus and the lack of need for unplanned surgery as definitions of success. Many women want timely resolution of miscarriage. The definition and time interval used to assess complete emptying of the uterus varies across studies. Importantly, the longer the time interval used, the higher the chance of success of both expectant and medical management. Considerable variation exists in the reporting of primary and secondary outcomes in miscarriage studies along with the measures used to assess them.

Moderate to high quality evidence shows that expectant management has a higher risk of incomplete miscarriage at two weeks and 6-8 weeks, with a higher need for unplanned surgical evacuation, more bleeding, and higher blood transfusion rates compared with surgery, as per a Cochrane review (seven randomised controlled trials, 1521 women). The costs are lower for expectant management. A subsequent randomised controlled trial (360 participants), however, reported no statistically significant difference in complete uterine evacuation at six weeks.

Expectant management

There is uncertainty regarding the length of time that women should try expectant management. Guidance from the National Institute for Health and Care Excellence (NICE) recommends expectant management for 7-14 days once miscarriage is confirmed on ultrasound. An exception is women with excessive bleeding in whom emergency surgery may be needed. Guidance from the American College of Obstetricians and Gynecologists (ACOG) suggests up to eight weeks of expectant management to achieve approximately an 80% success rate. If expectant management is unsuccessful, the woman is offered medical or surgical management.

Medical management

The Cochrane review found no evidence of a difference in the effectiveness of different misoprostol regimens in the completion of miscarriage. There is uncertainty around the optimal route of administration (vaginal or oral), and the additional value of mifepristone. The PreFaiR trial (300 participants) found a higher likelihood of expulsion of the gestational sac when mifepristone (200 mg orally) was used before misoprostol administration (800 µg vaginally) compared with misoprostol alone. NICE and ACOG guidance currently recommend an 800 µg dose of misoprostol given vaginally for missed miscarriage with a repeat dose of 600 or 800 µg for incomplete miscarriage. Following publication of the PreFaiR trial, ACOG also advises the administration of 200 mg oral mifepristone, if available, 24 hours before misoprostol.

Surgical management

Surgical uterine evacuation methods include suction curettage performed under general anaesthetic or a manual vacuum aspiration performed under local anaesthetic in an outpatient setting. Trials have compared costs, safety, and effectiveness of both surgical approaches but data to draw firm conclusions are lacking and either approach appears to be equally effective in achieving complete uterine evacuation. Complications and need for further surgery are rare, although these can be serious (bleeding, infection, and uterine perforation).
Is ongoing research likely to provide relevant evidence?

We searched the World Health Organization International Clinical Trials Registry Platform and the clinicaltrials.gov website using the term “miscarriage management” and identified five ongoing trials.\textsuperscript{20,24} Three of these trials investigate different regimens and routes of administration used in medical management. We are leading one of these trials (the MIFEMISO trial with a target of 710 participants; ISRCTN: 17405024) in the UK. One trial investigates the time to next pregnancy after medical versus surgical management. The last trial compares the use of topical lignocaine with placebo gel in manual vacuum aspiration.

We expect these trials will add to the evidence base to help women and clinicians choose the most suitable management option.

What should we do in the light of the uncertainty?

For women with abdominal pain or vaginal bleeding in early pregnancy, NICE guidance recommends prompt referral to the local early pregnancy clinic for ultrasound assessment of the pregnancy.\textsuperscript{1}

The choice of treatment depends on individual preferences as well as the clinical situation. Emergency surgery with suction curettage remains the treatment of choice in women who have excessive bleeding or who are haemodynamically unstable. Expectant management is advised for 7-14 days as per NICE guidance, except if the woman is bleeding or is at an increased risk of haemorrhage, has previously had a traumatic experience in early pregnancy, or if there is evidence of infection.\textsuperscript{1}

Recognise that this can be a difficult time for the woman and be sensitive to her needs and preferences. Provide accurate and consistent information regarding what each management option entails and the duration of each option to resolve the early miscarriage.

