Getting inflamed about canakinumab for CVD

In the good old days, human beings went around in a state of semi-permanent inflammation from parasites and infections, ate what they could, starved when they couldn’t, and rarely sat down. Few lived long enough to develop atherosclerosis. But in sedentary, well-fed modern people who live beyond 60, inflammation has come to be feared as a cardiovascular risk factor. In a much hyped study presented at the European Society of Cardiology, a monoclonal antibody targeting interleukin-1β called canakinumab was shown to reduce C reactive protein—a crude marker for inflammation first used in the 1930s—in over 10,000 people with previous myocardial infarction. In one dose group of three, this was associated with a statistically significant reduction in a composite outcome of non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death over four years. There were no differences in overall mortality. Canakinumab currently costs about $200,000 per person per year in the US and is associated with an increase in fatal infections.

*NEJM* doi: 10.1056/NEJMoal707914

Monitoring lipids on statin treatment

Next week I’ll be going to an international get-together of the various *Choosing Wisely* campaigns. Getting rid of useless medical practices needs the help of the public and of individual patients. We need to be humble and acknowledge that much of it is to do with saying that we got stuff wrong and now need to put it right. The world still contains hundreds of guidelines that recommend regular testing of blood lipids in people taking statins. Fortunately this practice is dying out in the UK, but is very much alive and well in the US. Here’s a study showing that in 90% of cases, it makes no difference to clinical decision making. Even when it does, it probably shouldn’t.


Screening for cancer in unprovoked venous thromboembolism

Now for another *Choosing Wisely* topic: should we screen for cancer in everybody who has an unprovoked episode of venous thromboembolism? The overall risk for having cancer detected in the year after unprovoked venous thromboembolism is one in 20. But it is not evenly distributed: the risk increases markedly over the age of 50. So there is probably a good case for screening older people after venous thromboembolism: but just how far should you go with testing (whole body computed tomography?) and what is the actual yield in terms of lives saved? The answers do not emerge clearly even though this is an exemplary systematic review and meta-analysis of individual participant data.

*Ann Intern Med* doi: 10.7326/M17-0868

The Importance of Being PURE

PURE is a five-continent observational study of diet in relation to cardiovascular disease in mortality in nearly 150,000 people. It is probably the best of its kind ever done, and concludes that “High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke.” But in these columns I have often implied that most dietary studies are bunk, and no observational study should be taken at face value unless it can be backed by randomised trial evidence. So believing PURE means sacrificing some intellectual purity. In this case I am willing to, because it seems the closest we are likely to get to the “truth” about diet and vascular disease. Follow-up was meticulous and households were studied as units, and the median time was 7.4 years. Above all, the main message was negative: there was no specific connection between carbohydrate intake and cardiovascular disease: the association was with total all-cause mortality. By contrast, eating more fat—including saturated—was associated with lower cardiovascular disease, meaning we can abandon the saturated-fat-cardiovascular disease hypothesis with some certainty.


So what does “healthy food” look like?

Plausibly, it looks like fruit, vegetables, and legumes. “Higher fruit, vegetable, and legume consumption was associated with a lower risk of non-cardiovascular, and total mortality. Benefits appear to be maximum for both non-cardiovascular mortality and total mortality at three to four servings per day (equivalent to 375–500 g/day).” Splendid. I’ll settle for fagioli con tonno, with lots of olive oil, followed by rib-eye steak swimming in a buttery sauce, a salad, fruit, cheeses, followed by strawberries and cream (no sugar).

Do patients at risk of infective endocarditis need antibiotics before dental procedures?

