**The false promise of regenerative medicine**

Over nearly two decades now, I’ve followed the progress of “regenerative medicine”—mostly stem-cell research—through phase 1 studies, most of them featured in the *Lancet*. The yield has been spectacularly low. And now comes a *Lancet* commissioned article beginning: “In this Commission, we argue that a combination of poor quality science, unclear funding models, unrealistic hopes, and unscrupulous private clinics threatens regenerative medicine’s social licence to operate.” To put it more bluntly, many people are beginning to think it is all rubbish, while others bankrupt themselves pursuing false hope. This article does not pull its punches: “…the number of poorly regulated clinics has grown; clinics that appeal to desperate patients and their families, who, in the absence of reliable clinical knowledge from trials, cannot be adequately informed to assess the risks and benefits…. The same environment is also permissive of one-off compassionate applications and poorly regulated trials.”

The article covers the full history of the subject and ends with robust recommendations for better science. Here for once is a great example of the *Lancet* living up to its long history as a radical and incisive presence in British medicine.

*Obinutuzumab*

Obinutuzumab may be a funny name, but anyone reading this paper will realise that follicular lymphoma is not a funny disease. Survival in this trial comparing obinutuzumab with rituximab was over 90% over a median of three years, but these years of augmented chemotherapy sound decidedly unpleasant. “Adverse events of grade 3 to 5 were more frequent in the obinutuzumab group than in the rituximab group (74.6% v 67.8%), as were serious adverse events (46.1% v 39.9).” I think this sentence is the one that patients need to know. The rest is an academic debate about the meaning of “progression-free survival,” which was slightly better with obinutuzumab. Yet if I got follicular lymphoma, I would only be interested in overall survival and quality of life—and for the latter rituximab is slightly superior.

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**PROs for happiness**

In reporting the above article, I gave you my individual patient preferences. These are not quite the same as patient reported outcomes (PROs in the USA, PROMs in the UK—the M standing for “measures”), the subject of a Perspective piece in this week’s *NEJM*. What a patient is asked to report might not be the same as what is most important to the patient. For example, the article states that “PRO collection has proliferated in oncology, where it has been linked to improved symptom management, enhanced quality of life, and longer survival.” That is not because of PRO collection in itself: it is because humane oncologists enter a dialogue with their patients in relation to their reported symptoms and the goals of treatment, and modify treatment accordingly. In a randomised trial, however, PROs can be collected by the armful, but scientific rigour demands that the study protocol should be followed inflexibly. But I digress. This piece is about improving clinical practice and patient care generally. Read it thoughtfully and think about how you could make PROs a force for good in your own practice.

Ann Intern Med doi:10.7326/M16-2726

http://meessi-ahf-risk.score.calculator-semes.portalsemes.org/
Which pain medications are effective for sciatica (radicular leg pain)?

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Sciatica is commonly seen in primary care. Its prevalence in the general population varies between 3% and 14%, depending on the definition used.1 The prognosis of acute sciatica is generally favourable: data from a prospective study of 183 patients with a median disease duration of 16 days show that in approximately one third of patients, symptoms improve greatly (ie, measured on a 4 point scale, 1–worsened, 2–remained unchanged, 3–improved, and 4–improved greatly) within two weeks, and about three quarters of patients reported improvement within 12 weeks.2 Nevertheless, in another study of 172 patients, 30% continued to report persistent and disabling symptoms after a year.3

Sciatica is a symptom rather than a specific diagnosis4 and is used broadly to refer to pain that radiates along the path of the sciatic nerve.4 The commonest cause of sciatica is impingement of lumbosacral nerve roots, as they emerge from the spinal canal, by a herniated intervertebral disc. Other causes of impingement include spondylolisthesis and spinal tumours or cysts (figure).5 For this reason, symptoms of sciatica often co-exist with low back pain, but disturbances along the course of the sciatic nerve can also arise from locations other than the lower back (ie, due to piriformis syndrome, diabetic radiculopathy, and hip fracture or dislocation).6

Patients with sciatica are more disabled and consume more health resources, including medication, than those with non-specific low back pain.6 There is no reference standard to classify radicular leg pain, however it seems reasonable to diagnose a patient with radicular leg pain if they report pain from the low back radiating down below the knee in one leg. Patients will often have a positive result on one or more neurological tests, indicating nerve root tension or neurological deficit.6 Box 1 shows key signs and symptoms commonly associated with radicular leg pain which can be used to distinguish it from non-specific low back pain. This is based on expert opinion.7 One of the first steps in managing a patient who presents with radicular leg pain is prescription of analgesia.6 There is uncertainty, however, about which pain medications are the most effective.