Most women will have a preference as to how they would like their miscarriage to be managed.\textsuperscript{1} For some women, the process of experiencing pain and bleeding is important in acknowledging their miscarriage and beginning the grieving process. Some women may have fears of medical or surgical intervention and therefore may wish to pursue expectant management. Others will wish to have an expedited process but want to avoid surgery, and therefore medical management could be the right option. Conversely, some women will want to manage their miscarriage as quickly as possible and would prefer surgery.\textsuperscript{1} The patient should be fully informed about the risks of surgery and general anaesthesia.

Respect a woman’s decision and explain the selected management processes clearly, offering support where required. You may wish to signpost the woman and her family to charities such as the Miscarriage Association (box “Information resources for patients”). Women undergoing early miscarriage may require an extended period to consider their choice of management, and may benefit from written information.

Competing interests: See bmj.com.
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Find the full version with references at http://dx.doi.org/10.1136/bmj.l643

WHAT PATIENTS NEED TO KNOW

- Miscarriages affect roughly one in every four pregnancies
- Most women will have a healthy pregnancy after a miscarriage
- Your doctor will be able to discuss your management options with you, including the risks and benefits of each option
- Broadly, you have three options if you have been diagnosed with a miscarriage:
  1. Expectant management—waiting for spontaneous miscarriage
  2. Medical management—using tablets to expedite the miscarriage
  3. Surgical management—undergoing a short surgical procedure, which can be done under local or general anaesthetic
- Current guidelines recommend expectant management for anywhere between 1 and 8 weeks after early miscarriage is diagnosed if there are no associated complications
- Surgery leads to more prompt resolution of miscarriage compared with other approaches, but it can have rare and sometimes serious risks. Expectant and medical management have comparable rates of complete miscarriage though these may take longer, and may sometimes require surgery later
- Discuss your preferences with your doctor to decide on the most suitable option

INFORMATION RESOURCES FOR PATIENTS

NHS: https://www.nhs.uk/conditions/miscarriage
Overview, symptoms, causes, diagnosis, what happens, aftercare, and prevention information
NICE: https://www.nice.org.uk/guidance/cg154/ifp/chapter/About-this-information
Information regarding miscarriage and its management
Miscarriage Association: https://www.miscarriageassociation.org.uk/
Support and information for anyone affected by the loss of a baby in pregnancy

EDUCATION INTO PRACTICE

- Based on reading this article, how would you discuss the management options for early miscarriage with women in your care?
- What options are available for miscarriage management at your local early pregnancy clinic? And what are the processes that are involved in each management option?
Duchenne muscular dystrophy

Hannah Fox, Luke Millington, Indu Mahabeer, Henriette van Ruiten

Duchenne muscular dystrophy (DMD) is a progressive and disabling neuromuscular condition that is often diagnosed late. In the UK the mean age of diagnosis has remained fairly static over the past 30 years, currently around 4.3 years of age. On average it takes 1.6 years from first parental concern to diagnosis of DMD, by which time muscle function has already declined (box 1, bmj.com). Delayed diagnosis of DMD can be devastating for patients and their families. Outcomes for people with DMD can be improved with optimum care at the earliest opportunity, and patients are now living into their fourth decades. Early diagnosis also enables parents to make informed decisions about family planning and can provide access to innovative treatments and clinical trials. International guidelines for diagnosis and management of DMD have been established by the DMD Care Considerations Working Group.

DMD is rare, with an estimated 2500 affected patients in the UK. Clinicians in primary care may never have seen patients with this condition, but are key to identifying DMD early and supporting patients and their families.

WHAT YOU NEED TO KNOW

- Consider Duchenne muscular dystrophy in boys with delayed motor milestones, positive Gowers' sign, abnormal gait, muscle pains, calf hypertrophy, unexplained elevated liver enzymes, learning difficulties, behavioural problems, or speech and language delay.
- Test for creatine kinase levels if you suspect any neuromuscular condition. Refer children with raised creatine kinase promptly to a neuromuscular specialist.
- Early diagnosis means early access to treatment, improved outcomes, and better informed family planning.
- Early genetic diagnosis is important, as it can enable entry into appropriate clinical trials.
- Where patients have breathlessness, palpitations and arrhythmias, morning headaches, and repeated chest infections or weight loss, suspect deterioration and refer for prompt specialist review.