Thomas J Cahill,1 Mark Dayer,2 Bernard Prendergast,3 Martin Thornhill4

Infective endocarditis is a life threatening disease with 30% one year mortality1 that affects 3-10 per 100 000 population per year—the average general practitioner will see one case every 20 years.2 Infective endocarditis occurs when bacteria enter the bloodstream through the mouth, gut, or skin, and replicate within the heart to form a “vegetation,” which is usually adherent to one of the valves (fig 1, fig 2). Specific patient subgroups are at increased risk of infective endocarditis as a result of damaged cardiac endothelium, abnormal blood flow, intracardiac prosthetic material, immunosuppression, or recurrent bacteraemia (box).3,4

Streptococci which colonise the mouth are the causative organism in 20%-40% of patients with infective endocarditis,5,6 and poor oral hygiene is a known risk factor.7 Invasive dental procedures that disrupt gingival integrity allow oral bacteria to access the circulation, which can lead to infective endocarditis in at-risk patients. Strategies that prevent bacteraemia or bacterial adherence might be expected to reduce the risk of infective endocarditis.

Oral antibiotic prophylaxis has been used for more than 50 years as a preventative strategy in at-risk patients undergoing invasive dental procedures.8 The efficacy of antibiotic prophylaxis has been confirmed in animal models, however the clinical evidence base is weak and its use has been challenged in the last decade. Nonetheless, guidelines from the European Society of Cardiology and the American Heart Association/American College of Cardiology committees continue to advocate antibiotic prophylaxis for those at highest risk.9,10 Controversially, in 2008 the UK National Institute for Health and Care Excellence (NICE) advised complete cessation of antibiotic prophylaxis to prevent infective endocarditis.11 In this article, we outline the evidence for and against antibiotic prophylaxis, the controversy surrounding its use, and ongoing research in the field. We provide a framework for clinical practice in the context of uncertainty.

UNCERTAINTIES

Do invasive dental procedures cause infective endocarditis? Invasive dental procedures cause bacteraemia, which is a necessary precursor to infective endocarditis,12 but it is unclear if dental interventions cause infective endocarditis. In a prospective Dutch cohort of 427 cases of infective endocarditis, 31 (11%) had undergone an invasive procedure (medical or dental) within the preceding 30 days.13 In a French case control study of 171 infective endocarditis cases and matched controls, there was no substantial difference in the number of dental procedures in the preceding three months (odds ratio 1.2, 95% confidence interval 0.7 to 2.1).14 In a similar case control study of 273 cases and matched controls, an invasive dental procedure was undertaken during the three months before infective endocarditis diagnosis in 36 cases (13.2%) and 27 controls (9.9%) (odds ratio 1.6, 95% confidence interval 0.8 to 3.4), suggesting no statistically significant risk associated with dental intervention. More recently, a retrospective analysis of 739 patients in Taiwan found no increased likelihood of exposure to dental procedures in the three month period before infective endocarditis hospitalisation, compared with a control period when infective endocarditis did not develop.15 These studies suggest that invasive dentistry is not the trigger for most

WHAT YOU NEED TO KNOW

• Patients with prosthetic heart valves, previous infective endocarditis, and some types of congenital heart disease are at highest risk of infective endocarditis
• Invasive dental procedures cause bacteraemia, which can be complicated by infective endocarditis in those at increased risk of the disease
• Antibiotic prophylaxis reduces the incidence of bacteraemia, but high level studies confirming that this reduces the incidence of infective endocarditis are lacking
• Warn high risk patients undergoing high risk dental interventions of the risk of infective endocarditis. Offer these patients antibiotic prophylaxis, and discuss with them the risks and benefits of this option
• Where patients are at moderate risk, encourage preventative measures, such as maintaining good oral hygiene and infection control, and discourage tattooing or piercing
cases of infective endocarditis; however, the studies were conducted in populations already using antibiotic prophylaxis, which might mask an association. All studies were underpowered to address the question.4–15

If invasive dental procedures are not the main trigger, an alternative explanation is that community acquired infective endocarditis might arise from low level bacteraemia occurring as bacteria translocate across the relatively permeable oral mucosa in the course of everyday activities, such as chewing, flossing, or tooth brushing (especially in those with poor oral hygiene or periodontal disease).17 The cumulative burden of this “everyday” bacteraemia is several orders of magnitude greater than rare episodes of “surgical” bacteraemia that result from dental procedures. This could explain why many cases of infective endocarditis arise in the absence of a preceding dental intervention.18

