3 February 2007 (Vol 334, No 7587, pp. 215-266)

**Editor's choice**

*Editor's choice: How much should doctors earn?*
Fiona Godlee
BMJ 2007;334, doi:10.1136/bmj.39112.522280.43

*US editor's choice: On dying and dyeing*
Douglas Kamerow
BMJ 2007;334, doi:10.1136/bmj.39113.523762.3A

**Editorials**

*Venlafaxine for major depression*
Andrea Cipriani, John R Geddes, Corrado Barbui

*Childhood intelligence and being a vegetarian*
Marcus Richards
BMJ 2007;334:216-217, doi:10.1136/bmj.39107.671412.80

*Leprosy after starting antiretroviral treatment*
Stephen D Lawn, Diana N J Lockwood

*Emergency care in the first 48 hours*
Peter Leman

*Allergy to hair dye*
John P McFadden, Ian R White, Peter J Frosch, Heidi Sosted, Jenne D Johansen, Torkil Menne

**Letters**

*This week's letters*

*Teenage pregnancy: Education programme has changed since study*
D Graham Mackenzie, John Taylor
BMJ 2007;334:221, doi:10.1136/bmj.39108.388345.1F

*Teenage pregnancy: Systematic review addresses socioeconomic inequalities*
Ginny Brunton, Ann Oakley, Angela Harden
BMJ 2007;334:221, doi:10.1136/bmj.39108.405139.1F
**Semantics:** Schizophrenia can and should be renamed
David G Kingdon, Yoshihiro Kinoshita, Farooq Naeem, Maged Swelam, Lars Hansen, Selveraj Vincent, Shanaya Rathod
BMJ 2007;334:221-222, doi:10.1136/bmj.39108.396852.1F

**Resuscitation orders:** Orthopaedic consultant is responsible in hip fracture
Paul Diggory
BMJ 2007;334:222, doi:10.1136/bmj.39108.393380.1F

**NHS cataract service:** ISTC programme is an expensive option
Simon P Kelly, Brenda Billington, Richard Smith, Rhod Daniel
BMJ 2007;334:222, doi:10.1136/bmj.39108.384572.1F

**News**

Ghost authorship of industry funded drug trials is common, say researchers
Sally Hargreaves
BMJ 2007;334:223, doi:10.1136/bmj.39108.653750.DB

Giving a voice to the unheard
Bryan Christie
BMJ 2007;334:223, doi:10.1136/bmj.39111.697315.DB

In Brief: News
BMJ 2007;334:224, doi:10.1136/bmj.39112.338889.43

Antibiotics in second trimester may reduce risk of preterm birth
Barbara Kermode-Scott
BMJ 2007;334:224, doi:10.1136/bmj.39111.364410.DB

Bush proposes plan to expand health insurance coverage
Janice Hopkins Tanne
BMJ 2007;334:225, doi:10.1136/bmj.39108.481042.DB

$500m investment in poor countries' health systems will boost vaccination
John Zarocostas
BMJ 2007;334:225, doi:10.1136/bmj.39111.668044.DB

MPs criticise £0.9bn PFI scheme for failing to consult doctors
Lynn Eaton
BMJ 2007;334:226, doi:10.1136/bmj.39111.537477.4E

More than 200 000 people ask Novartis to drop its challenge on drug patent
Sally Hargreaves
BMJ 2007;334:226, doi:10.1136/bmj.39111.596481.DB
Kidney patients should get more care from nurse practitioners and have dialysis closer to home
Roger Dobson

Publishers hire PR heavyweight to defend themselves against open access
Owen Dyer

Doctors disagree over detention of patients with extensively drug resistant tuberculosis
Peter Moszynski
BMJ 2007;334:228, doi:10.1136/bmj.39108.568368.DB

Dutch court acquits suicide counsellor of breaking the law
Tony Sheldon
BMJ 2007;334:228-229, doi:10.1136/bmj.39108.711794.DB

And the Oscar goes to . . . Salvarsan
Roger Dobson
BMJ 2007;334:229, doi:10.1136/bmj.39111.340023.DB