What is DMD?

DMD is an X-linked recessive genetic disorder that affects one in 3600-6000 male live births. DMD is caused by mutations in the dystrophin gene, resulting in a severe reduction or absence of functional dystrophin protein in muscle, which is crucial for maintaining muscle fibre strength and stability. Lack of functional dystrophin results in degeneration of muscle fibres.

Becker muscular dystrophy is also caused by dystrophin gene mutations. Typically it presents later and progresses more slowly.

When should I suspect DMD?

Warning signs for DMD are listed in box 2. Muscle weakness typically becomes evident at age 2 to 3. Children develop a progressive proximal to distal pattern of muscle weakness, starting with the lower limbs. There might be a delay in the development of motor milestones, such as walking, resulting in the child falling behind their peers developmentally. Other signs include difficulty with jumping, running, climbing steps, and rising from the floor. There may be a history of muscle pain, clumsiness, and frequent falls. Affected boys may display toe walking or a waddling gait. On examination the child may have poor head control, hypotonia, calf hypertrophy, or may demonstrate Gowers' sign (fig 1), a pattern of difficulty rising from the floor indicating proximal muscle weakness. A family history of DMD should raise suspicion.

Children with DMD have a high prevalence of learning and behavioural problems. This can make assessment more difficult, resulting in further diagnostic delay. Speech delay and failure to thrive may also coexist.

DMD is always associated with high levels of creatine kinase. Other enzymes, such as lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase, can also be raised reflecting muscle damage (not liver damage). DMD should therefore be considered if a patient has unexplained raised levels in liver function tests.

The Royal College of Paediatric and Child Health e-learning module and the MUSCLE mnemonic in fig 2 can help primary care professionals assess motor skills in children.
How is it diagnosed?

Diagnosis should be made early, ideally by age 2 to 3, when symptoms start to become evident. A simple, cheap, and readily available blood test, creatine kinase, has a high sensitivity for muscular dystrophy and results are quickly available, prompting referral to neuromuscular specialists for further investigation. If DMD is suspected, creatine kinase levels should be urgently checked. A markedly raised creatine kinase level warrants an urgent referral to a neuromuscular specialist. A mildly raised creatine kinase level of 1–2 times the normal range should be confirmed through a repeated test and followed up.

Although a normal creatine kinase result excludes DMD, not all neuromuscular conditions are associated with elevated creatine kinase. Therefore, if you suspect a muscle problem but creatine kinase levels are within the normal range, a referral to a neuromuscular specialist may still be warranted.

The diagnosis of DMD is confirmed by genetic testing. Approximately 70% of DMD cases are caused by a single or multi-exon deletion or duplication detectable by multiplex ligation dependent probe amplification (MLPA). Full sequencing of the dystrophin gene can detect small genetic changes, such as point mutations, when DMD is still suspected but MLPA has failed to identify an abnormality.

We suggest explaining to parents that a blood test can screen for certain muscle problems, keeping a broad mind rather than causing undue concern early in investigation.

What are the risks for female carriers of the DMD gene mutation?

Being an X-linked condition, DMD predominantly affects boys and men. Female relatives of patients with DMD should be offered genetic testing for carrier status. A small number of female carriers can develop muscle symptoms, such as pain, cramps, or weakness, and learning or behavioural problems. Female carriers are also at risk of heart problems, and regular cardiovascular monitoring is recommended. Women and girls of reproductive age who are carriers should be offered early counselling for family planning, including discussion about possible pre-implantation or prenatal genetic testing. Non-carrier mothers of sons with DMD still have a slightly higher risk of having another affected child compared with the general population and therefore should be offered counselling.