What is the evidence of the uncertainty?

Although most pain medications used for radicular leg pain in clinical practice have been investigated in randomised controlled trials, considerable uncertainty exists because of the low to moderate quality of most trials and the difficulty in comparing trials that differ in terms of population, intervention, comparator, outcomes, and study design.

This section and table 1 (see bmj.com) summarises evidence on the efficacy of each class of drugs. The emphasis is on evidence generated from randomised placebo controlled trials, including only patients with radicular leg pain and focusing on clinical endpoints. Where available, we report results from systematic reviews with meta-analysis, otherwise single trials are used to summarise the evidence.

Acetaminophen versus placebo

No randomised placebo controlled trials investigating the efficacy of acetaminophen for sciatica were identified.

NSAIDs versus placebo

A 2016 systematic review8 pooling data from three trials found that NSAIDs are no more effective than placebo in reducing pain or disability, but did find a statistically significant improvement in global improvement associated with non-steroidal anti-inflammatory drugs (NSAIDs) compared with placebo at short term follow-up (up to three weeks; n=753, risk ratio=1.14; 95% confidence interval 1.03 to 1.27). It should be noted, however, that the overall

What you need to know

- The most effective medication to treat patients with sciatica or radicular leg pain is unclear.
- In approximately one third of patients, symptoms improve within two weeks; in three quarters of patients, symptoms improve within 12 weeks, but about a third of patients have persistent and disabling symptoms after a year.3
- Medications used for the treatment of sciatica can have considerable side effects.

Box 1 | Key signs and symptoms that distinguish radicular leg pain from lower back pain

- Unilateral leg pain, which is worse than any associated back pain
- Pain radiating below the knee (and can radiate into the foot and toes)
- Numbness or pins and needles in a dermatomal distribution
- Positive result on a straight leg raise test (ie, radiating pain between 30 and 70 degrees of hip flexion)
- Weakness or reflex changes, or both, in a myotomal distribution
quality of evidence using the GRADE approach for these outcomes varies from low to very low.

Evidence from four trials suggests an increased risk of adverse events (n=967, risk ratio=1.40; 95% confidence interval 1.02 to 1.93) when using NSAIDs compared with placebo. Most adverse events identified in the 2016 systematic review were reported to be mild and consisted of headache, dizziness, and gastrointestinal problems, such as nausea, dyspepsia, epigastric burning, and abdominal pain.

Systemic corticosteroids versus placebo
In a 2012 systematic review from our group, a meta-analysis of two trials shows moderate quality evidence favouring corticosteroids over placebo in reducing pain (n=138, weighted mean difference on 0 to 100 scale=−12.2; 95% confidence interval −20.9 to −3.4) at short term follow-up (ie, more than two weeks and up to three months). In two subsequent trials the results were less favourable. One of these trials with moderate risk of bias (n=58; 8 mg of intravenous dexamethasone) reported pain relief at 24 hours (mean difference on a 0 to 10 scale=−1.86; 95% confidence interval −0.31 to −3.42) but not at six weeks. Another large trial with low risk of bias (n=269; 15 days of a reducing dose of oral prednisone), however, showed a small reduction in disability (without concomitant improvement in pain) in favour of corticosteroids at three weeks (mean difference on a 0 to 100 scale=−6.4; 95% confidence interval −10.9 to −1.9) and at one year (mean difference=−7.4; 95% confidence interval −12.5 to −2.2).

Evidence from the 2012 systematic review and the largest subsequent trial shows that adverse events, such as insomnia and nervousness, were more common in the corticosteroid group compared with the placebo group.

Benzodiazepines versus placebo
One small trial with low risk of bias (n=60) investigating the efficacy of benzodiazepines compared with placebo was identified and found no difference between groups for disability at one week and one year follow-up (table 1). The drug treatment was even associated with the lower likelihood of experiencing ≥50% improvement in pain at one week (risk ratio=0.5; 95% confidence interval 0.3 to 0.8) and a longer hospital stay (benzodiazepine group, median=10 days versus placebo, median=8 days; P=0.008) compared with placebo. Adverse events were not assessed in this trial.

