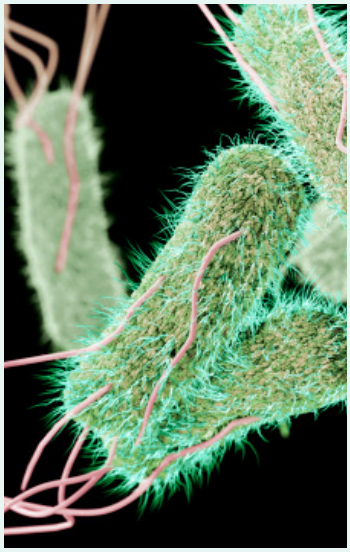
education

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



Promising new typhoid vaccine

The last typhoid outbreak in the UK happened in Aberdeen in 1964. I joined the queue to get vaccinated in far-off Sheffield, and then fainted at the bus stop. This was my only experience of syncope: it was very embarrassing to the adolescent RL, and I vowed never to go near doctors or needles again. Worldwide, there are still 2 million cases of typhoid a year (and 200 000 deaths), and newer, better typhoid vaccines are needed. It looks as if some that are already around and used in infants might be effective in adults as well: this trial compared Vi-conjugate, Vi-polysaccharide, or control meningococcal vaccine in 112 healthy volunteers. It will need proper field trials, but the study showed that Vi-conjugate is a highly immunogenic vaccine that substantially reduces typhoid fever cases when assessed using a stringent controlled model of typhoid infection.

Lancet doi:10.1016/S0140-6736(17)32149-9

Medicine: too big for the human brain?

A while back, there was a *New Yorker* cartoon consisting of a huge billboard in the middle of nowhere saying, "Stop And Think." Two small wayfarers stood beneath it, and one was saying, "It makes you stop and think, doesn't it?" Here is a perspective piece with the title "Lost in thought—the limits of the human mind and the future of medicine." Its central proposition is that the complexity of medicine now exceeds the capacity of the human mind. The article is open access and takes about 10 minutes to read slowly. Do you agree with the authors' formulation of the problem? Do you think the solutions they propose are valid? Don't send me your answers. Just stop and think.

N Engl J Med doi:10.1056/NEJMp1705348

Does primary care have a future?

It's difficult to address any meeting in the UK at present without being asked if you think general practice has a future. Seven years after retiring from my partnership, I'm not the best person to ask. But it's pretty clear that the old British model—which I think was wonderful in many ways—is collapsing and there is no sign of the political will or vision to put it back together again. But at least we are not America. If you want a bit of Schadenfreude, there are a few articles on the *JAMA Internal Medicine* website that bewail the demise of primary care over there. Just when humane, joined up thinkers are needed more than ever, they are being pushed out of the system, in the US even more comprehensively than in the UK. Stop and think. In an age of information overload and unfathomable new uncertainty, will IBM Watson suffice? Or will each ill and anxious person need an informed friend and advocate within the system?

JAMA Intern Med doi:10.1001/jamainternmed.2017.4991

Storage time and red cells for critically ill patients

Blood banks usually issue the oldest stored red cells in sequence, and in this five-nation study, that meant blood that was on average 22 days old. But perhaps the sickest patients needing acute transfusion would benefit from the most recently donated red cells, and in this trial that meant about 11 days. Here is a trial that recruited nearly 5000 critically ill adults, and its primary end point was death within 90 days. This was a common event, happening in 24.8% of those given freshest blood red cells and 24.1% in those given oldest blood red cells. So, this is another great trial addressing an important clinical question, and giving a clear answer: no difference.

N Engl J Med doi:10.1056/NEJMoa1707572

Within hospital age differences in myocardial infarction outcomes

Avedis Donabedian studied quality measures within health systems for about 30 years, and concluded that there were no metrics which were both simple and reliable. Survival and rehospitalisation following myocardial infarction might seem to be simple, but actually they are not. In the great tradition of the Center for Outcomes and Evaluation at Yale, Kumar Dharmarajan explores how these metrics can vary according to the age of patients. Hospitals that have the best outcomes for younger myocardial infarction patients are not necessarily the same as those with best outcomes for older people, and vice versa.

Ann Intern Med doi:10.7326/M16-2871

PRACTICE POINTER

Indications for anticoagulant and antiplatelet combined therapy

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CPD READING
0.5 HOURS

Antithrombotic medications reduce thromboembolic events by inhibiting platelet aggregation and coagulation. Antiplatelet drugs and oral anticoagulants are examples of antithrombotic medications and are among the most commonly prescribed drugs in both primary and secondary care.[1] However antiplatelets and oral anticoagulants are the drug classes most commonly implicated in adverse drug reactions occurring both in the community and in hospital.[2 3] Increasing numbers of patients have an indication for combination antiplatelet and oral anticoagulant therapy. For example, more than one million people in the UK have atrial fibrillation, of whom approximately one third also have an indication for antiplatelet therapy as secondary prevention.[4] Despite the need to understand the balance between benefit and risk, there are limited randomised data investigating antithrombotic co-prescription. Current guidelines are therefore based on expert opinion and the extrapolation of non-randomised data.

