

education

FROM THE JOURNALS Edited highlights of Richard Lehman's blog on <http://bmj.co/Lehman>

Bystander resuscitation efforts in cardiac arrest

Without a randomised trial, it's hard to be sure about the value of attempted out-of-hospital resuscitation for cardiac arrest. But since there's unlikely to be such a trial, we'll have to judge from observational evidence like this nationwide survey from Denmark. Data were available for 34 459 people, of whom 8.3% survived to 30 day discharge. Those who reached this point did somewhat better if they had received bystander cardiopulmonary resuscitation than if they hadn't, in terms of brain damage or nursing home admission. But we are talking about small subsets of the 8.3% subset. It's a signal for some effect, but there could be hidden confounders.

• *N Engl J Med* 2017 doi: 10.1056/NEJMoa1601891

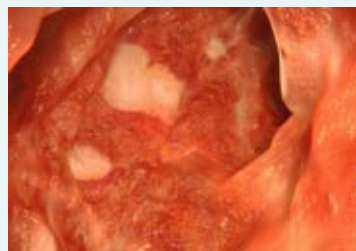
Antimicrobial training in Dutch hospitals

The Dutch Unique Method for Antimicrobial Stewardship is a thoroughly earnest exercise to improve the use of antimicrobial agents in hospitals. The acronym DUMAS commemorates the pleasure loving French writer best known for his counts and musketeers. In this trial, the clinicians could load their muskets as they chose, but were told which balls were most likely to reach the target. The results were then counted. There was a 13% reduction in the prescribing of the drugs deemed inappropriate, but total antibiotic prescribing did not fall.

• *JAMA Intern Med* doi:10.1001/jamainternmed.2017.0946

Alternate day fasting

Fasting seems to be a very widespread phenomenon, mostly associated with religious cleansing of the body. Even among New England Protestants, Solemn Days of Fasting were occasionally imposed up to the eighteenth century. In modern day



Janus kinase inhibitor for ulcerative colitis

"In patients with moderately to severely active ulcerative colitis, tofacitinib was more effective as induction and maintenance therapy than placebo." Is placebo the usual treatment for ulcerative colitis? Actually, this sentence in the abstract does not do justice to the design of the three OCTAVE trials that are bunched up in this article. The participants received lots of other treatment too: "Patients were required to have had treatment failure with or to have had unacceptable side effects from treatment with at least one of the following agents: oral or intravenous glucocorticoids, azathioprine, mercaptopurine, infliximab, or adalimumab. Permitted concomitant medications for ulcerative colitis were oral aminosalicylates and oral glucocorticoids (at a maximum dose of 25 mg per day of prednisone or a prednisone equivalent), provided that the medications were administered at a stable dose throughout the induction trials; in the maintenance trial, tapering of glucocorticoids was mandatory." So this paper about the Janus kinase inhibitor tofacitinib might be important, but it is unclear what role it has in the management of ulcerative colitis in 2017. This needs a careful network meta-analysis based on individual participant data, and hopefully Pfizer, who ran the trials, will make this possible right away.

• *N Engl J Med* doi: 10.1056/NEJMoa1606910

Chicago, 100 people who wanted to lose weight agreed to be randomised to alternate day fasting or a continuous calorie restricted diet for a year. You'll have read about this already. There was no difference between groups in weight loss achieved (a hefty 6%), adherence, or cardiovascular risk markers. More pain, same gain.

• *JAMA Intern Med* doi:10.1001/jamainternmed.2017.0936

Statins: pains in the mind or the muscles?

Statins are a pain in the mind. The worst migraine I've ever had came from trying to write an editorial about them for *The BMJ*. I gave up the attempt in the interests of personal survival. As a general practitioner, I prescribed statins liberally and with conviction for nearly two decades. If people came complaining about muscle pains, I would reassure them, stop the drug for a while, and then try a different one at lower dosage. Several patients, including some doctors, were desperate to continue because they had established coronary disease. But every time they tried to exercise, they hit a barrier, which disappeared after stopping the statin. Is this "muscle pain"? Would it have been classed as such in the lipid lowering arm of the Anglo-Scandinavian cardiac outcomes trial? I've no idea. I've no idea how many elderly people taking statins have stopped going out to the shops because of what they put down to old age, or how much of that could be due to statins. All I know is that, when authority figures remote from primary care dig out old studies to prove that it's all a figment of the imagination of the people who actually take or prescribe the drugs, I get rather cross and feel a migraine coming on. This silly argument can only be resolved with prospective studies and some understanding of how decisions are made in real life.