Anticonvulsants versus placebo
We identified four trials with moderate to low risk of bias testing anticonvulsants (gabapentin, pregabalin, and topiramate) against placebo in patients with chronic or mixed duration of symptoms. In the earliest trial (n=50) use of gabapentin was associated with a statistically significant reduction in pain (mean difference on a 0 to 100 scale=−26.6; 95% confidence interval −38.3 to −14.9) at two month follow-up, but subsequent trials, including a...
crossover trial\(^{13}\) (n=29), a trial\(^{14}\) using an enrichment trial design (n=217), and a 2017 randomised controlled trial\(^{17}\) (n=209), found that topiramate\(^{15}\) and pregabalin\(^{16,17}\) were no more effective than placebo to reduce pain and improve function at short and long term follow-up (table 1). All trials reported a similar proportion of adverse events in the anticonvulsant and placebo groups.

**Antidepressants versus placebo**

A small crossover trial\(^{14}\) (n=28) with a four arm design found no statistically significant differences in pain and disability between the antidepressant (nortriptyline) and placebo group at 10 day follow-up. However, another small crossover trial\(^{19}\) (n=25) found a statistically significant effect for reducing pain of antidepressants (duloxetine) over placebo (mean difference on a 0 to 10 scale\(=\)−1.8; 95% confidence interval −0.8 to −2.8) after a four week treatment period. In another trial with a three arm design\(^{19}\) (n=60), antidepressants (amitriptyline) were also more effective than placebo to reduce pain (mean difference on a 0 to 10 scale\(=\)−1.4; 95% confidence interval −0.1 to −2.8) after a two week treatment period. All trials reported a similar proportion of adverse events in the antidepressant and placebo groups.

**Opioids versus placebo**

One small crossover trial\(^{14}\) with a four arm design (n=28) including a comparison between morphine and placebo, was identified. This trial did not show a benefit from morphine over placebo to reduce pain (mean difference on a 0-100 scale\(=\)−3.0; 95% confidence interval −17.4 to 11.4) and disability (mean difference on a 0-100 scale\(=\)−4.8; 95% confidence interval −13.2 to 3.7) at 10 day follow-up. Adverse events, such as constipation, drowsiness, and dizziness, were more common in the opioid group compared with the placebo group.

**Biological agents versus placebo**

We identified a systematic review\(^{11}\) investigating the efficacy of biological agents (adalimumab, etanercept, and infliximab) targeting tumour necrosis factor α, compared with placebo. Pooled data from only randomised placebo controlled trials show that compared with placebo biological agents did not reduce pain (6 trials, n=211, mean difference on a 0-100 scale\(=\)−10.29; 95% confidence interval −24.03 to 3.45), and disability (6 trials, n=211, mean difference on a 0-100 scale\(=\)−2.8; 95% confidence interval −11.3 to 5.7), or increase the proportion of patients who expressed an improvement or recovery (3 trials, n=141, odds ratio\(=\)1.3, 95% confidence interval 0.5 to 3.7) at short term follow-up (ie, more than four weeks and up to six weeks). Similar effects were found for medium term (ie, six months) and long term (ie, 12 months) follow-ups. The proportion of adverse events did not differ between the biological agents and the placebo group.

**Ongoing trials of pain medication for radicular leg pain**

<table>
<thead>
<tr>
<th>Name of trial</th>
<th>Population (target sample size)</th>
<th>Intervention and comparison</th>
<th>Primary outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety and efficacy of nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids in acute sciatica – TÉAGS(^{13}) (France, 2013, NCT01816336)</td>
<td>Patient with clinical diagnosis of sciatica and concordant imaging evidence (n=50)</td>
<td>1. Corticosteroids 2. NSAIDs 3. Placebo</td>
<td>Leg pain (0-100 visual analogue scale)</td>
</tr>
<tr>
<td>Paracetamol vs IV Morphine vs Placebo in Sciatalgia(^{11}) (Turkey, 2015, NCT02504996)</td>
<td>Patient with sciatica diagnosed by clinical assessment alone (n=300)</td>
<td>1. Acetaminophen 2. Morphine 3. Placebo</td>
<td>Leg pain (0-100 visual analogue scale)</td>
</tr>
<tr>
<td>A randomised controlled trial of adalimumab injection plus physiotherapy compared with placebo plus physiotherapy for patients with sciatica(^{16}) (United Kingdom, 2014, ISRCTN14569276)</td>
<td>Patient with clinical diagnosis of sciatica and concordant imaging evidence (n=312)</td>
<td>1. Adalimumab 2. Placebo</td>
<td>Disability (Oswestry Disability Index)</td>
</tr>
</tbody>
</table>