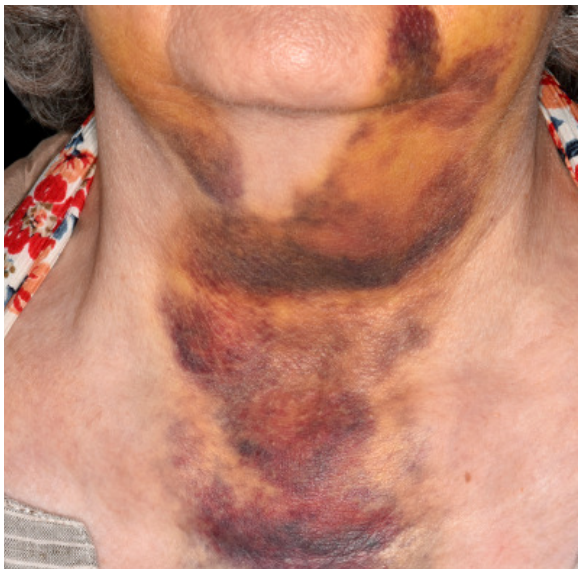
Who might need co-prescription?

Patients can develop independent indications for antiplatelet and oral anticoagulant therapy, but in most cases the pathophysiology will intersect. The relationship between cardiovascular disease and atrial fibrillation is the typical example, where one fifth of patients presenting with atrial fibrillation will subsequently require coronary intervention, and up to one fifth of acute coronary syndrome (including ST elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina) presentations develop atrial fibrillation.[5 6] Similarly, patients with essential thrombocythaemia and polycythaemia vera can be prescribed aspirin for primary prevention of cardiovascular disease, but may also require oral anticoagulation due to the high lifetime prevalence for venous thrombosis.[7]

Combination antithrombotic therapy increases the risk of fatal and non-fatal bleeding

WHAT YOU NEED TO KNOW

- Combination antithrombotic treatment increases the risk of bleeding, and this risk should be estimated and discussed with patients to guide treatment decisions (eg, using risk scores such as HAS-BLED)
- In most patients with independent indications for both antiplatelet and oral anticoagulant therapy the pathophysiology will intersect and combination antithrombotic treatment may not be necessary
- When co-prescribing, check that the patient is not prescribed medication that will increase bleeding risk further (eg, non-steroidal anti-inflammatory drugs) and consider the addition of an H_2 antagonist or proton pump inhibitor.



SPL

Bruising after tooth extraction in a patient taking warfarin

What are the risks of co-prescription?

Combination antithrombotic therapy increases the risk of fatal and non-fatal bleeding. In a Danish registry of patients with atrial fibrillation (n=82 854; mean follow-up over three years) the annual incidence of bleeding was less than 4% for aspirin or warfarin monotherapy, but rose to 15.7% for triple therapy comprising aspirin, clopidogrel, and warfarin.[8] The gastrointestinal tract is the most common site for bleeding, followed by upper airways.

Is the balance of benefit and risk quantifiable for an individual patient?

There are numerous scoring systems to prognosticate clinical outcomes (box), although none have been developed specifically in the context of combination antithrombotics. However, the patient cohort used to develop the CHA_2DS_2-VASc score was prescribed antiplatelet drugs in 74.0% of cases and so provides a reasonable estimation of annual stroke risk for patients already prescribed an antiplatelet drug.[9 10] In contrast, only 7.1% of the cohort used to develop the HAS-BLED score were co-prescribed an antiplatelet and oral anticoagulant, although subsequent investigation showed that HAS-BLED predicted bleeding events with moderate accuracy.[11 12] These two scoring systems are endorsed by European cardiovascular guidelines.[13]

Should everyone who has an indication for antiplatelet therapy plus oral anticoagulant be prescribed both?

The decision to co-prescribe antithrombotic medication must be based on the relative merit of each indication, the incremental risk of bleeding, and patient preference. Common clinical scenarios discussing possible indications for combination therapy are discussed below.

Primary prevention of cardiovascular disease

Antiplatelets are not licensed for the primary prevention of cardiovascular disease, although there is weak evidence that aspirin might confer some benefit in patients who are hypertensive and have impaired renal function or elevated risk for cardiovascular disease (10 year risk >20%).[14 15]

In patients who develop an indication for an oral anticoagulant, this should replace the antiplatelet agent for which evidence is weak.

Secondary prevention of cardiovascular disease

Antiplatelet therapy is recommended for the secondary prevention of cardiovascular disease.[16] In patients with stable coronary artery disease who have an additional indication for oral anticoagulation, it is recommended they are prescribed oral anticoagulant monotherapy unless they are very high risk for coronary events. In these patients the addition of aspirin or clopidogrel might be considered.[13]

Non-valvular atrial fibrillation and treatment after acute coronary syndrome or percutaneous coronary intervention

In patients with non-valvular atrial fibrillation who have acute coronary syndrome and/or undergo percutaneous coronary intervention, the combination and duration of antithrombotic therapy depend on stroke risk (CHA_2DS_2-VASc score), bleeding risk (HAS-BLED score), and clinical setting (stable coronary artery disease versus acute coronary syndrome).[13]

In general, it is recommended that patients receive triple therapy for the initial phase (four weeks to six months after the event), followed by dual therapy (antiplatelet plus oral anticoagulant) to complete 12 months of treatment.[13]

In patients at high risk of bleeding, the use of bare metal stents over drug eluting stents is recommended to shorten dual antiplatelet and anticoagulant therapy to four weeks.[13]

At 12 months after the event, treatment should be as per secondary prevention of cardiovascular disease (ie, antiplatelet only or oral anticoagulant if indicated).