• *Lancet* doi:10.1016/S0140-6736(17)31075-9

The evidence

The systematic review on the net benefit of knee arthroscopy compared with non-operative care pools data from 13 randomised trials for benefit outcomes (1668 patients) and an additional 12 observational studies for complications (>1.8 million patients).²¹ The figure below gives an overview of the patients included, the study funding, and patient involvement in the design of the studies.

Panel members identified three outcomes—pain, function, and quality of life—as the most important for patients with degenerative knee disease who are considering surgery. Although the included studies reported these patient-important outcomes, it is difficult to know whether changes recorded on an instrument measuring subjective symptoms are important to those with symptoms—for example, a change of three points might have completely different meanings in two different pain scales.

A second team performed a linked systematic review addressing what level of individual change on a given scale is important to patients,²⁰ a characteristic called the minimally important difference (MID).²² The study identified a range of credible MIDs for each key outcome; this range of MID estimates informed sensitivity analyses for the review on net benefit, informed discussions on the patient values and preferences, and was key to interpreting the magnitude of effect sizes as well as the strength of the recommendation.²⁰



What is degenerative knee disease?

- Degenerative knee disease is an inclusive term, which many consider synonymous with osteoarthritis. We use the term degenerative knee disease to explicitly include patients with knee pain, particularly if they are >35 years old, with or without:
 - Imaging evidence of osteoarthritis
 - Meniscus tears
 - Locking, clicking, or other mechanical symptoms except persistent objective locked knee
 - Acute or subacute onset of symptoms
- Most people with degenerative arthritis have at least one of these characteristics.¹ The term degenerative knee disease does not include patients having recent debut of their symptoms after a major knee trauma with acute onset of joint swelling (such as haemarthrosis)

DATA SOURCES

Use this information to gauge how similar your patients' conditions are to those of people studied in the trials

Characteristics of patients and trials included in systematic review of arthroscopic knee surgery

NUMBER OF TRIALS

13

NUMBER OF PATIENTS

1665

TRIAL CHARACTERISTICS

Trials in which more than 60% of people had meniscal tears



Trials which excluded patients with previous arthroscopic surgery



Trials which excluded patients with a single initial impact trauma event



Trials in which more than 50% of people had radiographic OA

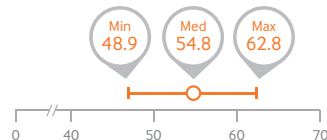


Trials in which all participants had previously used physiotherapy

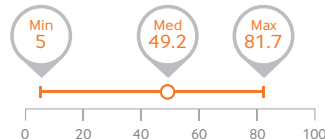


PATIENT CHARACTERISTICS

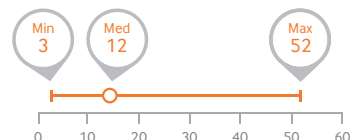
MEAN AGE



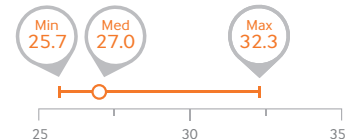
SEX % women



MEAN SYMPTOM DURATION months



MEAN BMI



12 of 13 trials were free of industry funding



No trials involved patients in design or conduct

Population



People with degenerative knee disease

Including people with or without:

- Radiographic evidence of osteoarthritis
- Mild to severe osteoarthritis
- Mechanical symptoms
- Acute onset knee pain
- Meniscal tears

Choice of intervention

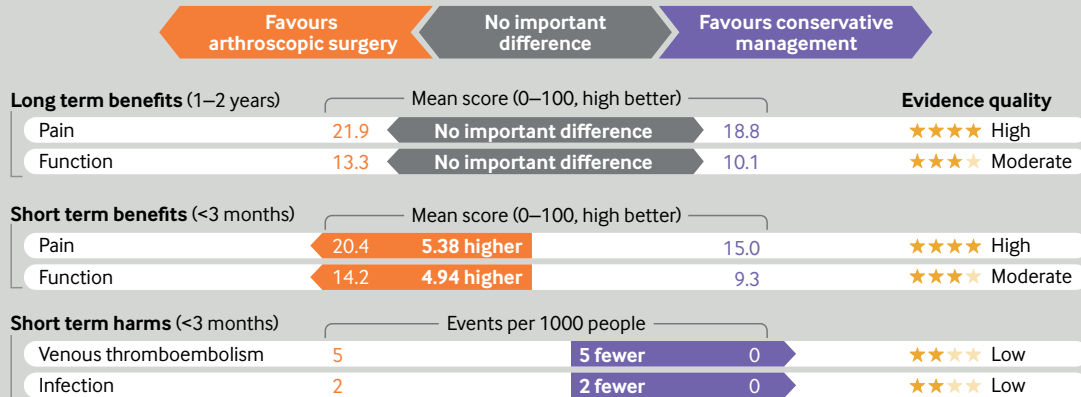
Arthroscopic surgery
Arthroscopic surgery with or without partial meniscectomy or debridement

