ART OF MEDICINE

What is it about the number of stitches?

It is a particular peculiarity of medicine that the interrupted suture count of a wound should serve as a lay index of injury severity. Many will recognise the invariable inquiry, “How many stitches will I have, doc?” as though this irrelevancy is the ultimate determinant of injury severity and not the damage that lies beneath the gaping wound. Why are patients fixated on an issue that is so arbitrary?

The usual suture count inquirer adopts a tone of excited curiosity more often than one of trepidation. A high count confers satisfaction and status, being an easily understood currency with which the magnitude of an injury and the work required to deal with it can be disseminated to friends, family, and more widely over social media. However, the range of suture counts that have a positive effect on the patient’s mood is not known; nor is it known whether increasing stitch count beyond a certain threshold becomes alarming and deleterious.

The disparity in importance attributed to suture counts has the potential to jeopardise the doctor-patient relationship. In our experience, predicting suture count preoperatively or recalling suture count postoperatively is unreliable and inaccurate. Few clinicians seize the narrow window between completion of wound closure and dressing application to humour their patient’s hankering.

We therefore suggest a simple strategy to pre-empt dissatisfaction: offer to show the sutured wound to the patient. This delegates the tedium of suture counting, while satiating the patient’s appetite for quantification of their misfortune—however unreliably.

Roshan Vijayan plastic surgery registrar, Queen Victoria Hospital, East Grinstead RH19 3DZ, UK Roshanvijayan@gmail.com
Greg Scott neuroscience research fellow, Imperial College NHS Healthcare Trust, London, UK
Foiz Ahmed plastic surgery registrar, Oxford University Hospitals NHS Trust, Oxford, UK

Cite this as: BMJ 2015;350:h1042

FAST FACT—HORMONAL CONTRACEPTION AND MOOD

It is not clear if combined hormonal contraceptives affect mood. However, women who attribute mood changes to their pill may simply stop taking the pill and put themselves at risk of pregnancy, so it is important to listen to their concerns and address them appropriately. As there is a wide range of contraceptives available, an alternative form of contraception may be offered to women who report continuing mood changes.

You can gain CPD points from your reading by recording what you have read in your appraisal folder. You should try to link your reading back to a learning need and also consider how you plan to improve your practice as a result of your learning. http://learning.bmj.com

We print a statement on financial interests and patient partnership with each education article because they are important to us. We have resolved to reduce the involvement of authors with financial interests that The BMJ judge as relevant. We encourage and make clear how patients have been involved and shaped our content. More details can be found on thebmj.com.

PRACTICE UPDATES

Asthma care bundle launched to reduce readmission rates

Technique and medication + Action Plan + Environment + Subsequent care (TAPES) is a care bundle that should be used for adults and children discharged from an emergency department after an acute asthma attack, recommends the British Thoracic Society (BTS). Five high-impact actions make up the TAPES bundle. Clinicians are advised to (a) check inhaler technique and (b) review medications before discharge, (c) stress the importance of medication adherence to patients and give them an asthma action plan covering how to manage care, (d) consider trigger and exacerbating factors in the patient’s local environment that might prevent future attacks, and (e) arrange follow-up in the community within two working days plus specialist care (according to criteria found in BTS/SIGN British guidelines on the management of asthma) within two weeks.

• http://bit.ly/1txFSIZ

NICE recommends GreenLight XPS laser in benign prostatic hypertrophy

GreenLight XPS laser uses photoselective vaporisation of prostatic tissue to treat benign prostatic hypertrophy. GreenLight XPS laser is supported by NICE for non-high risk patients. The new laser technology is at least as effective as transurethral resection of the prostate (TURP), but can more often be done as a day case procedure, after appropriate service redesign. There is not enough evidence to support GreenLight for high risk cases (patients with an increased risk of bleeding, prostates larger than 100 mL, or urinary retention).

• http://bit.ly/1S6Cvwo

What is it about the number of stitches?

It is a particular peculiarity of medicine that the interrupted suture count of a wound should serve as a lay index of injury severity. Many will recognise the invariable inquiry, “How many stitches will I have, doc?” as though this irrelevancy is the ultimate determinant of injury severity and not the damage that lies beneath the gaping wound. Why are patients fixated on an issue that is so arbitrary?

The usual suture count inquirer adopts a tone of excited curiosity more often than one of trepidation. A high count confers satisfaction and status, being an easily understood currency with which the magnitude of an injury and the work required to deal with it can be disseminated to friends, family, and more widely over social media. However, the range of suture counts that have a positive effect on the patient’s mood is not known; nor is it known whether increasing stitch count beyond a certain threshold becomes alarming and deleterious.