![Diagram to show Gowers’ sign, a pattern of walking arms up the thighs to stand up from a squatting position, indicative of proximal muscle weakness](image)

**Fig 1**

### Box 2 Warning signs for diagnosis of DMD

<table>
<thead>
<tr>
<th>Delayed motor developmental milestones</th>
<th>Abnormal gait</th>
<th>Speech delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Poor head control</td>
<td>• Waddling gait</td>
<td>• No words spoken in first 18 months</td>
</tr>
<tr>
<td>• Not walking independently by 18 months</td>
<td>• Tiptoe gait</td>
<td>• Unable to speak sentences by age 3</td>
</tr>
<tr>
<td>• Not running by age 3</td>
<td>• Frequent falls</td>
<td>• Any input from speech services (SALT)</td>
</tr>
<tr>
<td>• Struggling to hop, climb stairs, or get up from the floor in school age children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Frequent trips or falls</td>
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</tbody>
</table>

Unable to get up from the floor without using support from arms to push up (Gowers’ sign)

Muscle pain or cramps or calf hypertrophy

Episodes of myoglobinuria (cola-coloured urine)

Unexplained raised levels of lactate dehydrogenase, alanine aminotransferase, or aspartate aminotransferase

Learning difficulties and behavioural issues

Speech and language delay

Autistic spectrum disorder

![MUSCLE mnemonic, which demonstrates key features of DMD and the importance of early testing of creatine kinase](image)

**Fig 2**
What are the key elements of successful management?

Primary care

Every person diagnosed with DMD should be referred to a neuromuscular specialist for regular follow-up. However, primary care clinicians have an important role in their overall care.1 Care of patients with DMD involves optimising quality of life and proactively anticipating and treating complications as they arise. Recommendations for DMD based on international consensus were published in 2010 and updated in 2018.5,7 A family guide to help patients and carers to understand the condition and required management is also available.23

Corticosteroids are the mainstay of treatment. Moderate quality evidence shows that corticosteroids (0.75 mg/kg/day of prednisolone or 0.9 mg/kg/day of deflazacort on daily or intermittent regimens) improve muscle function and help prolong ambulation, delay the development of respiratory complications, postpone or avoid orthopaedic complications, and might delay cardiac complications.24‑28 Corticosteroid treatment is associated with notable side effects, however, including weight gain, cushingoid appearance, behavioural changes, delayed puberty, reduced growth, increased risk of fractures (including vertebral fractures), cataracts, and hirsutism.25‑27 An adjusted lower dose may be required for patients who develop unacceptable side effects on the recommended dose.

Multidisciplinary teams

Optimal care in DMD is best achieved by a multidisciplinary team, normally led by a neuromuscular specialist. Disease progression should be monitored every six months.5,29 A team of physiotherapists, orthotists, orthopaedic surgeons, and occupational therapists monitor muscle function, aiming to minimise contractures and deformities. Community paediatricians, community physiotherapists, speech and language therapists, and dietitians are also involved.29 Annual cardiac surveillance is essential from diagnosis onwards to screen for early signs of cardiac failure and promptly initiate and monitor cardiac treatment. Additional specialists, such as respiratory physicians, are involved as disease progresses. Psychological support, sometimes supplemented by mental health professionals, is integral to holistic care of patients and their families.

Box 3 | The role of primary care clinicians in management of DMD

Respiratory
- Ensure appropriate vaccination, such as the pneumococcal vaccine and yearly influenza vaccine.
- Avoid live vaccines for patients on steroids
- Chest infections can precipitate respiratory failure; prompt antibiotic treatment should be given if there are concerns about infection
- Look out for symptoms of nocturnal hypoventilation (table 1, see bmj.com), which should prompt referral to a respiratory specialist

Endocrine
- For patients on corticosteroids, reinforce the risk of adrenal insufficiency and of not stopping steroids suddenly. If unable to take steroids orally, or if unwell, consider giving a stress dose of steroids (intravenous or intramuscular hydrocortisone). Patients should have a steroid information card
- Monitor side effects of corticosteroids, such as delayed puberty, hypertension, diabetes mellitus, skin changes, infections

Gastrointestinal
- Monitor weight and nutrition; refer to dietitians if appropriate
- Consider gastroprotection for symptomatic patients on corticosteroids

Cardiac
- Encourage cardiovascular health and fitness, screen for cardiovascular risk factors such as hypertension (especially for patients on corticosteroids)