In the context of this uncertainty, a French population based cohort study published in this issue of the BMJ is timely (p 353).19 Among 138 876 adults with prosthetic heart valves, there was no statistically significant increase in the risk of oral streptococcal infective endocarditis between analyses might be explained by unrecognised differences between the overall cohort and infective endocarditis cases: for example, oral hygiene and dental status were unknown on account of the limitations of coding. The case crossover analysis is likely to control for individual patient risk factors and suggests that invasive dental procedures are associated with oral streptococcal infective endocarditis in some patients. Importantly, however, both analyses support the concept that most cases of infective endocarditis arise independently of invasive dental procedures.

It is not clear whether reduction in the incidence of bacteraemia translates into reduction in the incidence of infective endocarditis

95% confidence interval 0.90 to 2.53, P=0.08). Over median follow-up of 1.7 years, there were 267 cases—an incidence of oral streptococcal infective endocarditis of 93.7 per 100 000 person years and overall rate of oral streptococcal infective endocarditis of 1.4 cases per 10 000 invasive dental procedures.

However, these findings were not replicated in a case crossover analysis in the same study, in which each of the cases served as their own control. The analysis compared the frequency of invasive dental procedures in the three months before a diagnosis of infective endocarditis with earlier control periods. Exposure to invasive dental procedures was substantially more frequent during case than control periods (5.1% v 3.2%, odds ratio 1.66, 95% confidence interval 1.05 to 2.63, P=0.03).

This description of a large, representative, population at risk of infective endocarditis is a valuable addition to the evidence base. The apparently discordant findings between analyses might be explained by unrecognised differences between the overall cohort and infective endocarditis cases: for example, oral hygiene and dental status were unknown on account of the limitations of coding. The case crossover analysis is likely to control better for individual patient risk factors and suggests that invasive dental procedures are associated with oral streptococcal infective endocarditis in some patients. Importantly, however, both analyses support the concept that most cases of infective endocarditis arise independently of invasive dental procedures.
If invasive dental procedures cause infective endocarditis in some patients, does antibiotic prophylaxis reduce the risk?

Antibiotic prophylaxis has been shown to reduce bacteraemia in multiple studies: a recent meta-analysis of 21 trials of antibiotic prophylaxis in patients undergoing dental intervention showed a substantial reduction in the incidence of post procedural bacteraemia (risk ratio 0.53, 95% confidence interval 0.49 to 0.57, P<0.01).20 It is not clear, however, whether reduction in the incidence of bacteraemia translates into reduction in the incidence of infective endocarditis.

No randomised controlled trial of antibiotic prophylaxis for prevention of infective endocarditis has ever been conducted. The evidence base evaluating antibiotic prophylaxis is therefore derived from observational data. Meta-analysis of three case-control studies15-22 showed no statistically significant association between cases and failure to use antibiotic prophylaxis (odds ratio 0.59, 95% confidence interval 0.27 to 1.30, P=0.14).20 However, these studies were underpowered to address this question and were at high risk of intrinsic bias, so the overall level of evidence is weak.20 Many of the patients within these studies were not high risk and would not be eligible for antibiotic prophylaxis according to current guidelines. The study published in this issue found that the crude incidence of infective endocarditis in the three months after an invasive dental procedure was lower in patients taking antibiotic prophylaxis (78.1 [95% confidence interval 1.6 to 154.6] v 149.5 [95% confidence interval 56.8 to 242.2] per 100 000 person years). These rates were not statistically significantly different, however, possibly because of the small number of cases in each group.21 In a moderate size retrospective cohort study, a protective effect of antibiotic prophylaxis was identified in high risk patients with a prosthetic heart valve undergoing invasive procedures (a proportion of which were dental).21 Similarly, a population based cohort study found a protective effect of antibiotic prophylaxis in individuals with cardiac conditions, using extrapolated estimates of the incidence of infective endocarditis after protected or unprotected dental procedures.24