The disparity in importance attributed to suture counts has the potential to jeopardise the doctor-patient relationship. In our experience, predicting suture count preoperatively or recalling suture count postoperatively is unreliable and inaccurate. Few clinicians seize the narrow window between completion of wound closure and dressing application to humour their patient’s hankering.

We therefore suggest a simple strategy to pre-empt dissatisfaction: offer to show the sutured wound to the patient. This delegates the tedium of suture counting, while satiating the patient’s appetite for quantification of their misfortune—however unreliably.

Roshan Vijayan plastic surgery registrar, Queen Victoria Hospital, East Grinstead RH19 3DZ, UK Roshanvijayan@gmail.com
Greg Scott neuroscience research fellow, Imperial College NHS Healthcare Trust, London, UK
Foiz Ahmed plastic surgery registrar, Oxford University Hospitals NHS Trust, Oxford, UK

Cite this as: BMJ 2015;350:h1042

FAST FACT—HORMONAL CONTRACEPTION AND MOOD

It is not clear if combined hormonal contraceptives affect mood. However, women who attribute mood changes to their pill may simply stop taking the pill and put themselves at risk of pregnancy, so it is important to listen to their concerns and address them appropriately. As there is a wide range of contraceptives available, an alternative form of contraception may be offered to women who report continuing mood changes.

You can gain CPD points from your reading by recording what you have read in your appraisal folder. You should try to link your reading back to a learning need and also consider how you plan to improve your practice as a result of your learning. http://learning.bmj.com

We print a statement on financial interests and patient partnership with each education article because they are important to us. We have resolved to reduce the involvement of authors with financial interests that The BMJ judge as relevant. We encourage and make clear how patients have been involved and shaped our content. More details can be found on thebmj.com.
Assessment and initial management of major trauma: summary of NICE guidance

Jessica Glen, Margaret Constanti, Karim Brohi, on behalf of the Guideline Development Group

Trauma is a major contributor to the global burden of disease. Those who experience major trauma have serious and often multiple injuries associated with a strong possibility of death or disability. Nationally there are around 20 000 cases of major trauma per year in England, and over a quarter of these result in deaths. Trauma care is a developing field, and recent civilian and military research has led to changes in the assessment and management of severely injured patients. This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) on the assessment and initial management of major trauma. These guidelines sit as part of a suite of trauma guidelines and alongside the previously published guidelines on head injury. They are written in the context of the NHS, where trauma care was reorganised into major trauma networks in 2012. Here we focus on two central themes of the guidelines—the assessment of a patient with major trauma and the management of patients who are actively bleeding.

WHAT YOU NEED TO KNOW

• Use direct pressure dressings, tourniquets, and pelvic binders and move rapidly to damage control surgery or interventional radiology
• With actively bleeding patients, allow permissive hypotension and use blood rather than clear intravenous fluids
• Use whole body computed tomography (CT) in adults with blunt trauma and multiple injuries, but avoid unnecessary CT use, especially in children

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Committee members involved in this guideline included lay members who contributed to the formulation of the recommendations summarised here. Patient organisations were among the registered stakeholders who were consulted at both scoping and development stages.

1 National Guideline Centre, Royal College of Physicians, London NW1 4LE, UK
2 Centre for Trauma Sciences, Barts and the London School of Medicine, Queen Mary University of London
Correspondence to: K Brohi k.brohi@qmul.ac.uk
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 thebmj.com.
Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group’s experience and opinion of what constitutes good practice.

Assessment of the trauma patient in the hospital setting

The immediate assessment of trauma patients must be rapid and effective in identifying life threatening or life changing injuries. Diagnostic modalities such as emergency department ultrasound and computed tomography (CT) have the potential to streamline the assessment process. If used effectively within their diagnostic capabilities, they may provide faster, more accurate diagnoses to target lifesaving interventions. However, inappropriate use of these modalities may slow the assessment process and may lead to delays or in some cases inappropriate diagnoses. The guidelines use contemporary evidence and build on existing assessment frameworks (such as the primary and secondary surveys of the Advanced Trauma Life Support (ATLS) course) to direct the appropriate use of these imaging modalities during the immediate assessment of trauma patients. The ATLS course is a global training programme for trauma care that is updated every four years. The ATLS UK Steering Group will consider how the NICE guidelines inform their 10th edition due in summer 2017.