**Explain to patients the lack of evidence to support any particular pain medication**

To patients who express an improvement or recovery (3 trials, n=141, odds ratio\(=\)1.3, 95% confidence interval 0.5 to 3.7) at short term follow-up (ie, more than four weeks and up to six weeks). Similar effects were found for medium term (ie, six months) and long term (ie, 12 months) follow-ups. The proportion of adverse events did not differ between the biological agents and the placebo group.

**How patients were involved in this article**

One patient who suffered from sciatica in the past commented on the manuscript. This patient was treated with weak opioids (ie, tramadol) and emphasised the importance of communicating to patients about the lack of robust evidence for pain medications and the associated potential side effects.

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**EDUCATION INTO PRACTICE**

- When you next meet a patient taking medication for sciatica, what options would you consider?
- How would you discuss the relative benefits and harms of these options?
- Based on reading this article is there anything that you would do differently in your practice?
Is ongoing research likely to provide relevant evidence?
We searched for ongoing trials (table 2). Three (ie, one two-arm and two three-arm) ongoing randomised placebo controlled trials were identified. The largest trials identified are likely to provide evidence on the effectiveness of acetaminophen, opioids, and biological agents.

What should we do in the light of the uncertainty?
Explain to patients that there is a lack of evidence to support the prescription of any particular pain medication, and that these drugs can have side effects. Medication should be seen as one possible option within a range of conservative treatments for radicular leg pain. At the same time, clinicians should explain the natural history of radicular leg pain (as described earlier).

If drug treatment is desired, a reasonable approach is to make a personalised treatment plan depending on the duration and severity of pain, the patient’s age, history of medication use, and preference for medication, (co)morbidities and the safety profiles, and side effects of pain medications. If offering a NSAID as first line, discuss factors for adverse events (eg, being older, having kidney disease). Paracetamol is a simple and cheap alternative first-line analgesic, but its efficacy for treating radicular pain is unknown.

If NSAIDs are contraindicated, not tolerated, or have been ineffective, and the disc herniation is confirmed on imaging, systemic corticosteroids can be offered for patients with acute symptoms. The results of a 2015 large trial13 with low risk of bias shows that corticosteroids might benefit those patients with acute radicular leg pain with confirmed disc herniation and moderate disability (ie, at least 30 points on Oswestry Disability Index). Monitoring of side effects is also indicated during the course of treatment.

Patients with clinical features of chronic neuropathic pain (eg, allodynia or hyperalgesia), who had an inadequate response to NSAIDs might benefit from a trial of antidepressant medication. In this case, given the evidence from the latest trials19-20 on antidepressants, clinicians can consider the evidence based recommendation on the prescription of antidepressants from NICE guideline on neuropathic pain.21

Follow up patients regularly when prescribing any type of pain medication. In many cases patients do not find sufficient pain relief using pain medication, therefore encourage patients to try guideline endorsed non-drug treatments26 such as a (group) exercise or psychological programme, especially if there are psychosocial obstacles to recovery present.

After a course of conservative management including drug and non-drug treatments, refer patients with persistent and disabling sciatica (eg, after a 6-8 week period) to specialised care.

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Sin-drome—the phenomenon of missing-diagnosis

“We’ve had a new admission into bed”
“Great, I’ll be right there, what’s wrong with them?”
“He’sgot multorgan failure but was intubated mainly for respiratory failure”
“Ah OK, what’s wrong with him?”
“ARDS”
“Caused by what?”
“Sepsis I think”
“From what?”
“Pneumonia”
“What type?”
“Um….”

Speaking in terms of syndromes—ARDS (adult respiratory distress syndrome), IAH (intra-abdominal hypertension), AKI (acute kidney injury), MOF (multorgan failure), to name a few—makes communication easier and shortens the descriptions needed for referral, risk prediction, and effective handover but leads to the phenomenon of missing-diagnosis. This is precipitated by the acceptance of a syndrome as the end of a diagnostic process. I would like these conclusions renamed as a sin-drome.