General
- Liaise with specialists regarding referral to appropriate therapy services
- Monitor for red flags which might indicate clinical deterioration and refer appropriately (table 1, bmj.com)
- Provide access to psychosocial care for patients and their families
- Signpost families to advocacy groups and sources of support

Box 4 | Emerging treatments for DMD

Ataluren (also called Translarna), has now been approved by the National Institute for Health and Care Excellence (NICE) as a treatment for ambulatory patients with DMD in the UK under a management access agreement. Ataluren is a mutation-specific therapy, suitable for approximately 10‑15% of the DMD population. Other therapeutic approaches currently being evaluated in clinical trials include mutation-specific strategies to correct the underlying genetic cause of the disease (such as exon skipping), gene therapy, and non-mutation-dependent strategies including repurposing of existing drugs (tamoxifen, idebenone) and therapies to improve overall muscle function (givinostat, anti-myostatin). Innovative steroids (vamorolone) and NF-kB inhibitors (edasalonexent) are being investigated as potential alternatives to corticosteroids, aiming to maintain their efficacy while reducing or avoiding the side effects associated with traditional corticosteroids.

Emerging treatments

Management of DMD has changed substantially over the past five years as new potential therapeutic approaches have been developed (box 4). This rapid development of new therapies means that many clinical trials are currently running (www.clinicaltrials.gov, dmdhub.org). Early diagnosis and timely access to potential disease modifying therapies offers new hope for this group of patients.
What are the key complications and their recommended management?2-5

Cardiac
Absence of dystrophin in the heart muscle is associated with the development of a dilated cardiomyopathy in most patients. This presents with signs of heart failure or arrhythmias. All patients need annual cardiac surveillance by specialists, which may involve ultrasound echocardiograms, cardiac magnetic resonance imaging, and 24 hour holter monitoring. Many patients take cardioprotective medications, such as ACE inhibitors and β-blockers.32 33

Gastrointestinal
Consultation with a dietitian is important to encourage a balanced diet and help prevent obesity (commonly caused by corticosteroid treatment and limited mobility) or undernutrition (common in later stages of the disease). Speech and language therapy teams may help patients manage dysphagia. Gastroenterologists can manage gastric motility problems and may consider placement of a gastrostomy tube for undernutrition, dysphagia, and aspiration at a later stage. Gastroprotective therapy should be given in the presence of gastrointestinal symptoms.

Orthopaedic
Musculoskeletal problems require a multidisciplinary approach, including physiotherapy, occupational therapy, rehabilitation specialists, orthoses, or surgery.17 Patients need monitoring for the development of joint contractures and scoliosis. Widespread treatment with corticosteroids has reduced the risk of developing severe scoliosis and therefore reduced the number of patients requiring surgical correction.40

Endocrine and metabolic
Long term use of corticosteroids increases the risk of osteoporosis. Patients with DMD commonly develop pathological low trauma vertebral or long bone fractures.37 38 These can be asymptomatic. Annual dual energy x ray absorptiometry scans and lateral spine radiographs are recommended for surveillance every 1-2 years in patients treated with corticosteroids. Vitamin D supplementation and adequate calcium intake are recommended. Intravenous bisphosphonate is considered first line in patients with vertebral and long bone fractures because of DMD associated osteoporosis.3 Input from an endocrinologist may also be required to manage side effects associated with corticosteroid use, such as delayed puberty, glucose intolerance, and obesity.

Respiratory
Patients with DMD develop respiratory failure and are at risk of sudden respiratory complications. Serial monitoring of lung function and sleep studies are important in detecting respiratory impairment, more likely to occur in the later non-ambulant phase. Survival can be prolonged by lung volume recruitment, assisted coughing, nocturnal assisted ventilation, and continuous non-invasive ventilation.4 39

Emergencies
Adrenal crisis—a potentially life threatening complication of chronic corticosteroid treatment. It is important that families are aware of the risk, and know never to stop corticosteroids suddenly or omit doses. They should also know when to give a “stress” dose.

Fat embolism—a life threatening complication of fractures that can present with shortness of breath, tachycardia, or altered consciousness, and requires emergency care.