The guidelines make recommendations on immediate imaging for patients with suspected major haemorrhage and chest trauma, as well as the use of whole body CT in the assessment of patients with multiple injuries. Immediate imaging is focused on identifying the site of active bleeding to direct haemorrhage control, and the identification of other life threatening conditions.

Imaging for major haemorrhage

- Consider immediate CT for patients with suspected haemorrhage if they are responding to resuscitation or if their haemodynamic status is normal.
- Limit diagnostic imaging such as chest and pelvis x-rays or focused assessment with sonography for trauma (FAST) to the minimum needed to direct intervention in patients with suspected haemorrhage and haemodynamic instability who are not responding to volume resuscitation.
- Be aware that a negative FAST result does not exclude intraperitoneal or retroperitoneal haemorrhage.
- Do not use FAST or other diagnostic imaging before immediate CT in patients with major trauma.
- Do not use FAST as a screening modality to determine the need for a CT in patients with major trauma.
Imaging for chest trauma

- Consider immediate chest x-ray and/or extended focused assessment with sonography for trauma (eFAST) as part of the primary survey to assess chest trauma in adults (≥16 years old) with severe respiratory compromise.
- Consider immediate CT for adults with suspected chest trauma without severe respiratory compromise who are responding to resuscitation or whose haemodynamic status is normal.
- Consider chest x-ray and/or ultrasound for first line imaging to assess chest trauma in children (<16 years old).
- Do not routinely use CT for first line imaging to assess chest trauma in children.

Whole body CT of multiple injuries

- Use whole-body CT (consisting of a vertex-to-toes scanogram followed by a CT from vertex to mid-thigh) in adults (≥16 years) with blunt trauma and suspected multiple injuries. Patients should not be repositioned during whole body CT.
- Use clinical findings and the scanogram to direct CT of the limbs in adults with limb trauma.
- Do not routinely use whole body CT to image children (<16 years old). Use clinical judgment to limit CT to the body areas where assessment is needed.

Management of major haemorrhage in the hospital setting

Massive bleeding accounts for over a quarter of trauma deaths each year in England and Wales. Deaths from haemorrhage occur rapidly, and teams must be focused on the early identification of bleeding and rapid effective haemostasis.

Modern resuscitation focuses on providing volume resuscitation while protecting the body’s ability to form stable blood clots. The guidelines focus on the assessment and management of those who are suspected of having active ongoing bleeding, either visible external bleeding or suspected or known internal bleeding, which constitutes a threat to life.

Dressings, tourniquets and pelvic binders

- Use simple dressings with direct pressure to control external haemorrhage.
- In patients with major limb trauma use a tourniquet if direct pressure has failed to control life threatening haemorrhage.
- In the pre-hospital setting, if active bleeding is suspected from a pelvic fracture after blunt high-energy trauma:
  - apply a purpose-made pelvic binder or
  - consider an improvised pelvic binder, but only if a purpose-made binder does not fit.

Haemorrhage protocols

Major haemorrhage (or transfusion) protocols aim to rapidly and consistently deliver blood components to bleeding trauma patients.

- Hospital trusts should have specific major haemorrhage protocols for adults (≥16 years) and children (<16).
- For patients with active bleeding, start with a fixed ratio protocol for blood components and change to a protocol guided by laboratory coagulation results at the earliest opportunity.
- Use physiological criteria that include the patient’s haemodynamic status and his or her response to immediate volume resuscitation to activate the major haemorrhage protocol.
- Do not rely on a haemorrhagic risk tool applied at a single time point to determine the need for major haemorrhage protocol activation.

Haemostatic agents

Haemostatic agents may have a role to reduce or control bleeding. Tranexamic acid works by directly inhibiting clot breakdown, and its delayed use may be beneficial if there is evidence of hyperfibrinolysis (abnormally rapid clot breakdown), supported by blood tests such as D dimer and fibrinogen products.

- Use intravenous tranexamic acid as soon as possible in patients with major trauma and active or suspected active bleeding.
- Do not use intravenous tranexamic acid more than 3 hours after injury in patients with major trauma unless there is evidence of hyperfibrinolysis.
Volume resuscitation

These guidelines suggest high volume blood product resuscitation, avoiding the use of crystalloids and colloids in hospital. A restricted, or permissive approach to volume resuscitation involves accepting a lower blood pressure during active bleeding to reduce bleeding; and restricting fluid administration to avoid diluting the blood’s clotting ability.