or

Conservative management
Any conservative management strategy (exercise therapy, injections, drugs)

Recommendations

Comparison of benefits and harms



Key practical issues

Arthroscopic surgery

- Performed by a surgeon, in an operating theatre
- Recovery typically between 2 to 6 weeks
- At least 1–2 weeks off work, depending on speed of recovery and physical demands of job

Conservative management

- May be performed in hospital or the community
- No recovery time
- Time off work may be required for appointments, such as physiotherapy and injections

Interpreting the outcomes

The panel agreed “Minimally important difference” scores for pain and function, which represent what most patients would consider a worthwhile change:

Pain 12 Function 8

Preferences and values

The panel believes that almost everyone would prefer to avoid the pain and inconvenience of the recovery period after arthroscopy, since it offers only a small chance of a small benefit

Resourcing

Arthroscopy is not cost-effective from a societal perspective

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Understanding the recommendations

The infographic (opposite) provides an overview of the benefits and harms of arthroscopy in standard GRADE format. Estimates of baseline risk for effects comes from the control arms of the trials; for complications, comparator risk was assumed to be nil.

The panel is confident that arthroscopic knee surgery does not, on average, result in an improvement in long term pain or function. Most patients will experience an important improvement in pain and function without arthroscopy. However, in <15% of participants, arthroscopic surgery resulted in a small or very small improvement in pain or function at three months after surgery—this benefit was not sustained at one year. In addition to the burden of undergoing knee arthroscopy, there are rare but important harms, although the precision in these estimates is uncertain (low quality of evidence).

It is unlikely that new information will change interpretation of the key outcomes of pain, knee function, and quality of life (as implied by high to moderate quality of evidence).

The panel is confident that the randomised controlled trials included adequate representation from groups commonly cited to derive benefit from arthroscopic knee surgery for degenerative knee disease—notably those with meniscal tears, no or minimal radiographic evidence of osteoarthritis, and those with sudden but non-traumatic symptom onset. The recommendation applies to all or almost all patients with degenerative knee disease. Further, the evidence applies to patients with any severity of mechanical symptoms, with the only possible exception being those who are objectively unable to fully extend their knee (that is, a true locked knee). We did not consider young patients with sports related injuries or patients with major trauma in any age.

Trials that enrolled a majority of patients without radiographic osteoarthritis showed similar effect sizes to trials enrolling patients with radiographic evidence of osteoarthritis. Most of these trials exclusively included patients with meniscus tears. Meniscus tears are common, usually incidental findings, and unlikely to be the cause of knee pain, aching, or stiffness.¹ Mechanical symptoms were also a prominent feature for most trial participants, and many had sudden or subacute onset of symptoms.²³⁻²⁶ Given that there is evidence of harm and no evidence of important lasting benefit in any subgroup, the panel believes that the burden of proof rests with those who suggest benefit for any other particular subgroup before arthroscopic surgery is routinely performed in any subgroup of patients.

HOW THE RECOMMENDATION WAS CREATED

Our international panel including orthopaedic surgeons, a rheumatologist, physiotherapists, a general practitioner, general internists, epidemiologists, methodologists, and people with lived experience of degenerative knee disease (including both those who had undergone and not undergone arthroscopy) met to discuss the evidence. No person had financial conflicts of interest; intellectual and professional conflicts were minimised and managed.

The panel followed the *BMJ* Rapid Recommendations procedures for creating a trustworthy recommendation³⁵⁻³⁶ and used the GRADE approach to critically appraise the evidence and create recommendations.³⁷ The panel considered the balance of benefits, harms, and burdens of the procedure, the quality of evidence for each outcome, typical and expected variations in patient values and preferences, and acceptability of action.