Anaesthetic risk—aanaesthetic risk is increased for patients with DMD who need surgery. Depolarising muscle relaxants and inhaled anaesthetics should be avoided as they can lead to life threatening hyperkalaemia and rhabdomyolysis.

Additional educational resources for health professionals
Royal College of Paediatrics and Child Health https://www.rcpch.ac.uk/resources/recognising-neuromuscular-disorders-elearning
A free e-learning module that suggests a practical approach for the non-specialist to recognise children with neuromuscular disorders early. Accessible through RCPCH Compass (self-registration required, free to access)


Royal College of General Practitioners http://elearning.rgps.org.uk/course/info.php?popup=0&id=183
A RCGP e-learning module focusing on management of DMD in primary care. Free to those who are members of the RCGP.

Worth one accredited continued professional development point
Child Muscle Weakness https://childmuscleweakness.org/
A website targeted at health professionals to help identify children with neuromuscular disorders from “signs” and “clinical evaluation”

Detailed management guidelines for the diagnosis, investigation, and management of DMD. 5-7

These are also available free through the Treat MND network: http://www.treat-nmd.eu/care/dmd/diagnosis-management-DMD/

Paediatric Musculoskeletal Matters International http://www.pmmonline.org.doctor
A website to help health professionals better investigate and manage children with musculoskeletal problems

How this article was created
This article was created with the aim of providing a guide to help the non-specialist diagnose DMD early and manage patients’ ongoing care. A search of “Duchenne muscular dystrophy” from the Cochrane Collaboration in February 2019 yielded seven Cochrane reviews, of which five were included as they were relevant to the scope of this article. Diagnosis and management is written with reference to the international consensus DMD guidelines written by the DMD Care Considerations Working Group, updated in 2018.5 7 Evidence was also sought by signposting from experts in the care of DMD and from a personal archive of references.

How patients were involved in the creation of this article
We asked Luke, a patient with DMD, to review this article and to contribute his story. He has put his own thoughts down for the Patient’s perspective (bmj.com). We also asked the family of another child with DMD to share their experience of delayed diagnosis (box 1, see bmj.com)

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.l7012
An 18 month old girl presented to the children’s emergency department with five days of fever (up to 40°C) associated with painful swelling in the left side of her neck. She had no accompanying respiratory symptoms. On examination, she had tender cervical lymph node enlargement with the largest node measuring 3×3 cm at the left anterior cervical chain. In addition, there was redness and oedema over the previously healed site of her BCG vaccine inoculation on the left upper arm (fig 1) (she had received this vaccine at birth, as per the local vaccination schedule). She had no conjunctival injection, mucosal erythema, oedema over the extremities, or other rashes. Systemic examination was unremarkable.

Results of initial investigations are shown in the table.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White cell count</td>
<td>15×10⁹/L</td>
<td>5.00-15.00×10⁹/L</td>
</tr>
<tr>
<td>Absolute neutrophil count</td>
<td>8×10⁹/L</td>
<td>1.50-8.00×10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>402×10⁹/L</td>
<td>150-450×10⁹/L</td>
</tr>
<tr>
<td>Creatine protein</td>
<td>76 mg/L</td>
<td>0-10 mg/L</td>
</tr>
<tr>
<td>Erythrocyte sedimentation</td>
<td>97 mm/h</td>
<td>3-9 mm/h</td>
</tr>
</tbody>
</table>

Urinalysis was normal. Two dimensional echocardiogram showed mild left coronary artery dilatation.

What is the most likely diagnosis?

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Parental consent obtained.

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LEARNING POINT

Consider Kawasaki disease in children with high fever and BCG-itis when there is no obvious source of infection, especially if they are from countries where BCG vaccination is part of the immunisation schedule.

Kawasaki disease is a medium-vessel vasculitis of unknown aetiology that affects children; without treatment it can cause coronary complications.

Diagnostic criteria for classic Kawasaki disease are fever for five or more days with at least four of the following features: bilateral non-suppurative conjunctivitis, oral mucosal injection, polymorphous rash, cervical lymphadenopathy, and indurative oedema of the extremities followed by desquamation.