- For patients with active bleeding, use a restrictive approach to volume resuscitation until definitive early control of bleeding has been achieved.
- In hospital settings move rapidly to haemorrhage control, titrating volume resuscitation to maintain central circulation (central pulse or mean arterial pressure of 50 mm Hg) until control is achieved.
- For patients who have haemorrhagic shock and a traumatic brain injury:
  - If haemorrhagic shock is the dominant condition, continue restrictive volume resuscitation to maintain cerebral perfusion.
  - If traumatic brain injury is the dominant condition, use a less restrictive volume resuscitation approach to maintain cerebral perfusion.
- In hospital settings do not use crystalloids for patients with active bleeding. See NICE guideline Intravenous fluid therapy in adults in hospital (www.nice.org.uk/guidance/CG174) and the section on fluid resuscitation in the NICE guideline Intravenous fluid therapy in children and young people in hospital (www.nice.org.uk/guidance/ng29) for advice on tetrastarches.
- For adults (≥16 years old) use a ratio of 1 unit of plasma to 1 unit of red blood cells to replace fluid volume.
- For children (<16 years old) use a ratio of 1 part plasma to 1 part red blood cells and base the volume on the child’s weight.

Damage control surgery

Damage control surgery deals with the most life threatening aspects of patients’ injuries, often temporary bleeding control. Once haemorrhage control is achieved and normal homeostasis restored, further, definitive surgeries may be carried out.

- Use damage control surgery in patients with haemodynamic instability who are not responding to volume resuscitation.
- Consider definitive surgery in patients with haemodynamic instability who are responding to volume resuscitation.
- Use definitive surgery in patients whose haemodynamic status is normal.

Interventional radiology

- Use interventional radiology techniques in patients with active arterial pelvic haemorrhage unless immediate open surgery is needed to control bleeding from other injuries.
- Consider interventional radiology techniques in patients with solid organ (spleen, liver, or kidney) arterial haemorrhage.
- Consider a joint interventional radiology and surgery strategy for arterial haemorrhage that extends to surgically inaccessible regions.
- Use endovascular stent grafts in patients with blunt thoracic aortic injury.

Implementation

Major trauma systems around the world regionalise care into major trauma networks that include specialist major trauma centres for the most severely injured patients, trauma units (or a tiered system of lower level trauma centres) for all except the most severe trauma patients, and prehospital providers. Many of the recommendations in this NICE guidance are already established practice and, as such, the facilities, resources, and expertise are already available. Work may be needed to ensure consistent practices for all patients, across all providers, at all times of day and night.

Transfusion practice is already part of many major haemorrhage protocols, but it can be delivered inconsistently. Multidisciplinary groups meeting together and reviewing cases may ensure that blood products are delivered rapidly and consistently, while avoiding waste and over-transfusion.

These guidelines confirm the place of interventional radiology services as integral to haemorrhage control for some injuries, such as pelvic trauma. In the UK, such services are part of the national service specification for major trauma, but there is variation in their provision, and between in-hours and out-of-hours services. Trusts and providers might consider the same standards as emergency surgery in terms of access and provision.

Further information on implementation tools provided by NICE can be found at www.nice.org.uk/guidance/ng39/resources and www.nice.org.uk/guidance/ng40/resources

Cite this as: BMJ 2016;353:i3051
Find this at: http://dx.doi.org/10.1136/bmj.i3051

Massive bleeding accounts for over a quarter of trauma deaths each year in England and Wales. Deaths from haemorrhage occur rapidly, and teams must be focused on the early identification of bleeding and rapid effective haemostasis.
The QT interval is measured from the beginning of the QRS complex to the end of the T wave on a surface electrocardiogram and represents the period from onset of depolarisation to completion of repolarisation of the ventricular myocardium. The interval varies greatly and is affected by age, sex, sympathetic tone, and diurnal pattern. Because it increases as heart rate falls, measurements of QT interval are usually corrected for heart rate (QTc). Several methods have been used (box 1).

Measurement of the QT interval is not straightforward. There is currently no agreed consensus on how to measure the QT interval in patients with broad complex ventricular conduction abnormalities or paced ventricular rhythm, and measurement in patients with atrial fibrillation requires special consideration. The QT interval also differs between electrocardiograph (ECG) leads. In addition, details of algorithms used in semi-automated ECG machines are not always readily available. QTc intervals of 450 ms and 460 ms are generally accepted as the upper limits of normal for adult men and women, respectively.