An alternative observational approach has been to examine changes in the incidence of infective endocarditis after guideline amendments to restrict the use of antibiotic prophylaxis. In 2008, NICE recommended the cessation of antibiotic prophylaxis in the UK for all patients. Subsequent follow-up showed an 88% reduction in the use of antibiotic prophylaxis and an increase in the incidence of infective endocarditis above the projected historical trend (corresponding to an additional 35 cases in England per month).2 This study, however, lacked microbiological data to confirm that this change was secondary to an increase in oral streptococci infective endocarditis. In July 2016, NICE updated its guidance to indicate that antibiotic prophylaxis is not recommended “routinely” and that “this amendment should make clear that in individual cases antibiotic prophylaxis may be appropriate.”25

What are the risks and benefits of antibiotic prophylaxis?

There are legitimate concerns that the risks and low cost-effectiveness of antibiotic prophylaxis might outweigh the benefits.37 Widespread use of antibiotic prophylaxis might contribute to antibiotic resistance, although this has not been linked specifically to single dose antibiotic prophylaxis, and the risk of anaphylaxis might exceed the protective effect of antibiotic prophylaxis. However, recent analysis of UK adverse event reporting identified only two adverse events per year and no deaths from antibiotic prophylaxis with single dose amoxicillin, and clindamycin antibiotic prophylaxis (used in penicillin allergic patients) resulted in twice as many adverse events and one death every three years.25 Risk benefit analysis suggests that reinstatement of antibiotic prophylaxis for those at moderate or high risk of infective endocarditis would be associated with beneficial clinical effects overall.39 Moreover, such a change would lead to cost savings of £5.5-£8.2 million and health gains of >2600 quality adjusted life years in England per annum.40

Is ongoing research likely to provide relevant evidence?

Infective endocarditis rarely arises after a dental intervention, so conducting a randomised controlled
Fig 3 | Identifying patients at risk of infective endocarditis who might benefit from antibiotic prophylaxis and other preventative measures

Is this patient with a predisposing cardiac condition at high risk of infective endocarditis?

- Patients with any prosthetic valve
  - Transcatheter valves
  - Bioprosthetic valves
  - Homografts
- Patients with previous infective endocarditis
- Patients with congenital heart disease
  - Any type of cyanotic congenital heart disease
- Patients in whom any prosthetic material was used for cardiac valve repair

Is the dental intervention high risk?

- Involves manipulation of the gingival region of the teeth
  - Including extractions and scaling
- Involves perforation of oral mucosa
  - Excluding local anaesthetic injections
- Involves manipulation of periapical region of the teeth
  - Including root canal procedures

Offer antibiotic prophylaxis

after outlining risks and benefits and background of limited high quality evidence. See ESC guidelines (reference 10) for suggested antibiotic regimen

Then

1. Educate regarding symptoms of infective endocarditis
2. Advise maintenance of good oral hygiene; dental follow-up twice a year in high risk patients; yearly in others
3. Advise importance of infection control: disinfection of cutaneous wounds, curative antibiotics and benefits and for any focus of bacterial infection
4. Discourage piercing/tattooing and injecting drug use

EDUCATION INTO PRACTICE

- How do you identify patients at high and moderate risk of infective endocarditis? How could you make this process more robust?
- Has this article given you new ideas about how to discuss antibiotic prophylaxis for invasive dental procedures with patients at risk of infective endocarditis?
- Do you routinely give all high risk patients an infective endocarditis patient leaflet?
- Are you aware of the cardinal symptoms of infective endocarditis? Do you make sure that your high risk patients are aware of how to spot and respond to these symptoms?

trial is challenging. It is unclear whether even an international multicentre trial would be able to recruit sufficient numbers of patients in a pragmatic timescale. In the last decade, national funding agencies in both the US and UK have balked at the projected cost. Since the standard of care recommended by the European Society of Cardiology and American Heart Association/American College of Cardiology guidelines is that patients at highest risk of infective endocarditis should receive antibiotic prophylaxis, it is unclear whether a placebo controlled, “no antibiotic prophylaxis” trial would receive international ethical approval.