Valvular heart disease

Oral anticoagulant therapy is recommended for all patients with native valvular heart disease and atrial fibrillation.[17] Choice of oral anticoagulant is limited to warfarin, as clinical trials for direct oral anticoagulants (DOACs) in valvular heart disease have not been undertaken.

The target international normalised ratio is determined by a combination of prosthesis thrombogenicity and patient related risk factors.[17]

The addition of an antiplatelet to oral anticoagulants reduces the risk of valve thrombosis and arterial thromboembolism but at an increased risk of major bleeding.[18]

Oral anticoagulants are recommended lifelong for patients with a mechanical prosthesis, with the possible addition of low-dose aspirin in patients with concomitant atherosclerotic disease.[17]

Bioprosthetic values might not require oral anticoagulants beyond three months after insertion unless there is another indication such as atrial fibrillation.

Risk factors for stroke in atrial fibrillation (CHA_2DS_2-VASc) and for bleeding in patients on anticoagulation (HAS-BLED)

For details on calculation of these scores and how to use them to guide therapy, see nice.org.uk/guidance/cg180/chapter/key-priorities-for-implementation

CHA_2DS_2-VASc

- Congenital heart failure
- Hypertension
- Age 65-74, or ≥ 75 years
- Diabetes mellitus
- Stroke, transient ischaemic attack, or thromboembolism
- Vascular disease
- Female sex

HAS-BLED

- Hypertension
- Abnormal liver function
- Abnormal renal function
- Stroke
- Bleeding
- Labile international normalised ratios
- Age › 65 years
- Drugs that predispose to bleeding (ie, antiplatelet medications or non-steroidal anti-inflammatory drugs)
- Alcohol

Usually, aspirin should be prescribed as the first line antiplatelet agent

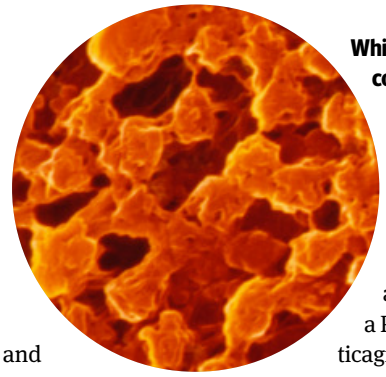
Venous thromboembolism

Acute deep vein thrombosis in patients prescribed antiplatelets should be treated with oral anticoagulants for a minimum of three months.[19] In patients with intermediate to high risk of bleeding, consider stopping any antiplatelet for the duration of the treatment unless there is an acute indication (eg, recent cardiac event).

On completion of treatment for a provoked deep vein thrombosis the patient should return to their pre-event antithrombotic regimen. Patients who have had an unprovoked deep vein thrombosis should be investigated and might continue long term oral anticoagulants in place of the pre-event antithrombotic regimen.[19 20]

Myeloproliferative disorders

Patients with essential thrombocytosis or polycythaemia vera are prescribed low-dose aspirin to mitigate their increased thrombotic risk. There is insufficient evidence to suggest that thromboembolism in this population should be treated differently from the regimen described above.[21]



Effective haemeostasis relies on platelet-to-platelet adhesion

Which antiplatelets and oral anticoagulants can be combined?

Aspirin should be prescribed as the first line antiplatelet agent unless the patient is intolerant or has a compelling contraindication. In patients receiving dual antiplatelet therapy, for example after percutaneous coronary intervention without an indication for an oral anticoagulant, then a $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, or ticagrelor) is added. The novel $P2Y_{12}$ inhibitors

Combining antiplatelets and anticoagulants

Antiplatelets

APL

Monotherapy

ASP Aspirin

Aspirin should be prescribed as the first-line antiplatelet agent unless the patient is intolerant or has a compelling contraindication

+

Dual therapy

For dual antiplatelet therapy, a $P2Y_{12}$ inhibitor can be added:

CLO Clopidogrel

PRA Prasugrel

TIC Ticagrelor

Combining novel $P2Y_{12}$ inhibitors with oral anticolaguants increases risk of bleeding, and cannot currently be recommended

Oral anticoagulants

OAC

WAR Warfarin

Warfarin is the most commonly used anticoagulant

DOAC

Direct oral anticoagulants

These are thought to be a safe alternative to warfarin, although there remains uncertainty about risks versus benefits

Patients should be prescribed the lower licenced dose of a DOAC when combined with an antiplatelet

API Apixaban

DAB Dabigatran

RIV Rivaroxaban

Example clinical scenarios

1 Cardiovascular disease

Primary prevention

ASP

Antiplatelets are not licensed for the primary prevention of cardiovascular disease. However, there is weak evidence that aspirin may confer some benefit in patients who are hypertensive and have impaired renal function or elevated risk of CVD

If a patient develops an indication for an OAC, this should replace the antiplatelet agent

~~APL~~ OAC

Secondary prevention

APL

Antiplatelet therapy is recommended for the secondary prevention of cardiovascular disease

If a patient develops an indication for an OAC:

~~APL~~ OAC

Stable coronary artery disease

OAC monotherapy is recommended instead of antiplatelet

Very high risk for coronary events

Consider adding aspirin or clopidogrel to OAC

OAC + ASP/CLO

2 Non-valvular atrial fibrillation

Generally, patients who have an acute coronary syndrome and/or undergo percutaneous coronary intervention could benefit from:

4-6 months
Triple therapy
ASP + CLO + OAC

To complete 12 months
Dual therapy
APL + OAC

After 12 months
As per secondary prevention of CVD

Combination and duration depends on stroke risk, bleeding risk, and clinical setting

In patients who are at high risk of bleeding, the use of bare-metal stents over drug-eluting stents is recommended to shorten dual antiplatelet and anticoagulant therapy to four weeks

3 Deep vein thrombosis

APL + OAC

DVT in patients prescribed antiplatelets should be treated with OACs for a minimum of three months

In patients with intermediate-to-high bleeding risk, consider stopping any antiplatelet for the duration of the treatment–unless there is an acute indication (such as a recent cardiac event)

~~APL~~

4 Valvular heart disease

WAR Warfarin is recommended for all patients with native valvular heart disease and atrial fibrillation

Clinical trials for direct oral anticoagulants (DOACs) in valvular heart disease have not been undertaken

DOAC ?

+ ASP/CLO

The addition of an antiplatelet reduces risk of valve thrombosis and arterial thromboembolism but at an increased risk of major bleeding

OAC

Oral anticoagulants are recommended lifelong for patients with a mechanical prosthesis

Bioprosthetic values might not require oral anticoagulants beyond three months after insertion

EDUCATION INTO PRACTICE

- How do you monitor whether the indications continue to be clear and appropriate for co-prescription of oral anticoagulants and antiplatelets?
- Does this article give you any ideas about how to approach a discussion with patients about the risk:benefit of prescribing oral anticoagulants and antiplatelets?
- What will you do differently as a result of reading this article?

(prasugrel and ticagrelor) are reserved for patients with acute coronary syndrome as they inhibit platelet activity to a greater extent than clopidogrel and so increase the risk of bleeding.[22-24] The combination of novel $P2Y_{12}$ inhibitors with oral anticoagulants increases the risk of bleeding, and cannot currently be recommended. In patients with atrial fibrillation and coronary artery disease, the dose of warfarin should be carefully regulated to a target INR 2.0-2.5.[13] DOACs (apixaban, dabigatran, rivaroxaban) have been generally shown to be a safe alternative to warfarin for the management of both atrial fibrillation and venous thromboembolism, although there remains uncertainty with regards to real world risk:benefit.[25-27] Prescribe patients the lower licensed dose of a DOAC when combined with an antiplatelet. In patients on warfarin with a stable international normalised ratio there is no indication to switch to a DOAC.[13] Where prescribers choose to switch between oral anticoagulants, it is important that they check both the licensed indications and contraindications of the new medication, as these differ between oral anticoagulants.

CASE STUDIES

Case 1

A 63 year old, post-menopausal woman visits her general practitioner having noticed intermittent blood in her urine. These episodes have been associated with dysuria, but she denies increased frequency or vaginal discharge. She reports that her urine has been a light pink colour and that she first noticed this after commencing rivaroxaban 20 mg once daily five weeks ago for an unprovoked, below knee deep vein thrombosis. Her medical history includes stable ischaemic heart disease, for which she takes clopidogrel 75 mg once daily (she is intolerant of aspirin). Clinical examination is unremarkable. Her heart rate is 65 beats/min and blood pressure 145/76 mmHg. Urine is coloured pink; dipstick reveals 4+ blood and trace protein. Is it appropriate to attribute the haematuria to antithrombotic therapy? Should her antithrombotic therapy be stopped?

Discussion Perform a full blood count and screening for renal function and coagulation as initial investigations. Don't attribute macroscopic haematuria to antiplatelet and/or anticoagulant therapy without urological investigation, and so refer the patient on a two week wait cancer pathway.[30 31] The rivaroxaban is required to prevent propagation of deep vein thrombosis and/or embolism and so should be continued unless bleeding is sufficient to require inpatient assessment. The clopidogrel is prescribed for secondary prevention and so short-term cessation is low risk.

Case 2

A 71 year old man undergoes an angiogram after acute coronary syndrome and receives two drug eluting stents in an uncomplicated percutaneous coronary intervention. His medical history includes non-valvular atrial fibrillation for which he takes warfarin. Prognostic scoring shows that he is high risk for stroke (CHA_2DS_2-VASc) and intermediate risk for bleeding (HAS-BLED). What is the optimum antithrombotic strategy?

Discussion The patient should receive triple antithrombotic treatment for six months, at which point aspirin can be stopped. At 12 months after the percutaneous coronary intervention, switch the patient to oral anticoagulant monotherapy.[13]

What else needs to be considered when co-prescribing?

Pharmacology

Check that the patient is not prescribed medication that will increase bleeding risk further (eg, non-steroidal anti-inflammatory drugs).

Consider the addition of an H_2 antagonist or proton pump inhibitor to reduce the risk of gastrointestinal bleeding.

Patient factors

Discuss the risk:benefit of treatment with all patients, with specific emphasis on the required duration of treatment if they are undergoing any procedure that will necessitate co-prescription (eg, coronary stent insertion).

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We asked two patients to review the article, both of whom are prescribed antiplatelet medication for secondary prevention and involved in research governance. Feedback focused on the "partnership between patient and practitioner" when making prescribing decisions, and that, due to the stress that can be caused by excessive bleeding, "each case should be carefully considered with respect to the balance struck between the protection of a patient's medical welfare and their quality of life." In response we put greater emphasis on considering the risk:benefit balance throughout the article. The case studies in this article are hypothetical.