Although QT prolongation is associated with torsades de pointes (TdP) and sudden cardiac death, it is an imperfect predictor. Many patients with prolonged QT never experience TdP, whereas many who experience TdP have a normal QT before the episode. Similarly, some drugs (eg amiodarone) can markedly prolong QT but are rarely associated with TdP. Both the QT interval and increase in QT duration predict the risk of developing TdP. Each 10 ms increase in QTc is associated with a 5-7% increase in the risk of developing TdP; and when the absolute QTc is >500 ms, the risk of TdP is generally regarded as markedly increased and intervention considered necessary.

Conditions that affect the QT interval
A variety of genetic and acquired conditions can cause QT prolongation. Some congenital long QT syndromes (LQTS), such as Romano-Ward syndrome and Jervell and Lange-Nielsen syndrome, have long been recognised to be associated with a high risk of arrhythmia and premature sudden death. These syndromes are caused by mutations predominantly in genes encoding potassium and sodium channels that help regulate the duration of the cardiomyocyte action potential. The mutations contribute to delayed cardiac repolarisation and increased risk of arrhythmia. Variants of at least 13 separate genes have been shown to cause LQTS, but those underlying LQTS types 1-3 (KCNQ-1, KCNH-2, and SCN-5A) account for about 90% of all genotype positive cases. These classic forms of LQTS are typically associated with different abnormal T-wave morphologies on ECG and arrhythmic triggers (eg sleep, exercise, sudden loud noises). A clinical history of presyncopal and syncopal symptoms (eg palpitations, chest pain, dyspnoea) and a family history of sudden cardiac death may be used to support

**WHAT YOU NEED TO KNOW**
- Measurement of the QT interval is not straightforward
- QT prolongation is associated with torsades de pointes and sudden death
- Prolongation of QT is often caused by drugs in the presence of at least one other factor such as electrolyte disturbance, or renal impairment
- Before prescribing a drug that may increase QT offer those at risk baseline and follow up ECG, information on arrhythmia and advice on when to seek help
- If QTc is >500 ms discontinue the drug, repeat the ECG and seek advice

---

**Box 1 | Formulas used to correct the QT interval for heart rate**
- Bazett method: QTc=QT/(√RR)
- Fridericia method: QTc=QT/(RR/3)
- Framingham method: QTc=QT+0.154(1-RR)

RR, the interval between two successive R waves.
the diagnosis of LQTS. Patients with such symptoms and history, or those with QT prolongation, should be referred for specialist investigation. If a diagnosis of LQTS is confirmed, patients should be offered counselling, risk stratification, screening of family members, drug therapy (eg β blockers) and, where appropriate, be considered for cardiac sympathetic denervation or an implantable cardiac defibrillator. Gene specific management is based on the underlying genetic profile.16

Congenital LQTS is rare, with an estimated prevalence of about one in 2000 infants,7 and drugs are the most common cause of prolonged QT (box 2). Even so, drug induced QT prolongation and TdP are relatively uncommon.16 Furthermore, TdP is a rarely reported adverse drug reaction, with one study estimating that drug related TdP represented about one in 700 reported adverse drug reactions.16

Drugs that can cause QT prolongation

Other than a drug itself, various factors increase or amplify the risk of drug induced QT prolongation and TdP (box 3). Most clinical cases of drug induced QT prolongation occur in the presence of at least one of these risk factors, with over 70% occurring in the presence of two or more risk factors.17

How do drugs affect QT?

Most drugs that prolong QT do so through inhibition of the rapid component of the delayed rectifier potassium (IKR) channel, encoded by the human ether-a-go-go related gene (hERG), which is affected in LQTS type 2.18 However, drug induced QT prolongation is not specific to inhibition of the IKR current, as not all drugs that block this current cause TdP.

In general, the risk of drug induced QT prolongation is directly related to the dose and plasma concentration of the drug. Pharmacokinetic and pharmacodynamic interactions can also cause QT prolongation.8 Drug-drug interactions that inhibit drug metabolism may increase the plasma concentration of the affected drug and precipitate QT prolongation. Similarly, QT prolongation may occur when two drugs have an additive effect. Differences in individual susceptibility to QT prolongation may relate to specific genetic factors.19

Minimising the risks of drug induced QT prolongation

Screening during drug development

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, which includes drug regulatory authorities and drug companies in Europe, Japan, and the United States, has published guidance for monitoring the effect on QT through preclinical and clinical phases of drug development.20 Potential new drugs are routinely screened in preclinical development for interaction with the hERG encoded potassium channel with in vitro and in vivo studies.21 In the early clinical phase of drug development, a “thorough QT/QTc test” is undertaken to determine a drug’s effect on QT and the dose-response association of any effect detected.21 This often involves testing the drug at therapeutic and supratherapeutic doses, with comparisons made against placebo as well as active controls with known QT prolonging properties. A positive result is recorded when the upper limit of the 95% one sided confidence interval for the largest time matched placebo corrected mean effect of the drug on QTc exceeds 10 ms. Generally, a positive QT/QTc test will almost always lead to a requirement by regulatory authorities for expanded ECG monitoring and safety evaluation during later stages of development.