In this context, the priority is to clarify further the link between infective endocarditis and invasive dental procedures. To do this, we are conducting an observational study, the IDEA Study, to link NHS Digital hospital admissions data to the NHS Business Services Authority Dental Database and to determine whether the frequency of invasive dental procedures is higher in the three months before the diagnosis of infective endocarditis, compared with earlier three month “control” periods (https://www.journalslibrary.nihr.ac.uk/programmes/hta/155732/#/). This study will be highly powered to assess the link between invasive dentistry and infective endocarditis: in the proposed period of study between April 2009 and March 2015, there are data for 10 593 infective endocarditis admissions and 90.6 million invasive dental procedures. The study will be conducted in the English population, for whom antibiotic prophylaxis was not recommended during this period, thereby fully exposing any potential link between invasive dental procedures and infective endocarditis and the case crossover design will reduce any effect from residual confounders. Refuting a link between dental interventions and infective endocarditis would logically support a move away from antibiotic prophylaxis as a preventative strategy. Conversely, confirmation of the link would provide further justification for a randomised trial.

What should we do in light of the uncertainty?

The first step is to risk stratify the patient (fig 3). Consistent with European Society of Cardiology and American Heart Association/American College of Cardiology guidelines, we advocate that antibiotic prophylaxis is only considered for high risk patients: those with prosthetic valves, previous infective endocarditis, or certain types of congenital heart disease. We also suggest dental risk stratification: high risk procedures are those in which there is manipulation of the gingival or periapical region of the teeth (fig 3).

If both the patient and dental procedure are high risk, it is reasonable to offer the option of antibiotic prophylaxis. When offering antibiotic prophylaxis, you could:

- outline what is known about the potential risks and benefits
- explain that the evidence base is weak
- reassure the patient that the overall risk of infective endocarditis after a dental intervention is extremely low (even in those at high risk)
- For patients who choose antibiotic prophylaxis, we advise single dose amoxicillin 3 g given orally 60 minutes before the procedure, or clindamycin 600 mg in those who are allergic to penicillin.

Early diagnosis of infective endocarditis can be life saving but it requires a high index of suspicion among dentists, general practitioners, and hospital doctors.

Competing interests: See bmj.com.

Cite this as: BMJ 2017;358:j3942
Find the full version with references at http://dx.doi.org/10.1136/bmj.j3942

RESEARCH, p 353
Diagnosis and treatment of endometriosis
Laura Kuznetsov, Katharina Dworzynski, Melanie Davies, Caroline Overton

Endometriosis is one of the most common gynaecological disorders, affecting an estimated 10% of women in the reproductive age group (usually 15-49 years old), and in the UK it is the second most common gynaecological condition (after fibroids). It is a long term condition causing pelvic pain, painful periods, and subfertility. Endometriosis presents a diagnostic and clinical challenge, with many women left undiagnosed, often for many years. The diagnostic delay is not limited to adults; endometriosis is also often missed in adolescent girls.

This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) on diagnosis and management of endometriosis. The recommendations were based on consideration of the available evidence, which was mostly of very low quality and seldom of moderate or high quality, and the expert opinion of the Guideline Committee (GC).

The overall aim of the guideline is to improve the diagnosis and management of endometriosis in community services, gynaecology services, and specialist endometriosis services. This summary focuses on investigation, early management, and referral for women with suspected endometriosis, and is aimed mainly at general practitioners and healthcare professionals in community services.

WHAT YOU NEED TO KNOW

- Endometriosis can be difficult to diagnose, with some studies showing a delay in diagnosis of 4-10 years, resulting in decreased quality of life and disease progression
- Endometriosis cannot be ruled out by a normal examination and pelvic ultrasound
- Hormonal treatments for endometriosis suppress menstruation and reduce pain. They are contraceptive, but have no effect on fertility after discontinuation
- Refer women to a gynaecology service if they have severe, persistent, or recurrent symptoms of endometriosis, if they have pelvic signs of endometriosis, or if initial management is not effective, not tolerated, or is contraindicated
- Endometriosis can be a long term condition, with substantial physical, sexual, psychological, and social impact

Recommendations

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

When to suspect endometriosis

Recommendations on endometriosis symptoms and signs are summarised in the box on p 374, and a pathway for initial management of suspected endometriosis is presented in the infographic.