It is true that patients can sometimes get better when the aetiology of illness is uncertain—by using the triad of surgery, antibiotics, and time. However, many cannot get better without a correct diagnosis: the patient shocked due to autoimmune Addison’s disease, the patient with sepsis due to hidden aortic valve Staphylococcus aureus endocarditis, the young patient with multiorgan failure due to Behçet’s disease.

To arrive at the correct diagnosis, we need to overcome cognitive biases—including anchoring bias (the patient with “sepsis” who actually has acute gallstone pancreatitis) and confirmation bias ("Ah yes, it does look like pneumonia on the chest x ray” in the patient with systemic lupus erythematosus related diffuse alveolar haemorrhage).

Avoidance of the sin-drome is also important in evidence based medicine. My own field of “sepsis” research has suffered countless “negative” trials partially due to grouping together patients with soft tissue infection from causes as different as Streptococcus pneumonia and Staphylococcus aureus. These entities are not the same despite falling under the umbrella of causing “septic shock.”

If we are to have personalised medicine we will need to focus on a diagnosis and not simply a sin-drome.

Matt Morgan, is an intensive care consultant, scientist, computer programmer, teacher, and geek interested in machine learning, medical education, and public engagement (@matrix_mania)
High quality handovers are essential for safe healthcare and are used in many clinical situations. Miscommunication during handovers can lead to unnecessary diagnostic delays, patients not receiving required treatment, and medication errors. Miscommunication is one of the leading causes for adverse events resulting in death or serious injury to patients. The process of handovers can be improved, and the aim of this article is to provide practical guidance for clinicians on how to do this better.

What is a handover?
A handover involves the transfer of professional responsibility and accountability for some or all aspects of care for a patient, or groups of patients, to another person, such as a clinician or nurse, or professional group on a temporary or permanent basis. Ideally a professional can take over responsibility for a patient only if he or she receives all relevant information to continue the treatment or care effectively and safely.

Why is handover important?
Patients can be handed over up to 15 times during a five day hospitalisation, and a doctor might participate in 3000 handovers a month. The figure illustrates the potential interactions for patients in an acute setting.

A narrative review including 69 studies and systematic review of 38 studies showed that poor communication between team members can lead to errors, patient harm, discontinuity of care, inefficient use of resources, and dissatisfied patients. There are several well studied ways to improve handovers. Systematic reviews of 36 quasi-experimental or observational studies and 29 studies (two randomised controlled trials and 27 uncontrolled studies) and an intervention study showed that implementing structured handover tools improved information transfer and increased professional satisfaction. Shift-to-shift handovers at the bedside instead of away from the patient also improved satisfaction for patients and staff in a systematic review which included 41 studies.

Another systematic review of 10 studies showed that educational interventions and non-technical skill based approaches to improve handovers such as simulation, group discussions, and lectures were beneficial.

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**WHAT YOU NEED TO KNOW**

- Information shared during clinical handover includes, as a minimum, the patient’s current health status, medications, and treatment plans as well as advance directives and any important changes in the patient’s status.
- Tools and handover structures such as SBAR (Situation, Background, Assessment, Recommendation) have been shown to improve the quality of handovers.
- Involving patients and carers in handovers—including scheduling a timely discharge conversation to discuss aspects of their admission and follow-up plan that includes a personalised discharge letter—is of great value.
What is best practice internationally?
In 2007 the Joint Commission International (JCI) and the World Health Organization suggested implementation of a standardised approach to handover communication by using the SBAR (Situation, Background, Assessment, Recommendation) technique. Effective communication is one of the JCI’s main patient safety goals and one of the elements assessed during hospital accreditation. Handover needs to fulfil the criteria of being timely, accurate, complete, unambiguous, and understood by the recipient. Guidance is available to help clinicians improve handovers (see box overleaf and additional educational resources on bmj.com).

How to do it better
Changing handover practice at an organisational level is complicated and requires effective strategies for implementation, reinforcement, and education on why it is important. Nevertheless, everyone can work on their handover practice by taking some practical steps that are relevant to all types of handovers. These include:

- Assessing the key people that need to be involved in the handover (physicians, nurses, patients and carers)
- Choosing a calm environment with minimal distractions
- Using a structured format such as SBAR
- Providing the person you are handing over to with the opportunity to ask questions and checking if they have understood correctly (report back).