---

| Box 2 | Drugs that can cause QT prolongation | 23 71 15 |
| Anti-arrhythmic drugs | Amiodarone, disopyramide, dronedarone, flecainide, sotalol |
| Other cardiac drugs | Ranolazine, macrolides (eg erythromycin, clarithromycin, azithromycin), quinolones (eg levofloxacin, moxifloxacin) |
| Antifungals | Fluconazole, ketoconazole |
| Antimotility and antiemetic agents | Domperidone, granisetron, ondansetron |
| Antimalarials | Quinine, chloroquine |
| Antihistamines | Hydroxyzine |
| Antipsychotics | Chlorpromazine, clozapine droperidol, fluphenazine, haloperidol, olanzapine, pimozide, paliperidone, quetiapine, risperidone |
| Antidepressants | Amitriptyline, citalopram, escitalopram, dosulepin doxepin, fluoxetine, imipramine, lofepramine |
| Miscellaneous | Methadone, antiretrovirals (eg foscarnet), protein kinase inhibitors (eg sorafenib, sunitinib) |

---

| Box 3 | Risk factors for torsades de pointes with drug induced QT prolongation | 14 71 2 |
| Demographic | Female sex, advanced age |
| Biochemical | Electrolyte disturbances (eg hypokalaemia) |
| Genetic | Genetic predisposition, ion channel abnormalities |
| Systemic conditions | Hepatic impairment, renal impairment |
| Cardiac | Occult long QT syndrome, bradycardia, baseline QT prolongation, recent cardioversion with QT prolonging drug, underlying heart disease (heart failure, left ventricular hypertrophy, myocardial infarction) |
| Drug therapy | Concurrent use of more than one QT prolonging drug, concurrent diuretic therapy, digoxin, rapid rate of intravenous infusion of QT prolonging drug, high concentration of QT prolonging drug |

---

Each 10 ms increase in QTc is associated with a 5–7% increase in the risk of developing torsades de pointes.
Regulation and postmarketing surveillance
At a regulatory level, judgments have to be made about the degree of QT prolongation, risk of life threatening arrhythmia, and clinical benefits associated with a drug. The risk-benefit assessment is influenced by the size of the prolongation in the QT/QTc interval, whether the effect occurs in most patients or only in certain defined outliers, and the utility and feasibility of risk management options. Generally, a mean prolongation in QTc of 5 ms is considered the threshold of concern, with a prolongation >20 ms considered to be associated with a substantial likelihood of the drug being proarrhythmic. Irrespective of the degree to which a drug prolongs the QT/QTc interval, decisions to grant marketing authorisation for a drug depend on several factors: morbidity and mortality associated with the untreated disease; the demonstrated benefits of the drug—especially when compared with other therapeutic options; the overall benefit of the drug; whether the drug has clear advantages over existing drugs; and whether available therapeutic options meet the needs of most patients. Where drugs with the potential to prolong QT offer sufficient benefit, appropriate warnings and monitoring requirements are specified in the summary of product characteristics.

Clinical trial programs are not usually large enough to determine most unwanted adverse effects, including the proarrhythmic potential of a drug with modest QT prolonging effects. Postmarketing surveillance is therefore crucial to an ongoing assessment of risk of TdP and cardiac arrhythmia with drugs that have the potential to prolong QT. In fact, QT prolongation is one of the main reasons for withdrawal of drugs from markets across the world (eg astemizole, cisapride, grepafloxacin, terfenadine, and thioridazine).

Minimising risks in clinical practice
Few recommendations exist for managing the risk of drug induced QT prolongation. Precise estimates of relative and absolute risks of QT prolongation and TdP with individual drugs are not readily available. Although some information is available in the BNF and summaries of product characteristics, we are not aware of any regularly updated UK based list of drugs associated with QT prolongation. In the US, lists of drugs that have a risk of QT prolongation and cardiac arrhythmia are maintained on the CredibleMeds website, under a contract with the Food and Drug Administration (https://crediblemeds.org/healthcare-providers/; registration on the CredibleMeds site is required so that users can be notified when the lists have been revised).