Investigating suspected endometriosis

Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, ultrasound scan, or magnetic resonance imaging is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation (see below).

Imaging: ultrasound scanning

- Consider transvaginal ultrasound:
  - To investigate suspected endometriosis even if the pelvic and abdominal examination is normal
  - To identify endometriomas and deep endometriosis involving the bowel, bladder, or ureter.
- If a transvaginal scan is not appropriate (for example, in women who have never had sexual intercourse), consider a transabdominal ultrasound scan of the pelvis.

Imaging: magnetic resonance imaging (MRI)

- Do not use pelvic MRI as the primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis.
- Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder, or ureter.

Blood tests: cancer antigen 125 (CA-125)

- Do not use serum CA-125 to diagnose endometriosis.
- If a coincidentally reported serum CA-125 level is available, be aware that:
  - A raised serum CA-125 titre (≥35 IU/mL) may be consistent with having endometriosis
  - Endometriosis may be present despite a normal serum CA-125 level (<35 IU/mL).

Diagnostic laparoscopy

- Consider laparoscopy to diagnose endometriosis in women with suspected endometriosis, even if the ultrasound scan was normal.
**Endometriosis–initial management**

Based on NICE guidance—Endometriosis: diagnosis and management

### At first presentation

#### Symptoms and signs

- Suspect endometriosis in women (including young women aged ≤ 17 years) with 1 or more of:
  - Chronic pelvic pain
  - Period related pain (dysmenorrhoea)
  - Deep pain during or after sex
  - Period related or cyclical symptoms
  - Gastrointestinal particularly painful bowel movements
  - Urinary particularly blood in the urine or pain passing urine
  - (These symptoms may be associated with infertility)

#### Investigations

- Offer abdominal and pelvic examination to identify:
  - Reduced organ mobility and enlargement
  - Tender nodularity in the posterior vaginal fornix
  - Visible vaginal endometriotic lesions
  - Consider an ultrasound scan

#### Assess needs

- Assess women’s individual information and support needs:
  - Circumstances
  - Symptoms
  - Daily living
  - Physical needs
  - Psychosexual needs
  - Priorities
  - Work and study
  - Cultural background
  - Emotional needs
  - Desire for fertility

#### Initial treatment

- **Analgesics**
  - Short trial (for example, 3 months) of paracetamol or NSAID alone or in combination

- **Hormonal treatment**
  - Combined contraceptive pill or progestogen

- **Treatment with neuromodulators**
  - Refer to the NICE guideline on neuropathic pain

#### Consider referral

- If trial of analgesics does not provide adequate pain relief
- If initial hormonal treatment for endometriosis is not effective, contraindicated, or not tolerated

#### If fertility is a priority

- Management by multidisciplinary team with input from a fertility specialist
- Diagnostic fertility tests
- Consider other recommended fertility treatments such as assisted reproduction

#### Referral

- **Gynaecology service**
  - Refer to this service if:
    - Severe, persistent, or recurrent symptoms of endometriosis
    - Pelvic signs of endometriosis
    - Initial management is not effective, not tolerated or is contraindicated

- **Specialist endometriosis service**
  - Refer to this service if:
    - Suspected or confirmed deep endometriosis involving:
      - Bladder
      - Bowel
      - Ureter

- **Paediatric and adolescent gynaecology**
  - Refer young women (aged ≤ 17 years) to this service
  - If no service available, refer to specialist endometriosis service

---

Disclaimer: This infographic is not a validated clinical decision aid. This information is provided without any representations, conditions or warranties that it is accurate or up to date. BMJ and its licensors assume no responsibility for any aspect of treatment administered with the aid of this information. Any reliance placed on this information is strictly at the user’s own risk. For the full disclaimer wording see BMJ’s terms and conditions: http://www.bmj.com/company/legal-information/
They have severe, persistent, or recurrent symptoms

How laparoscopic surgery could affect endometriosis

The possible need for further planned surgery for deep endometriosis that conservative treatments have been unsuccessful, unless the woman shows signs of deep endometriosis involving the bowel, bladder, or ureter.