EDUCATION INTO PRACTICE

- Project: how many arthroscopic procedures are scheduled in your organisation for degenerative knee disease?
- Based on this article, is there anything which you might alter your practice?
- To what extent might you use this information to alter the conversations with patients with degenerative knee disease, or those considering surgery?

Practical issues

It takes between two and six weeks to recover from arthroscopy, during which time patients may experience pain, swelling, and limited function.²⁷⁻²⁸ Most patients cannot bear full weight on the leg (that is, they may need crutches) in the first week after surgery, and driving or physical activity is limited during the recovery period.²⁷ See bmj.com for an outline of the key practical issues for those considering arthroscopic knee surgery versus non-surgical management for degenerative knee disease.

Degenerative knee disease is a chronic condition in which symptoms fluctuate. On average, pain tends to improve over time after seeing a physician for pain,²¹⁻²⁹ and delaying knee replacement is encouraged when possible.⁴

Values and preferences

Our strong recommendation against arthroscopy reflects a low value on a modest probability (<15%) of small or very small improvement in short term pain and function that does not persist to one year, and a higher value on avoiding the burden, postoperative limitations, and rare serious adverse effects associated with knee arthroscopy. The panel, including the patient participants, felt that almost all patients would share these values. The recommendation is not applicable to patients who do not share these values (that is, those who place a high value on a small, uncertain, and transient reduction in pain and function, and a low value on avoiding the burden and postoperative limitation associated with arthroscopy).

As new evidence is published, a group will assess the new evidence and make a judgment on to what extent it is expected to alter the recommendation.

Competing interests: See bmj.com.

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Find the full version with references at <http://dx.doi.org/10.1136/bmj.j1982>

LINKED ARTICLES IN THIS *BMJ* RAPID RECOMMENDATIONS CLUSTER

- Brignardello-Petersen R, Guyatt GH, Schandelmaier S, et al. Knee arthroscopy versus conservative management in patients with degenerative knee disease: a systematic review. *BMJ Open* 2017;7:e016114. doi:10.1136/bmjopen-2017-016114
- Devji T, Guyatt GH, Lytvyn L, et al. Application of minimal important differences in degenerative knee disease outcomes: a systematic review and case study to inform *BMJ* Rapid Recommendations. *BMJ Open* 2017;7:e015587. doi:10.1136/bmjopen-2016-015587
- MAGICapp (www.magicapp.org)

Contraception advice for women with epilepsy

Inuka Kishara Gooneratne,¹ Mayurika Wimalaratna,²
A K Probhodana Ranaweera,³ Sunil Wimalaratna⁴

See <http://learning.bmj.com> for linked learning module

¹Department of Neurology, Kettering General Hospital

²Wendover Health Centre, Buckinghamshire

³Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Colombo, Sri Lanka

⁴Neurology Department, John Radcliffe Hospital, Oxford University Hospital

Correspondence to: IK Gooneratne kishig@gmail.com

A 22 year old student attends your practice asking for contraception. She has idiopathic generalised epilepsy diagnosed five years ago, which is controlled with lamotrigine. She does not plan to conceive in the near future.

Active epilepsy affects around 6.4 per 1000 persons,¹ Globally, 50% of women and girls with epilepsy are in the reproductive age range.² Counsel women about the potential teratogenic effects of anti-epileptic drugs and provide information on contraception to avoid an unplanned pregnancy.³ Consider interactions between anti-epileptic drugs and hormonal contraceptives because using them together can reduce the efficacy of contraception or of seizure control.⁴

Competing interests: None declared.

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Find the full version with references at <http://dx.doi.org/10.1136/bmj.j2010>

HOW PATIENTS WERE INVOLVED

The manuscript was discussed with a woman of childbearing age with epilepsy. She wanted information on robust contraceptive methods to prevent an unplanned pregnancy. She also expressed a need to know about safe anti-epileptic drugs if she were to conceive.

EDUCATION INTO PRACTICE

- Do you routinely discuss pregnancy and contraception with women who are receiving epilepsy treatment?

WHAT YOU NEED TO KNOW

- Anti-epileptic drugs such as carbamazepine, phenytoin, and phenobarbital can reduce the efficacy of hormonal contraceptives.
- Consider long acting reversible contraceptives such as medroxyprogesterone acetate depo injection, copper intrauterine device, and levonorgestrel releasing intrauterine systems in patients on enzyme inducing anti-epileptic drugs.
- Sodium valproate is not recommended in women of childbearing age because of high teratogenicity.