QT prolonging drugs should not be used in patients with congenital LQTS. When they are used in patients without inherited LQTS but who are at risk of QT prolongation, patients should be educated on the common symptoms of cardiac arrhythmias, such as dizziness, palpitations, and syncope, and advised on when to seek medical attention.

Before starting a QT prolonging drug, patients should be assessed for risk factors for QT prolongation and their overall risk of drug induced QT prolongation. The evaluation should include risk factors for inherited LQTS (see box 3) and concomitant drugs that might interact and increase the risk of QT prolongation. An assessment of the risk-benefit balance of initiating the QT prolonging drug should be carefully made. If possible, modifiable risk factors for QT prolongation (eg electrolyte abnormalities) should be corrected. Where a patient has a high risk of drug induced QT prolongation or is already taking a drug that can enhance QT prolongation, an alternative drug not known to prolong QT should be prescribed instead.

There is no agreed consensus on when to undertake ECG monitoring and follow-up for patients started on drugs with the potential to prolong QT. It has been estimated that about 16 000 screening ECGs are needed to identify a single case of asymptomatic long QT syndrome. Therefore, while it is probably impractical to perform an ECG before prescribing a drug that may prolong QT (particularly in primary care), it is prudent to consider baseline ECGs on a patient by patient basis. For instance, where the risk of drug induced QT prolongation is deemed high (eg where use of an alternative non-QT prolonging drug is not possible in a patient at risk of drug induced QTc prolongation), an ECG should be performed both at baseline and when the added drug reaches steady state. Where a QT prolonging drug is associated with a QTc of 470–500 ms in men, 480–500 ms in women, or an increase in QTc ≥60 ms, dose reduction or discontinuation is advised. If the QTc reaches or exceeds 500 ms, the drug should be discontinued, the ECG repeated, and specialist advice sought.

Conclusion
Several rare inherited LQTS can cause prolongation of QT, but it is more often caused by drugs, typically in the presence of additional risk factors for QT prolongation. Although measurement of the QT interval can be problematic, it is required by regulatory agencies when determining and managing the risk of drug induced cardiac arrhythmias during drug development, and in subsequent clinical practice. However, it is of concern that there is no readily accessible and regularly updated UK based list of drugs that prolong the QT interval.

This article was originally published in Drug and Therapeutics Bulletin (DTB 2016;54:33-36 doi:10.1136/dtb.2016.3.0390).

DTB is a highly regarded source of unbiased, evidence based information and practical advice for healthcare professionals. It is independent of the pharmaceutical industry, government, and regulatory authorities, and is free of advertising.

DTB is available online at http://dtb.bmj.com.
CASE REVIEW

Assessment of cardiovascular risk in primary care

A 41 year old white man presented to his general practitioner for a routine blood pressure check. He was asymptomatic and had an initial reading of 154/115 mm Hg. Subsequent ambulatory blood pressure monitoring (ABPM) showed that the average daytime reading was 137/89 mm Hg. On further assessment he had no evidence of left ventricular hypertrophy on electrocardiography, and no silver wiring or other abnormalities were found on funduscropy. Laboratory tests showed total cholesterol 6.8 mmol/L (reference range <5 mmol/L), triglycerides 5.9 mmol/L (0.45-1.69), high density lipoprotein (HDL)-cholesterol 0.76 mmol/L (0.9-1.6). There was no evidence of urinary microalbuminuria.

He drank a moderate amount of alcohol at weekends only and smoked 10 cigarettes a day. He had a medical history of depression and dyspepsia for which he took sertraline and omeprazole daily. He had no family history of cardiovascular disease (CVD).

His QRISK2 score was calculated as 10.3%. He was worried about what this meant for his health and wanted help in making decisions about how to proceed.

SPOT DIAGNOSIS

What is the diagnosis?

A 55 year old man had chest and abdominal discomfort after a long haul flight. The chest discomfort resembled his usually stable angina pectoris. On admission his heart rate was 90 beats/min and his blood pressure was 95/52 mm Hg. Electrocardiography showed T wave inversion in the inferolateral leads, compatible with ischaemia, although serum troponin and D-dimer tests were negative. His arterial blood gases, pH, and lactate were normal. What does the supine abdominal radiograph show and what sign suggests the diagnosis (figure)?
Reversible cognitive decline diagnosed on ear examination

A 65 year old man presented with a six week history of rapidly progressive cognitive decline, fevers, and ataxia. He had auricular swelling, inflammation of the cartilaginous portion of the pinna (with lobe sparing), ocular inflammation, and symmetrical small joint polyarthropathy. T2 weighted magnetic resonance imaging showed diffuse, white matter hyperintense lesions. There was lymphocytic pleocytosis of the cerebrospinal fluid. Relapsing polychondritis causing cerebral vasculitis was suspected clinically and confirmed histologically by brain and auricular biopsy. Relapsing polychondritis is a rare (3.5/1 000 000 population/year), severe inflammatory condition of cartilaginous structures. Rarely it causes cerebral vasculitis and is an important, potentially treatable, cause of cognitive decline.