Evidence suggests endometriosis is often not suspected in young women and, because of this they are often not referred to the right services for endometriosis.

The management of endometriosis-related subfertility should have multidisciplinary team involvement with input from a fertility specialist.

Surgical management if fertility is a priority

The management of endometriosis-related subfertility should have multidisciplinary team involvement with input from a fertility specialist.

Competing interests: We declare the following interests based on NICE’s policy on conflicts of interests (available at http://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/code-of-practice-for-declaring-and-managing-conflicts-of-interest.pdf): MD and CO have private practice that may include treating women with endometriosis. These authors’ full statements can be viewed at www.bmj.com/content/bmj/358/bmj.3935/related#datasupp.

Cite this as: BMJ 2017;358:j3935

Find the full version with references at http://dx.doi.org/10.1136/bmj.j3935
CASE REVIEW

Peri-orificial rash in an infant

A 6 month old girl was brought to the paediatric dermatology outpatient clinic with a rash, irritability, and poor weight gain for two months. She was born at 32 weeks’ gestation with intrauterine growth restriction as a result of placental insufficiency. She was exclusively breastfed. There was no family history of skin disorders. On examination, she had scaly erythematous plaques around her eyes, nose, mouth, ears, and neck (figure).

She had been recently prescribed mild topical corticosteroids to treat presumed atopic dermatitis, but there had been no improvement.

Skin swabs and scraping for bacterial and fungal microscopy and culture were taken. The serum zinc level of the child and her mother, and the full blood count and liver function tests for the child were obtained.

1 What are the differential diagnoses?
2 Which differential diagnosis is most likely?
3 What is the most appropriate initial management for this condition?

Submitted by Hui Min Liew and Jin Ho Chong
Parental consent obtained.

Cite this as: BMJ 2017;358:j3606

SPOT DIAGNOSIS

Abnormalities on computed tomography of the pancreas

A 35 year old man described 16 kg weight loss over the past six months, low mood, and poor appetite. He was concerned that he might have cancer. He reported that he smoked 10 cigarettes per day. He had been a carrier of hepatitis B virus for 10 years, and had been taking entecavir for three years although not consistently. Before the age of 28, he drank 500 mL of high concentration spirits daily until an episode of acute pancreatitis five years ago, and had not drunk alcohol since.

Physical examination revealed mild abdominal tenderness. In laboratory tests, serum lipase was 65 U/L (normal level 60 U/L), aspartate amino transferase was 380 U/L (normal range 0-40 U/L), amino alanine transferase was 210 U/L (0-40 U/L), and fasting blood glucose was 4.72 mmol/L (3.82-6.11 mmol/L).

A computed tomography (CT) scan of the patient’s abdomen was taken (fig 1). What abnormalities are shown on the CT image?

Submitted by Lin-Hai Yan, Li Li, and Jian-Si Chen
Patient consent obtained.

Cite this as: BMJ 2017;358:j3979

Abnormalities on computed tomography of the pancreas

The extensive high density shadow analogous to a bony structure is a calcified suffused pancreas, suggesting advanced chronic pancreatitis. A thickened duodenum and mild splenomegaly are also visible (fig 2).

1 Abnormalities on computed tomography of the pancreas

Fig 1 | Extensive calcification in pancreas (arrow 1), mild splenomegaly

Fig 2 | Extensive calcification in pancreas (arrow 1), mild splenomegaly, and thickened duodenal wall (arrow 2).
**MINERVA A wry look at the world of research**

**Siderosis bulbi: out of sight, out of mind?**

A 57 year old man presented to the emergency department with a foreign body in the cornea after drilling metal. The object was removed and no further injury suspected. He was referred to the cataract service 11 months later after noticing gradual deterioration in vision and reduced night vision. On examination, brown discoloration of the lens and iris transillumination were detected (figure). A computed tomography scan found a metal intraocular foreign body. Electrodiagnostics showed evidence of siderosis bulbi, a rare cause of visual loss. Ionised iron is toxic to ocular tissues. On presentation, patients with high velocity injury should undergo dilated fundus and iris transillumination examinations to promptly detect and subsequently remove any intraocular foreign body.