0.5 HOURS



See <http://learning.bmj.com> for linked learning module



GAROPHANIE/ALAMY

Consider patient preference, relative efficacy of each contraceptive, and interactions with prescribed anti-epileptic drugs

WHAT YOU SHOULD COVER

Consider asking about

- **Current status of epilepsy**
Age at onset of seizures? Are seizures well controlled? What anti-epileptic drugs is the woman taking? Does she experience any adverse effects from taking these drugs?
- **Preferred contraceptive**
Does she use any contraception at present or has she tried any before? What has been her experience? Has she had recent unprotected sexual intercourse?
- Her plans and wishes regarding pregnancy and contraception to gauge whether short or long term contraception is needed
- History of sexually transmitted infections or symptoms such as vaginal discharge, pelvic pain, pain during sex, or lesions in the vaginal area, which might suggest the need for treatment and might influence method of contraception
- Menstrual history to assess regularity of cycles and excessive bleeding. Consider whether she could currently be pregnant
- Previous pregnancies with outcomes
- Medical illnesses such as diabetes, hypertension, ischaemic heart disease, stroke, venous thromboembolism, migraine, and liver and renal disease, which could preclude use of hormonal contraceptives

WHAT YOU SHOULD DO

If the woman has missed her periods, offer her a pregnancy test. If pregnancy is confirmed, advise her on the need to see an obstetrician to manage the potential teratogenic effects of anti-epileptic drugs.

If the woman reports unprotected sexual intercourse in the last five days, discuss options for emergency contraception. In a patient taking enzyme inducing anti-epileptic drugs, the copper intrauterine device is recommended.

Alternatively, offer a 3 mg dose of levonorgestrel. Ulipristal acetate is not recommended in patients on enzyme inducing anti-epileptic drugs.⁵

If a current pregnancy is unlikely (as determined above) and the woman does not plan to conceive in the near future, offer long acting contraception. Barrier methods alone have high failure rates (15%-20%), and are therefore discouraged in women with epilepsy, as failure can result in an unplanned pregnancy and risk of teratogenicity.⁶ Consider patient preference, relative efficacy of each contraceptive, and interactions with prescribed anti-epileptic drugs in choosing the appropriate contraceptive.^{5,7}

Enzyme inducing anti-epileptic drugs (table 1) increase the activity of hepatic cytochrome

enzyme P450. Thereby, metabolism of oestrogen and progestogen is increased with reduced blood concentrations.⁸ In patients taking these drugs, contraceptive failure can occur when using combined oral contraception pills, progestogen only pills, and progestogen implants (Nexplanon/etonogestrel).⁶ The efficacy of combined oral contraceptives can be improved by increasing the oestrogen dose (50 ug-70 ug), by tri-cycling (taking three packets back to back without a pill free interval), and reducing the pill free interval to four days, although evidence is variable.⁶ Advise women taking anti-epileptic drugs who wish to use combined oral or progestogen only contraceptives, transdermal patches, vaginal rings, or implants also to use barrier methods such as condoms or a vaginal diaphragm.

Enzyme inducing anti-epileptic drugs do not alter the efficacy of medroxyprogesterone acetate depo injections, intrauterine devices, and levonorgestrel releasing intrauterine systems; therefore these methods of contraception can be considered in patients on enzyme inducing anti-epileptic drugs.

Non-enzyme inducing anti-epileptic drugs do not affect hormonal contraceptive efficacy. Women on these medications can choose any contraceptive and emergency contraceptive method.⁴

Barrier methods alone have high failure rates and are discouraged in women with epilepsy

Lamotrigine, a non-enzyme inducing anti-epileptic drug, has minimal effects on the efficacy of combined oral contraceptives. However, combined oral contraceptive pills reduce blood concentrations of lamotrigine by 40%–60%, which can result in poor seizure control.⁹ If combined oral contraceptives are chosen, the dose of lamotrigine might need to be increased. To reduce the risk of anti-epileptic drug toxicity, extend the cycle so that there is no pill free interval.⁹

Ask the woman to come back if she decides to stop contraception and plan a pregnancy, as aspects of preconception care differ for women with epilepsy.¹⁰

If a patient is planning to conceive in the foreseeable future, explain the risks of fetal malformation with different anti-epileptic drugs (table 2). Valproate has the highest teratogenic risk and affects long term neurodevelopment.^{11,12} Lamotrigine and levetiracetam have lower teratogenic risk and are recommended over other anti-epileptic drugs during pregnancy. Consider referral to a neurologist for switching drugs if the patient is on valproate and plans to conceive in the near future.