What is the best approach to handover in a hospital setting?
Schedule sufficient time for the handover adjusted to the complexity of the patient’s situation. Start by introducing yourself and create an environment in which participants feel free to ask questions. Emphasise important elements during your handover, such as expected actions within the next shift or details of any treatment restrictions such as avoiding giving fluids. When handing over to a team of care professionals, give specific orders to every individual. Check if the receiver of the handover has understood the
What tools can help improve handover?

The use of structured handover tools, such as SBAR\(^1\) or I-PASS (Illness severity, Patient summary, Action list, Situation awareness and contingency plans, and Synthesis by receiver)\(^2\) have been shown to improve information transfer and healthcare professionals’ satisfaction with handovers.\(^7\) The clinical questions included within the fixed format of a handover tool can be decided on at an organisational level or, depending on the type of handover, department, patient group or individual user. An example of SBAR is shown below.

Information correctly by asking them to report back, and record necessary information in the patient’s record.

Be aware of barriers for effective communication when multiple disciplines are involved, such as differences in training, communication styles, lack of confidence, and hierarchy.\(^8\) Standardised handover tools and simulations may help to overcome these.\(^9\)

What is the best approach to handover between hospitals and community settings?

For handovers at discharge, several important elements have been identified.\(^10\)\(^11\) Start planning the discharge early and structure the discharge process so everyone knows what to expect in terms of responsibilities, coordination of tasks within the team, and content of discharge information. The medical discharge information for a patient should at least include active problems, diagnosis, medications, any services required, warning signs of a worsening condition, safety-netting (who to contact in case of an emergency), and a follow-up plan. Involve the patient and carer in the discharge by providing verbal information and written information in a personalised patient discharge letter with information on diagnosis, treatment, potential complications, medication, lifestyle advice, and who to contact with questions.\(^12\) Aim to send the (preliminary) discharge letter to the community care professional in good time, and, if possible, call to inform them if you feel this might enhance safe handover.

How should I involve patients in handovers?

The patient is the only constant factor in the care process and can therefore provide valuable information during the handover process. Commonly used tools to structure handovers usually do not include patient involvement; therefore, you need to incorporate this as an additional element. Keep in mind that, as a patient receives an overwhelming amount of information during admission, having a carer present during the handover can be valuable. Try to involve the patient and carer whenever possible; not only during the more informal moments when talking to the patient at the bedside, but also during formal handovers.

Establish individual patients’ need, wishes, and capacity for participation and understanding during the handover process, and discuss the level of involvement that they feel comfortable with.\(^13\) Patients can be more actively involved by conducting handovers at the bedside, providing the patient with understandable information about their condition and treatment plan, and allowing them to ask questions.\(^14\) For this to succeed, aim to set a specific time and place so patient and carer(s) know when to expect you. Create a situation in which patients feel comfortable to participate, for example, by introducing yourself, sitting down instead of standing next to the patient, making eye contact, and encouraging questions. Protect patients’ privacy during bedside handovers by avoiding discussing sensitive issues in front of other patients in the room.

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CASE REVIEW

Acute constipation and vomiting with the “coffee bean” sign

A 44 year old woman with cerebral palsy and multiple sclerosis—which was diagnosed at the age of 16—presented to the emergency department with four days of acute constipation and vomiting.

She had a history of chronic constipation that resulted from neurogenic bowel dysfunction. The dysfunction was secondary to her underlying cerebral palsy and multiple sclerosis and was initially managed with laxatives. In the last year, the constipation had become severe enough to warrant insertion of a sacral anterior root stimulator.

On physical examination, the abdomen was markedly distended, diffusely tender, and bowel sounds were absent. There was no guarding, rigidity, or sign of previous incisions, and all hernia orifices were intact.

The patient was tachycardic (140 beats/min) and tachypnoeic, normotensive (130/60 mmHg), and had oxygen saturation in room air of 98%. Arterial blood gas showed normal pH of 7.36, hypocapnea (PCO₂ 29 mmHg, normal range 35-45 mmHg), hyperlactataemia (20 mg/dL, 9-16 mg/dL), and no hypoxaemia (PO₂, 99 mmHg). White blood cell count was 10 500 cells/mm³ (73% neutrophils), and C reactive protein was 3.25 mg/dL (0-1 mg/dL).

Plain abdominal radiography (fig 1) and a computed tomography (CT) scan were performed.

1 What is the most likely diagnosis?
2 What differential diagnoses should be considered?
3 What are the treatment options for this condition?