Use the CHA_2DS_2-VASc and HAS-BLED scores to aid this discussion.

Risk stratification is a dynamic process, and is best performed at regular intervals (ie, on a yearly basis).[13] Consider the patient's ability to adhere to the medication regimen and take steps to assist as necessary (eg, dosette box, care package).

Physician factors

Discharge patients on medications that are available for prescription on community formularies.

Ensure that suitable follow-up is arranged to review termination or continuation of antithrombotic treatment as appropriate.

How might recommendations change in the future?

There is emerging evidence that triple antithrombotic therapy results in no better cardiovascular outcome and an increase in bleeding when compared with clopidogrel plus oral anticoagulant.[28 29] Upcoming studies aim to report on whether aspirin provides any benefit when prescribed with novel $P2Y_{12}$ inhibitors, the optimum DOAC dose when combined with an antiplatelet, and the duration of antiplatelet therapy after acute coronary syndrome.

Competing interests: None declared.

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Faltering growth in children

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Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on bmj.com.

CPD READING
0.5 HOURS

Growth in infants and preschool children is a common cause for parental and professional concern. Some weight loss is common in the early days of life, while establishing feeding, and is usually a physiological phenomenon associated with fluid shifts.[1] The term "faltering growth" is used to describe a pattern of slower weight gain than expected for age and sex in infants and preschool children after these early days and is most often due to inadequate nutritional intake.

Concerns about faltering growth arise in up to 5% of infants and preschool children, depending on the definition used.[2 3] This article summarises the recent National Institute for Health and Care Excellence (NICE) guidance on the recognition and management of infants and preschool children with faltering growth,[5] focusing particularly on recommendations for primary care professionals.

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 are based on the experience and opinion of the Guideline Committee of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Weight loss in the early days of life

The pattern of initial weight loss and return to birth weight varies between infants.

Assessment and management of early weight loss and faltering growth is presented in the infographic. Initial assessment usually involves joint working between GP and other professional such as a health visitor or midwife.

- Be aware that:
  - It is common for infants to lose some weight during the early days of life
  - This weight loss usually stops after 3 or 4 days of life
  - Most infants have returned to their birth weight by 3 weeks of age.
- If infants in the early days of life lose more than 10% of their birth weight:
  - Perform a clinical assessment, looking for evidence of dehydration or of an illness or disorder that might account for the weight loss
  - Take a detailed history to assess feeding (see NICE guideline on postnatal care up to 8 weeks after birth[6])
  - Consider direct observation of feeding
  - Ensure observation of feeding is done by an individual with appropriate training and expertise (for example, in relation to breastfeeding and bottle feeding)
  - Perform further investigations only if they are indicated by the clinical assessment.
- Provide feeding support (see NICE guideline on postnatal care[6]) if there is concern about weight loss in infants in the early days of life.
- If infants lose more than 10% of their birth weight in the early days of life, or they have not returned to their birth weight by 3 weeks of age, consider:
  - Referral to paediatric services if there is evidence of illness, marked weight loss, or failure to respond to feeding support (see NICE guideline on postnatal care[6])
  - When to reassess if not referred to paediatric services.
- Be aware that supplementary feeding with infant formula in a breastfed infant may help with weight gain but often results in cessation of breastfeeding.
- If supplementation with an infant formula is given:
  - Support the mother to continue breastfeeding
  - Advise expressing breast milk to promote milk supply, and
  - Feed the infant with any available breast milk before giving any infant formula.

A clear cause of faltering growth may not always be identified

Faltering growth after the early days of life

Thresholds for concern

- Consider using the following as thresholds for concern about faltering growth in infants and children (a centile space being the space between adjacent centile lines

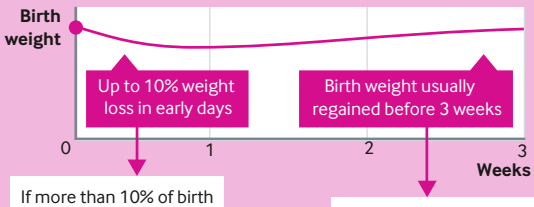
WHAT YOU NEED TO KNOW

- Weight loss of up to 10% of birthweight is common in the early days of life and is usually regained before 3 weeks of age
- Faltering growth after early days of life is characterised by a slower rate of weight gain than expected for age, sex, and current weight, and is usually due to insufficient energy intake
- Investigations for faltering growth involve clinical, developmental, and social assessment and physical examination
- Initial interventions for faltering growth include strategies to increase energy intake and advice on managing feeding and eating behaviours
- Providing or signposting emotional support to parents and carers is important as they often feel blamed for a child's slow growth

Faltering Growth

Weight loss in the early days of life

Normal weight pattern



If more than 10% of birth weight lost in early days

If not returned to birth weight by 3 weeks

Clinical assessment

Take a detailed history to assess feeding

Look for evidence of:

- Dehydration
- An illness or disorder that might account for weight loss

Further investigations

Only if indicated based on clinical assessment or concern about amount of weight loss

Observation

Consider direct observation of feeding

Consider referral

Refer to paediatric services if there is evidence of illness, marked weight loss, or failure to respond to feeding support →

In the early days of life some weight loss is common and is usually a physiological phenomenon associated with fluid shifts. The term 'faltering growth' is used to describe a pattern of slower weight gain than expected for age and sex in infants and preschool children, and it is most often due to inadequate nutritional intake.