This patient has not had a seizure for five years, therefore you could discuss the option of withdrawing anti-epileptic drugs and advise referral to a neurologist.¹³

Table 1 | Enzyme inducing and non-enzyme inducing anti-epileptic drugs

Enzyme inducing anti-epileptic drugs	Non-enzyme inducing anti-epileptic drugs
*carbamazepine	Acetazolamide
eslicarbazepine acetate	clobazam
oxcarbazepine	clonazepam
phenobarbital	ethosuximide
phenytoin	gabapentin
primidone	lacosamide
rufinamide	levetiracetam
topiramate	*Lamotrigine
perampanel	piracetam
	pregabalin
	sodium valproate
	stiripentol
	tiagabine
	vigabatrin
	zonisamide

* Commonly used anti-epileptic drugs are in bold

** in doses >200mg

*** Efficacy reduced by combined oral contraceptive drugs

Table 2 | Fetal malformation risk (data from pregnancy registries)

Drug	Malformation risk	Most frequent major congenital malformation
Valproic acid	4.7%-10%	Neural tube defects, hypospadias, cardiac malformations
Topiramate	4.2%-7.7%	Orofacial clefts
Phenobarbital	5.5%-7.4%	Cardiac malformations
Phenytoin	2.9%-6.7%	Cardiac malformations
Carbamazepine	2.6%-5.6%	Cardiac malformations
Lamotrigine	2.0%–3.4%	Cardiac malformations, orofacial clefts
Oxcarbazepine	1.8%-3.3%	*Orofacial clefts
Levetiracetam	0%-2.4%	*Cardiac malformations, *Neural tube defects

Registries: International Register of Antiepileptic Drugs and Pregnancy, North American Antiepileptic Drug Pregnancy Register, UK Epilepsy and Pregnancy Register,

Medical Birth Register of Norway,

Swedish Medical Birth Register

*Rarely reported

Are you “satisfied” with clinical decision support?

A 60 year old woman goes to her doctor with dizziness and poor balance. Her doctor is not sure what is wrong but thinks about postural hypotension, Meniere’s disease, and benign positional paroxysmal vertigo. He cannot find anything on examination, and all tests come back negative. He tells the patient that he cannot find a physical cause for her poor balance and suggests physiotherapy. A year later, the symptoms have got worse, and the patient is eventually diagnosed with multiple sclerosis. She wonders why she couldn’t have been diagnosed earlier.

So why couldn’t she have been diagnosed earlier? One possibility is that her doctor was “satisfied” with the differential diagnosis too quickly. Satisficing is a portmanteau of satisfy and suffice. It means that when you make a decision, you think through alternatives until you decide that you have done an acceptable job. But the problem is that the threshold for acceptability is subjective, and many people are “satisfied” too soon.



Sherbino and colleagues tried teaching medical students cognitive forcing strategies to overcome satisficing and other biases, but it didn’t work—the students who received the training were no better at diagnostic decision making than controls.

Clinical decision support at the point of care seems like the way forward. Too often, doctors still rely on memory. Most exams in medicine are closed-book exams, and students learn tremendous amounts by heart. But this is no

longer the real world. Today learners have constant access to a range of evidence based, practical, and continually updated knowledge on their mobile. During cardiopulmonary resuscitation, there is literally no time to look things up and you have to know what to do immediately. But in most other cases, there is time to check. There just needs to be the will and the right culture and environment.

Kieran Walsh, clinical director of BMJ Learning and BMJ Best Practice

I’m an uncertainty specialist

A middle aged woman had been told by our practice nurse that she had pre-diabetes and was prescribed metformin. She wanted to speak to me to understand what pre-diabetes meant. “Have I got a disease or not, Dr Marshall?” she asked, “And do I have to take these tablets?”