Fig 1 Plain radiograph of the abdomen (lateral decubitus view)

Submitted by Salomone Di Saverio, Alice Piccinini, Arianna Brindelli, Carlo Fabbri, and Stefano Pretolani

Patient consent obtained.

Cite this as: BMJ 2017;358:j4414

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

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0.5 HOURS

the bmj | 14 October 2017
Rash in the returning traveller
A 26 year old woman was referred to the dermatology clinic after an itchy rash on her foot (figure) had not responded to topical corticosteroids or antifungals.
She reported that the rash had developed six days after returning from Barbados, and had started as a small blister. On examination, there was an erythematous, serpiginous rash on the dorsum of her right foot. The diagnosis was made clinically as likely cutaneous larva migrans. The patient was treated with a single dose of ivermectin, an anthelmintic. On clinical review 10 days later, the rash had resolved.
Cutaneous larva migrans is the result of a zoonotic infection from nematode parasites (such as *Ancylostoma braziliense*) of the hookworm family, which do not use humans as the definitive host.

Anaemia after Roux-en-Y gastric bypass
Long term follow-up of people who had received a Roux-en-Y gastric bypass for treatment of obesity reveals that the risk of anaemia is substantial and that it increases over time (JAMA Surg doi:10.1001/jamasurg.2017.3158). Ten years after surgery, more than half had haemoglobin concentrations below 135 g/L (men) or 120 g/L (women). The anaemia was normocytic and probably caused by multiple deficiencies of vitamins and minerals.

Probiotics for infants
The hygiene hypothesis, which explains the rising prevalence of asthma, eczema, and allergy in the developed world as a consequence of reduced or delayed exposure to microorganisms in early life, continues to stimulate investigations. *Paediatrics* has a trial of supplements of *Lactobacillus rhamnosus* given to infants with at least one atopic parent over the first six months of life (Paediatrics doi:10.1542/peds.2016-3000). However, no beneficial effects on rates of eczema, asthma, or rhinitis were apparent at age 2.

Trauma resuscitation
What is the experience of trauma resuscitation like from a patient’s point of view? A qualitative study interviewed 30 victims of both violent and non-violent trauma. Many participants had been highly aware of what had been happening and said they were satisfied with the expertise, efficiency, and clear communication between members of the trauma team (JAMA Surg doi:10.1001/jamasurg.2017.1088). They also remembered whether they had received words of explanation and reassurance. These are useful insights because it’s when assessment and treatment are most urgent that doctors are most likely to ignore patients’ fears and anxieties.

The death of the P value
The poor reproducibility of much medical research has prompted journals and grant-giving bodies to demand higher standards and greater methodological rigour. An essay in the *American Journal of Epidemiology* argues that this misses the point, blaming instead an obsession with P value (Am J Epidemiol doi:10.1093/aje/kwx261s). The author reckons that a system of selecting results for further investigation based on significance testing is bound to yield not only a low proportion of repeatable results but also a high proportion of effects that are initially overestimated.

Surgery for epilepsy
A retrospective review of nearly 700 patients who had undergone surgery for their epilepsy explored variables that influenced the likelihood of a seizure free outcome (J Neurol Neurosurg Psychiatry doi:10.1136/jnnp-2017-316211). Overall, 50% of patients were still free of seizures five years post-operatively. Those with hippocampal sclerosis had the best outcomes, while those whose magnetic resonance image showed no abnormality did least well. Seizure recurrence was also more likely when the surgery involved structures beyond the temporal lobe.

Outlook for people with SLE
Between 1950 and the mid 1990s there was a striking improvement in survival in patients with systemic lupus erythematosus, according to a systematic review of longitudinal studies in *Annals of the Rheumatic Diseases* (Ann Rheum Dis doi:10.1136/annrheumdis-2017-211663). Since then, there has been little change. Interpreting these time trends isn’t straightforward. Although some of the improvement can be attributed to better treatment, some of it can also be put down to the inclusion of milder cases after antinuclear antibody testing became available.

Preventing pneumothorax
Recurrence is common after spontaneous pneumothorax and a systematic review in *Thorax* leaves little doubt that chemical pleurodesis is an effective preventive treatment (Thorax doi:10.1136/thoraxjnl-2015-207967). Unfortunately, there have been few randomised trials and the review is unable to say whether any one of the numerous chemical agents that have been tried is better than the others. Another clear deficiency in the data are the lack of information about patient preferences and adverse effects.