Faltering growth is complex and often multifactorial. Parents may feel 'blamed' for their child's slow weight gain. Health care professionals should remain alert to the possibility of a safeguarding concern, but should be sensitive to the emotional impact of caring for a child with faltering growth.

Faltering growth after the early days of life

Birth weight	All birth weights	Below 9th centile	9th–91st centile	Above 91st centile
Thresholds for concern	Current weight is below the 2nd centile for age	1+ A fall across 1 or more weight centile spaces	2+ A fall across 2 or more weight centile spaces	3+ A fall across 3 or more weight centile spaces

Offer assessments

- Clinical
- Social
- Developmental

Take a detailed history of feeding or eating

Observations

Consider direct observation of feeding or meal times

Further investigations

Consider investigations for:

- Urinary tract infection
- Coeliac disease

Management strategies

Food and drink choices

If necessary, based on the assessment, advise on food choices that:

- are appropriate to the child's developmental stage in terms of quantity, type, and food texture
- optimise energy and nutrient density

In infants or children who need a further increase in the nutrient density of their diet beyond that achieved through advice on food choices, consider:

- short-term dietary fortification using energy-dense foods
- referral to a paediatric dietitian →

Advise the parents or carers of infants or children with faltering growth that drinking too many energy-dense drinks, including milk, can reduce a child's appetite for other foods.

Feeding and mealtime strategies

Discuss possible strategies with parents or carers, based on assessments, history, and observations

- Encouraging relaxed and enjoyable feeding and mealtimes
- Eating together as a family or with other children
- Encouraging young children to feed themselves
- Allowing young children to be 'messy' with their food
- Making sure feeds and mealtimes are not too brief or too long
- Establishing regular eating schedules
- Setting reasonable boundaries for mealtime behaviour while avoiding punitive approaches
- Avoiding coercive feeding

Consider referral

Is there any evidence of any of the following?

- Symptoms or signs that may indicate an underlying disorder
- Rapid weight loss
- Slow linear growth
- Unexplained short stature
- Safeguarding concerns
- Failure to respond to interventions in primary care
- Severe undernutrition

No → Consider management strategies, and when to reassess

Yes → Discuss with or refer to an appropriate paediatric specialist care service →

REX/SHUTTERSTOCK

on the UK-WHO growth charts (see figure on bmj.com):
- A fall across ≥1 weight centile spaces, if birth weight was below the 9th centile
- A fall across ≥2 weight centile spaces, if birth weight was between the 9th and 91st centiles
- A fall across ≥3 weight centile spaces, if birth weight was above the 91st centile
- When current weight is below the 2nd centile for age, whatever the birth weight.

The guideline also includes recommendations about measuring length or height, assessing weight change over time and linear growth (using UK WHO growth charts), and calculating the body mass index in those over 2 years to identify undernutrition.

How to assess a child with faltering growth?

- If there is concern about faltering growth:
  - Perform a clinical, developmental, and social assessment
  - Take a detailed feeding or eating history
  - Consider direct observation of feeding or meal times
  - Consider investigating for:
    - Urinary tract infection (follow the principles of assessment in the NICE guideline on urinary tract infection in children under 16 years old[7])
    - Coeliac disease, if the diet has included food containing gluten (follow the principles of assessment in NICE guideline on coeliac disease[8])
  - Perform further investigations only if they are indicated based on the clinical assessment.
- Recognise that in faltering growth:
  - A range of factors may contribute to the problem, and it may not be possible to identify a clear cause
  - There may be difficulties in the interaction between an infant or child and the parents or carers that may contribute to the problem, but this may not be the primary cause.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

The Guideline Committee included two lay members

Management strategies in faltering growth

- Together with parents and carers, establish a management plan with specific goals for every infant or child for whom there are concerns about faltering growth. This plan could include:
  - Assessments or investigations
  - Interventions
  - Clinical and growth monitoring
  - When reassessment to review progress and achievement of growth goals should happen.
- When there are concerns about faltering growth, discuss the following, as individually appropriate, with the infant's or child's parents or carers:
  - Encouraging relaxed and enjoyable feeding and mealtimes
  - Eating together as a family or with other children
  - Encouraging young children to feed themselves
  - Allowing young children to be "messy" with their food
  - Making sure feeds and mealtimes are not too brief or too long
  - Setting reasonable boundaries for mealtime behaviour while avoiding punitive approaches
  - Avoiding coercive feeding
  - Establishing regular eating schedules (such as three meals and two snacks in a day).
- If necessary, based on the assessment, advise on food choices for infants and children that:
  - Are appropriate to the child's developmental stage in terms of quantity, type, and food texture
  - Optimise energy and nutrient density.
- In infants or children who need a further increase in the nutrient density of their diet beyond that achieved through advice on food choices, consider:
  - Short term dietary fortification using energy-dense foods
  - Referral to a paediatric dietitian.
- Advise the parents or carers of infants or children with faltering growth that drinking too many energy-dense drinks, including milk, can reduce a child's appetite for other foods..

What are the challenges to management?

Faltering growth is complex and often multifactorial, and a specific underlying cause may not be identified. There is a risk that children may undergo excessively frequent monitoring or unnecessary investigations looking for an underlying disorder. Parents may feel blamed for their child's slow weight gain, whereas neglect is an uncommon cause of faltering growth. Healthcare professionals should remain alert to the possibility of a safeguarding concern but should be sensitive to the emotional impact of caring for a child with faltering growth.