These are good questions. I could have introduced a bit of artificial certitude (a George Bushism) into the consultation, but, for once, I wasn’t running late. I felt like answering “Yes, you have, and no, you haven’t” to first question, and “Maybe, but maybe not” to the second. Classic answers to questions that arise from the

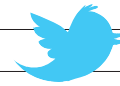
zone of uncertainty that GPs operate in for so much of the time. The fundamental problem, which I appreciated only later that evening over a glass of wine with my wife, was that I thought we were preventing a disease by prescribing metformin, but the patient thought we were giving her one.

My uncertainty problem is that screening for pre-diabetes is both a good and a bad thing, a paradox. Most importantly, it is an arbitrary judgment. The cut off point for diagnosing so called pre-diabetes was recently reduced by a group of experts in the US from a fasting glucose of 6.0% to one of 5.7%. Overnight, this increased the prevalence of pre-diabetes threefold. Does this sound OK? Are we creating illness?

Huxley said that, “medical science has made such tremendous progress that there is hardly a healthy human being left.” So where do you stand? Are you a disease denier or a disease monger? Good GPs can only make sense by being both at the same time. Such is the paradox of being an uncertainty specialist.

Martin Marshall, GP, Newham; professor of healthcare improvement, UCL





CASE REVIEW

A man with chest tightness and burning limbs

A 73 year old man arrived at the cardiac clinic complaining of chest tightness when walking or speaking loudly. He had oedema in both legs and intermittent burning pain in his abdomen and extremities, especially the forearms and ankles, which had persisted for one month. He had no history of diabetes mellitus, rheumatic disease, or cerebral haemorrhage, and his vital signs were normal. Physical examination revealed acrocyanosis and hyperpigmentation on his abdomen, and tenderness to palpation across his entire chest area. He showed no jugular venous distension or pulmonary rales.

The patient had

- haemoglobin of 10.9 g/dL (normal range 12.0~15.5 g/dL)
- red blood cell count of $3.36 \times 10^{12}/L$ ($4.0 \sim 5.5 \times 10^{12}/L$)
- white blood cell count of $4.98 \times 10^9/L$ ($4 \sim 10 \times 10^9/L$)
- platelet count of $112 \times 10^9/L$ ($100 \sim 300 \times 10^9/L$)
- normal erythrocyte sedimentation and C reactive protein
- a 16172 pg/mL concentration of N-terminal prohormone brain natriuretic peptide (<400 pg/mL)
- <0.01 ng/mL troponin T (normal range <0.1ng/mL).

An echocardiogram showed a bi-atrial enlargement (left atrium, 58x51 mm; right atrium, 53x43 mm) and left ventricular concentric hypertrophy (ventricular septum thickness, 14 mm; posterior wall thickness, 14 mm). The left ventricular ejection fraction was 65%. Cardiac magnetic resonance imaging showed concentric thickening of the left ventricular wall and global transmural late gadolinium enhancement.

- 1 What is the most likely diagnosis?
- 2 What steps can physicians take to confirm the most likely diagnosis?
- 3 How would you manage this patient?

Submitted by Zhong Yi, Yen Shu Huang, Lei Wang, and Yun-Tao Zhao
Patient consent obtained.

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SPOT DIAGNOSIS

A young man with elbow pain



A 24 year old man presented with pain and reduced pronation/supination of his right elbow that had been worsening over the past three months. He had sustained a traumatic brain injury six months before presentation and was undergoing inpatient rehabilitation for a right hemiparesis. Radiographs of the elbow were taken (figs 1, 2). Based on these images and the patient's history, what is the diagnosis?

Submitted by Julia Myers
Patient consent obtained.

Cite this as: *BMJ* 2017;357:j1820

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>



SPOT DIAGNOSIS A young man with elbow pain
There is extraskeletal bone formation in the soft tissue adjacent to the radial tuberosity. This is consistent with neurogenic heterotopic ossification (Fig 3, arrows).

- 1 Cardiac amyloidosis.
- 2 Differential diagnoses include amyloid A amyloidosis, acquired transthyretin amyloidosis wild type, mutant transthyretin amyloidosis, and light chain type amyloidosis. To distinguish between these, serum and urine free light chains, Congo red staining with apple green birefringence under polarised light, and laser microdissection with mass spectrometry can be used.
- 3 Treatment of light chain type cardiac amyloidosis involves chemotherapy aimed at halting the amyloidogenic plasma cell dyscrasia, and optimal treatment for heart failure.

CASE REVIEW
A man with chest tightness and burning limbs

answers



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

0.5 HOURS



Articles with a "learning module" logo have a linked BMJ Learning module at <http://learning.bmj.com>.