Consider IKD if these criteria are not fully met but one or more of the following features are present: BCG-itis, raised inflammatory markers, leucocytosis, thrombocytosis, hypoalbuminaemia, anaemia for age, elevated transferase level, and/or pyuria.

Prompt treatment with intravenous immunoglobulin (IVIG) reduces the risk of coronary artery involvement.


discovery

SPOT DIAGNOSIS

Oedema over an inoculation site

New onset erythema and oedema on the child’s left upper arm

ENDGAMES

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
A herpes type 1 skin infection in a newborn

This is a localised umbilical vesicular bullous eruption that evolved over four days in a newborn baby. The baby was 8 days old, afebrile with no neurological symptoms, and was feeding normally. Viral culture of the fluid was positive for herpes simplex virus (HSV)-1. The baby’s mother had a negative history for HSV, which is not unusual because most neonatal HSV infections are acquired at birth from a mother with an asymptomatic primary genital HSV infection. HSV skin infections classically present as a cluster of vesicles, but in neonates HSV may present as a bullous eruption. *Staphylococcus aureus* (bullous impetigo) also presents as a bullous eruption. Without treatment, both could disseminate and become serious: bullous impetigo by cutaneous dissemination, and HSV by spread to uninfected skin and internal organs, including the brain.

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Parental consent obtained. Cite this as: *BMJ* 2020;368:m17076

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

Monitoring flu by Fitbit

A few years ago there was hope that internet search data and social media outlets could be used to monitor trends in infectious diseases. But they proved to be unreliable indicators because it was impossible to know whether activity was caused by people trying to find out about their own symptoms, or if it was just a reflection of heightened awareness. Data from wearable devices may get around the problem by using information about heart rate and sleep. Retrospectively evaluated against rates of flu-like illness reported by the US Centers for Disease Control and Prevention, anonymised Fitbit data showed the potential to improve surveillance of flu (*Lancet Digital Health* doi:10.1016/S2589-7500(19)30222-5).

Fat tongue

Using a combination of sleep monitoring, magnetic resonance imaging of the upper airway, and an intervention to promote weight loss, investigators explored why obesity is such a strong risk factor for obstructive sleep apnoea. It seems that what matters most is the fat volume of the tongue. People who succeeded in losing weight experienced a reduction in the volume of several soft tissues in the upper airway and a lessening in the severity of sleep apnoea. Reduction in tongue fat was the strongest correlate of improvement—a finding that remained statistically significant even after controlling for weight loss (*Am J Respir Crit Care Med* doi:10.1164/rcrm.201903-0692OC).

Molecular mechanisms of touch

Genetic investigation of patients with profoundly reduced proprioception and vibration sensation led to the identification of two genes, PIEZO 1 and 2, that encode ion channels able to convert mechanical forces into electrical impulses at sensory nerve endings. Cryo-electron microscopy has just shown what this channel looks like and how it might work. Three Piezo proteins form the spiral arms of a propeller shaped structure that straddles the plasma membrane. Mechanical strain in the membrane straightens the arms and opens a central pore (https://www.nature.com/articles/d41586-019-03955-w).

Overdose with migraine treatments

Although migraine is common, deliberate overdose with drugs used to treat acute attacks—triptans and ergotamine—is unusual according to a review of nationwide data from the US. Risk of serious harm was low with only six deaths among 1489 cases recorded over five years (*Neurology* doi:10.1212/WNL.0000000000008685). All deaths occurred in people who had taken other drugs too. Characteristic features of triptan toxicity were hypertension, tachycardia, and drowsiness, while the main toxic effects of ergotamine were nausea, vomiting, abdominal pain, and vertigo.

Microbiota transplantation for irritable bowel syndrome

The gut microbiota of patients with irritable bowel syndrome differs from that of healthy people, which provides a rationale for a trial of faecal transplantation. Patients were randomly allocated either to faecal transplants from a donor or to placebo (their own faeces) administered via an endoscope into the distal duodenum. At one and three months after the transplant, more than three quarters of patients who received donor material showed a substantial improvement in symptoms and quality of life (*Gut* doi:10.1136/gutjnl-2019-319630). Only a quarter of patients in the placebo group improved. Cite this as: *BMJ* 2020;368:m260