**Zika virus**

On the subject of infectious agents and neurological disease, a series of cases from a tertiary care centre in Rio de Janeiro, Brazil, suggests that Zika virus is responsible for a recent rise in admissions for Guillain Barré syndrome and encephalitis (JAMA Neurol doi: 10.1001/jamaneurol.2017.1703). Out of 40 patients with new-onset para-infectious or neuro-inflammatory disease admitted between December 2015 and May 2016, 35 showed molecular or serological evidence of acute Zika virus infection in blood or cerebrospinal fluid samples.

**Multiple sclerosis in the armed forces**

An analysis of occupational mortality in England and Wales from 1979 to 2010 finds that deaths from multiple sclerosis among men in the armed forces are two to three times commoner than expected (Occup Med doi: 10.1093/occmed/kqox083). If chance, bias, and confounding can be ruled out, and the investigators argue they can, there must be an underlying occupational hazard. One possibility is that the close proximity in which military recruits live and work facilitates the transmission of an infectious agent.

**Frailty index**

Frailty is usually defined in terms of reduced physiological reserves and impaired ability to cope with stressors, such as surgery. So there’s an element of circularity in a study from the US which finds that 30 day readmission rates and postoperative complications are greater in people with high scores on the Modified Frailty Index (JAMA Surg doi: 10.1001/jamasurg.2017.1025). None of the individual components of the frailty index exerted a particularly strong influence, which must limit the potential for effective preoperative intervention.

**Overtreating diabetes**

Insulin and oral antidiabetes drugs come second only to warfarin and antiplatelet agents as iatrogenic causes of hospital admission in older people. A survey of prescribing data in 16 UK general practices helps explain why (Diabetic Med doi: 10.1111/dme.13380). Among nearly 4000 people aged over 70 with type 2 diabetes, more than a third were taking sulfonylureas or insulin. Neither the drugs chosen nor the glycaemic targets that were set seemed to take account of the high prevalence of both chronic kidney disease and cognitive impairment.

**Measuring arterial stiffness with bathroom scales**

Aortic pulse wave velocity, a measure of aortic elasticity, might be a useful predictor of cardiac risk but it’s difficult to evaluate it outside the laboratory. An ingenious new method uses bathroom scales as a ballistocardiograph to detect aortic valve opening, and a simple impedance plethysmograph to pick up the arrival of the pulse wave at the foot (Am J Hypertens doi: 10.1093/ahj/hpx059). The time difference between the two, divided by the person’s height, estimates arterial pulse wave velocity with surprising accuracy.

**The value of genograms**

Genogram is the technical name for the symbolic family histories that medical students are taught to record. Later in their careers, unless they become geneticists or family therapists, many doctors cease to bother with them. An article in the Postgraduate Medical Journal explains why this is a mistake (Postgrad Med J doi: 10.1136/postgradmedj-2017-135241). These little diagrams pack a lot of potentially useful information into a small space and they’re quick and easy to record. What’s more, constructing them provides an opportunity for patient and doctor to work together.

**Chronic low back pain**

Pregabalin and gabapentin, both analogues of gamma-aminobutyric acid, are sometimes helpful in treating neuropathic pain. However, a systematic review in PLoS Medicine reckons that there is no justification for extending their use to people with chronic low back pain (PLoS Med doi: 10.1371/journal.pmed.1002369). Although gabapentin was slightly better at relieving symptoms than placebo, pregabalin proved less effective than conventional analgesics. Any benefits from these drugs were outweighed by the risk of adverse effects, which included dizziness, fatigue, and visual disturbances.

Cite this as: BMJ 2017;358:j4073