Haemangioma of the tympanic membrane

A 45 year old woman was referred to the ear, nose, and throat department with a three month history of imbalance associated with a “warm glow” sensation that arose from her right ear. Her hearing was normal. On examination, a haemangioma of the right tympanic membrane was identified in its posterosuperior aspect (right). The haemangioma was cauterised under a brief

general anaesthetic. A haemangioma is a benign vascular tumour. They predominantly affect men in their sixth decade of life and are often accompanied by non-specific otological symptoms, but can be asymptomatic.

Declan C Murphy (declan.murphy@uea.ac.uk), Norwich Medical School, Norwich, UK; John Phillips Patient consent obtained.

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Individual targets for blood pressure

The “one target fits all” model for lowering high blood pressure makes little sense, but it is proving difficult to replace. In 2015 the SPRINT trial (*N Engl J Med* doi:10.1056/NEJMoa1511939) showed that having a lower target blood pressure in high risk patients reduced the number of cardiovascular events, though with a high number needed to treat and more serious adverse events. A team led by John Spertus in Texas has analysed the published data and developed prediction models to tailor the intensity of blood pressure control based on the projected risk and benefit for each patient (*Circ Cardiovasc Qual Outcomes* doi:10.1161/CIRCOUTCOMES.117.003624). This model, and others like it, will now need to be tested in long term studies.



Long term opioid use after surgical analgesia

Chronic opioid use, and with it opioid related death, is soaring in the USA. To see how surgeons might be contributing to it, a Michigan team examined national statistics for prescribing opioids after major and minor surgery (*JAMA Surg* doi:10.1001/jamasurg.2017.0504). They found that around 6% of patients who were given opioids were still claiming prescriptions for them three to six months later.

Avoiding cystourethrography in infants

Voiding cystourethrography is a difficult and unpleasant procedure to carry out on infants who have had febrile urinary infection under the age of 3 months, but it could also be important to detect high grade vesicoureteral reflux. Happily, a Swiss study carried out on 122 such infants shows that, if the infection was caused by *Escherichia coli* and urinary tract ultrasound is normal, voiding cystourethrography can be safely avoided (*Arch Dis Child* doi:10.1136/archdischild-2016-311587).

Deciding for double mastectomy

Four years after Angelina Jolie revealed she had undergone bilateral mastectomy, repercussions are still being felt in an increased demand for *BRCA* testing and bilateral mastectomy in quite different circumstances. Two papers in *JAMA Surgery* describe this dialogue. In a study from Los Angeles and Georgia, about a quarter of women start off suggesting bilateral removal, and it is often done inappropriately unless surgeons recommend against it (*JAMA Surg* doi:10.1001/jamasurg.2016.4749). Another report on this study shows that, when surgeons do recommend against, this does not substantively increase patient dissatisfaction, the use of second opinions, or loss of the patient to a second surgeon (*JAMA Surg* doi:10.1001/jamasurg.2017.0458).

Should I see a doctor about this?

A questionnaire survey of the Danish population shows that approximately every fifth symptom reported by individuals from the general population leads to contact with a general practitioner (*BJGP Open* doi:10.3399/bjgpopen17X100761). Not surprisingly, important factors were the effect of symptoms on daily life, anxiety about their cause,

and their overall burden. The number of symptoms in female responders was larger, but the proportion of these that led to GP contact was the same as for men.

Fifty shades of grey

When systematic reviewing was a new art in the 1990s, retired people with grey hair volunteered to hand search for papers that might have eluded the search engines of the day. However, this probably isn't the origin of the term “grey literature,” which covers at least 50 shades of article that might be remotely connected with the material you are looking for. And a survey of its use—for example, non-English publications and unpublished dissertations—shows that searching for it seldom affects the findings of a review (*BMC Med Res* doi:10.1186/s12874-017-0347-z).

Babies and Ramadan

Mothers who know they are pregnant during the Muslim month of Ramadan are excused from keeping a fast from dawn to dusk. But for some it might be too early in pregnancy to know, or others might conceive during those four weeks. A study based in Bradford looked to see whether this might have any effect on the birth weight of babies born to Muslim mothers whose likely date of conception fell seven days before Ramadan until the end of the fast (*J Epidemiol Community Health* doi:10.1136/jech-2016-208800). According to routine birth weight data, it makes no difference at all.



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