R J Ellis (rjellis@doctors.net.uk), B D Michael, M Doran, Walton Centre NHS Foundation Trust, Liverpool

Patient consent obtained.

Cite this as: BMJ 2016;352:i1215

Statins for all type 2 diabetes?

It used to be so easy. The Quality and Outcomes Framework command was issued, and party commissars presented every patient with diabetes with a suit made of a statin and a couple of other drugs. Disobedience was punished by fines and disgrace. But “type 2 diabetes” is a risk state that differs for each person, and an analysis of data from three statin trials with large numbers of people with type 2 diabetes has been used to create and validate an absolute risk reduction score that can be used for individual patients (Circoutcomes doi:10.1161/ CIRCOUTCOMES.115.001980). Risk levels vary widely. Shared decision making needs to replace the one-suit-fits-all model.

AUDAKUT

AUDAKUT stands for antenatal ultrasound diagnosed anomalies of the kidney and urinary tract. A study of more than 50 000 cases in Denmark gives a prevalence of 0.39%, which is much lower than some previous surveys (Arch Dis Child doi:10.1136/ archdischild-2015-309784). A key measurement seems to be the anterior-posterior diameter of the renal pelvis (APD). Babies with an APD of >10 mm in the third trimester or >12 mm at first postnatal ultrasonography are at a 25% risk of having a febrile urinary infection or needing surgery.

A good death—agreed

Patients with advanced local or metastatic cancer in the catchment of two hospitals and five hospices in southern England were given a questionnaire about factors that they would consider important in achieving a “good death” (BMJ Support Palliat Care doi:10.1136/ bmjspcare-2015-001085). At the same time, the people looking after them at home were given the same questions. Happily, there was good agreement between the answers, although widespread reluctance to complete a formal advanced care plan.

AKI in hospitals

Stage 3 acute kidney injury is a threefold rise in serum creatinine or creatinine levels greater than 354 µmol/L, and it happened to 15 647 patients in 46 UK hospital trusts over five months in 2012. The median age of patients with adequate follow-up data was 75, and their overall mortality within one month was 38% (QJM doi:10.1093/qjmned/bcw072). The study found wide variations in management and outcomes between hospitals.

Down’s syndrome and congenital heart disease

In Sweden, most pregnancies found positive for trisomy 21 are aborted, so that babies born with Down’s syndrome are a different population from those decades ago. A population-wide survey (Paediatricshhttp:// bit.ly/1UenEaZ) finds that congenital heart defects are still found in 54% of infants with Down’s syndrome, but the rate of complex defects has decreased by almost 40%. Another finding is that although atrioventricular septal defect was far more common than isolated ventricular septal defect in 1992 to 1994, they were equally common in 2010 to 2012.

Increase the brown puffer?

“If you feel a cold or a wheeze coming on, increase your brown puffer,” the asthma nurse or doctor always said. But a newly updated Cochrane review (doi:10.1002/14651858.CD007524.pub4) finds that increasing inhaled steroids at the time of exacerbations makes no difference to the need for medical attendances or the use of rescue oral corticosteroids. Three of the studies were in children and five in adults.

Weed and the gum

If you live in Dunedin, New Zealand, you are very likely to stay there, and more likely to have smoked cannabis (65%) than daily tobacco (47%), according to a cohort of 1037 people with 95% follow-up at age 38. Investigators looked for evidence of physical harm in early middle life from up to 20 years of cannabis use, but could only find an increase in periodontal disease (JAMA Psychiatry doi:10.1001/ jamapsychiatry.2016.0637).

Work as hedonic deficit

A study of 124 adults in the “peri-retirement period” (early 60s) measured their pleasure in life and concludes “enjoyment of everyday activities increased after retirement and remained increased for at least 12 months (Age Ageing doi:10.1093/ageing/afw099). Work appears to constitute a relative hedonic deficit.” So perhaps work should be redefined as PDS, or pleasure deficiency syndrome, whereas retirement could be LBS, the first letter standing for lucky.

Cite this as: BMJ 2016;353:i3385

Find this at: http://dx.doi.org/10.1136/bmj.i3385