Such challenges can be overcome by thoughtful explanation and discussion, by ensuring the availability of support and consistent advice from a multidisciplinary team, and by working with families to agree plans for investigation, intervention, monitoring, and onward referral if required.

GUIDELINES INTO PRACTICE

- How do you involve the parents and carers of children with faltering growth in establishing a management plan?
- Are you aware of available resources to provide information and support to parents and carers of children with faltering growth?
- How do you ensure the multidisciplinary team gives consistent advice about monitoring, nutrition, and managing mealtime behaviour?

Competing interests: We declare the following interests based on NICE's policy on conflicts of interests (available at www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/code-of-practice-for-declaring-and-managing-conflicts-of-interest.pdf): RP received payments to present a BMJ Mastercourses webinar on common problems in newborns and infants and a webinar on feeding problems in infants, and to conduct teaching with BMJ Learning.

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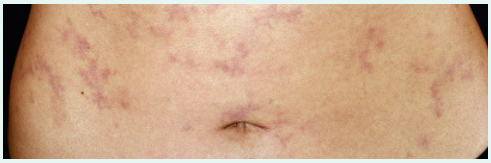
Find the full version with references at http://dx.doi.org/10.1136/bmj.j4219



CASE REVIEW

Neuropathy and a rash

A 26 year old woman was referred to dermatology with a one year history of a rash on her lower legs, abdomen, and arms, and a six month history of paraesthesia in her right hand and left foot. She had no history of fatigue, weight loss, fever, or arthralgia.

There was palpable retiform erythema and broken livedo on her abdomen, arms, and legs (above). She had reduced sensation to light touch in the right ring and little fingers, the lateral palmar and dorsal hand, the left lateral calf, and the dorsum of the left foot. She had a feeling of clumsiness in her right hand that caused her difficulty with writing, but there was no weakness.

Blood tests were normal, including a full autoimmune screen. Skin biopsy showed medium vessel vasculitis with fibrinoid necrosis. Electromyography showed sensory damage in the right ulnar nerve and asymmetrical superficial sensory damage in the peroneal nerve, with the left side being affected to a greater extent.

1 What is the most likely diagnosis?
2 How can differential diagnoses be ruled out?
3 How should this condition be managed?

Submitted by Fangyi Xie and Daniel Creamer

Patient consent obtained.

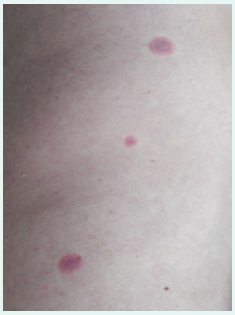
Cite this as: *BMJ* 2017;359:j4109

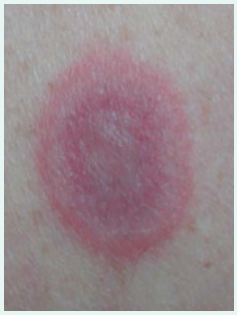
CASE REVIEW

The diagnosis is in the rings

A 62 year old man reported a history of recurrent oral ulcers, sometimes with laryngitis, and conjunctivitis. He consulted his doctor in 2011 for acute onset fever (39°C), odynophagia, and laryngitis lasting two days, and was prescribed ibuprofen and clarithromycin. Two days later, conjunctivitis, oral mucous membrane erosions, and cutaneous lesions appeared (above). The patient was hospitalised on suspicion of Stevens-Johnson syndrome.

Dermatological examination showed several target lesions on the trunk, lower limbs, and scrotum, conjunctivitis, and diffuse erosions of the mucous membranes involving the mouth (palate, tongue, buccal mucosa, and lips), and glans. Examination of ear, nose, and throat showed diffuse nasal erosion, crusts, and epiglottal erosion.





Blood examination showed normal blood cell counts, increased C reactive protein (160 mg/L), negative herpes simplex virus culture from the mouth and skin, and negative HIV, herpes simplex virus, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* serologies. Skin biopsy showed a dense lichenoid lymphocytic infiltrate with necrotic keratinocytes in the basal layer. Direct and indirect immunofluorescence tests were both negative.

1 What is the diagnosis?
2 What differential diagnosis needs to be excluded before deciding whether the patient can use ibuprofen and clarithromycin in the future?
3 When should patients with this condition be referred to a dermatologist?

Submitted by Saskia Ingen-Housz-Oro, Nicolas Ortonne, and Olivier Chosidow

Patient consent obtained.

Cite this as: *BMJ* 2017;359:j3817

answers

CASE REVIEW

Neuropathy and a rash

1 Mononeuritis multiplex due to cutaneous polyarteritis nodosa.
2 Full blood count, glycated haemoglobin, hepatitis screen, anti-nuclear antibody, extractable nuclear antigens, anti-neutrophil cytoplasmic antibodies, rheumatoid factor, and complement levels can help to rule out other vasculitides, diabetes, connective tissue disorders, infections, and malignancy.
3 Oral corticosteroids are required to treat the inflammatory response. Cyclophosphamide or azathioprine might be required to treat the vasculitis.

CASE REVIEW

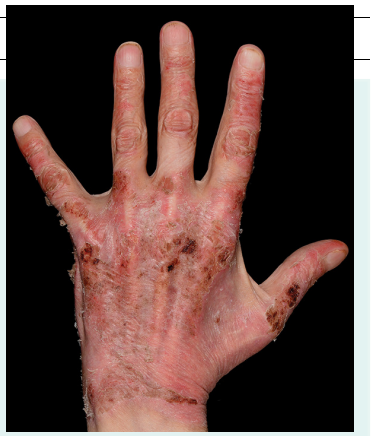
The diagnosis is in the rings

1 A diagnosis of erythema multiforme major is supported by the typical target lesions with three concentric rings, and the widespread oral, ocular, and genital mucous membrane erosions, suggestive of the subtype "major" erythema multiforme.
2 Severe cutaneous adverse reactions of the epidermal necrolysis spectrum, such as Stevens-Johnson syndrome and toxic epidermal necrolysis. These conditions are drug-induced in 85% of cases.
3 Where the lesions are atypical and diagnosis is doubtful (skin biopsy might be necessary); or for management of the acute phase of severe erythema multiforme major; and in any case of erythema multiforme that is difficult to treat.

CPD READING
0.5 HOURS

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

A rash that appeared on holiday



A 64 year old man developed a severe, erythematous, blistering rash that required hospital admission (right). His face, neck, forearms, and lower legs were also affected. The eruption developed within four hours of arriving on holiday in Spain, and was present only on sites that were exposed to sun. He was taking fusidic acid and doxycycline 100 mg twice daily and begun the previous week for septic arthritis. After topical treatment and analgesia, he made a full recovery.

Doxycycline is a tetracycline antibiotic with a broad spectrum of action. It can induce a severe photosensitivity reaction on sunlight exposure. This is reported to be a common, dose-dependent reaction present in up to 35% of patients on doses of 150-200 mg per day. Clinicians prescribing doxycycline are reminded to advise avoidance of direct sun exposure and sunbathing.

Melanie Page (melanie.page@nnuh.nhs.uk), clinical fellow in dermatology, Abby Macbeth, consultant dermatologist, Norfolk and Norwich University Hospital, Norwich, UK

Patient consent obtained.

Cite this as: *BMJ* 2017;359:j4338

Tattoos

Not long ago, only sailors and bikers sported tattoos. Today, nearly a third of adults in the US have at least one. The American Academy of Pediatrics has issued a report on tattooing, piercing, and other forms of body modification, which gives a worryingly long list of potential adverse effects including infection, inflammation, vasculitis, granuloma formation, and keloids (*Paediatrics* doi: 10.1542/peds.2017-1962). However, it admits that, in view of the large number of these procedures carried out every day, the rate of complications is probably very low.

Antibiotics for children with acute otitis media

Trials have shown that antibiotic treatment is effective in children with acute otitis media. On the other hand, they've also shown that about half of children with the condition get better fairly quickly without antibiotics. What clinical features help doctors decide whether children need antibiotics immediately or if they can be safely delayed? A secondary analysis of data from a recent trial suggests that, if there is bulging of the tympanic membrane, it's better to give antibiotics right away (*Paediatrics* doi:10.1542/peds.2017-0072).

Drowning in childhood

With the important exception of epilepsy, an analysis of deaths by drowning in childhood finds no evidence that other medical conditions increase risk. Childhood is the age group in which the hazards of unintentional fatal drowning are greatest but, providing they are adequately supervised, there seems no reason why children with asthma, autism, or learning difficulties can't enjoy aquatic activities (*Arch Dis Child* doi: 10.1136/archdischild-2017-31268).

Statins and colorectal cancer

Several studies have suggested that people with colorectal cancer who take statins have a reduced mortality. A registry based investigation from Denmark that followed more than 20 000 people with stages I to III colorectal cancer confirms this finding. However, it failed to detect any influence of statin use on cancer recurrence rate (*Am J Epidemiol* doi:10.1093/aje/kww245). The investigators think this means that statins have no direct effect on cancer and that the association with mortality is an artefact of healthy user or lead time bias.

Diagnosing giant cell arteritis

Ultrasound measurements of the intima-media thickness of the walls of the superficial temporal artery show good specificity and sensitivity for diagnosing giant cell arteritis, according to a study in *Rheumatology* (*Rheumatology* doi:10.1093/rheumatology/kex143). The approach has yet to be tested outside the setting in which it was developed, but it might provide a less invasive and more accurate option than the hit or miss of temporal artery biopsy.

Vasectomy and prostate cancer

It's hard to prove a negative, but a systematic review of 53 cohort, case-control, and cross-sectional studies is confident that any association between vasectomy and prostate cancer is clinically insignificant. Among these studies, those of higher quality, better design, and low risk of bias gave estimates of effect close to zero. Overall, the absolute increase in lifetime risk of prostate cancer after vasectomy was less than 1% (*JAMA Intern Med* doi:10.1001/jamainternmed.2017.2791).

Twelve cranial nerves

Herophilus, the father of anatomy, identified seven pairs of cranial nerves in the third century BCE. But it wasn't until 1778 that the German physician Samuel Thomas Soemmerring, below, described the 12 cranial nerves we recognise today. He was 23 years old, and the observation was part of his doctoral thesis. Soemmerring's system was rapidly accepted across continental Europe, but it took many years before it was recognised in Britain. It wasn't included in *Gray's Anatomy* until the 11th edition of 1887 (*Adv Clin Neurosci Rehab*http://www.acnr.co.uk/wp-content/uploads/201709/Naming-the-cranial-nerves-6.pdf).

Cite this as: *BMJ* 2017;359:j4516