Ontario starts colorectal cancer screening programme for adults aged 50-74
David Spurgeon
BMJ 2007;334:229, doi:10.1136/bmj.39108.509167.DB

NICE proposes incentives to keep addicts free of drugs
Susan Mayor

Politicians should not be making healthcare decisions, survey says
Anne Griffin
BMJ 2007;334:229, doi:10.1136/bmj.39111.379688.DB

National director calls for five point plan on care of older people
Lynn Eaton
BMJ 2007;334:229, doi:10.1136/bmj.39111.622176.4E

UK minister is questioned about recruiting too many GPs
Adrian O'Dowd
BMJ 2007;334:229, doi:10.1136/bmj.39108.561470.DB

World's first public-private cord blood bank launched in United Kingdom
Susan Mayor
BMJ 2007;334:229, doi:10.1136/bmj.39114.689850.DB
Shortcuts from other journals: Drug safety is too important to leave to industry

Shortcuts from other journals: Citalopram lifts depression after heart disease

Shortcuts from other journals: One fracture predicts another, especially in men

Shortcuts from other journals: Surgery still best treatment for fibroids
BMJ 2007;334:231, doi:10.1136/bmj.334.7587.231

Shortcuts from other journals: Antibodies to myelin don't predict progression to multiple sclerosis
BMJ 2007;334:231, doi:10.1136/bmj.334.7587.231-a

Shortcuts from other journals: High school linemen are too heavy for their health
BMJ 2007;334:231, doi:10.1136/bmj.39108.435938.BE

Feature

One for the album: First pictures
Geoff Watts

Head to head: Is doctors' self interest undermining the National Health Service
Alan Maynard
BMJ 2007;334:234, doi:10.1136/bmj.39066.452847.68

Head to head: Is doctors' self interest undermining the National Health Service?
Laurence Buckman

Observations

THE WEEK IN MEDICINE: So how much do doctors really earn?
Michael Day

ATLANTIC CROSSING: Is the president's plan dead even before arrival?
Uwe E Reinhardt
Analysis

Defining limits in care of terminally ill patients
Ursula K Braun, Rebecca J Beyth, Marvella E Ford, Laurence B McCullough
BMJ 2007;334:239-241, doi:10.1136/bmj.39048.475046.68

Research

Risk of suicide during treatment with venlafaxine, citalopram, fluoxetine, and dothiepin: retrospective cohort study
Annalisa Rubino, Neil Roskell, Pat Tennis, Daniel Mines, Scott Weich, Elizabeth Andrews

IQ in childhood and vegetarianism in adulthood: 1970 British cohort study
Catharine R Gale, Ian J Deary, Ingrid Schoon, G David Batty

Clinical review

Endometriosis
Cynthia Farquhar

Practice

Masterclass for GPs: Headaches
Geraint Fuller, Claire Kaye
BMJ 2007;334:254-256, doi:10.1136/bmj.39090.652847.DE

Penetrating trauma to the junctional zone needs aggressive management
J Ahmad, G C Beattie, R Kennedy, J A Kennedy, W D B Clements
BMJ 2007;334:257-258, doi:10.1136/bmj.39055.459248.80

10-minute consultation: Newly diagnosed iron deficiency anaemia in a premenopausal woman
Tony Todd, Tim Caroe
BMJ 2007;334:259, doi:10.1136/bmj.39003.602338.94

Views & reviews

Personal views: Collecting feathers in the health service

REVIEW OF THE WEEK: Telling the inside story?
Jeanne Lenzer
BMJ 2007;334:261, doi:10.1136/bmj.39108.525810.59

FROM THE FRONTLINE: Flagging up a necessary division
Des Spence
BMJ 2007;334:262, doi:10.1136/bmj.39111.450301.59
Drug tales and other stories: On the cheap
Ike Iheanacho

BETWEEN THE LINES: "Remember: people—and animals"
Theodore Dalrymple

MEDICAL CLASSICS: Tropical Diseases
W F Bynum
BMJ  2007;334:263, doi:10.1136/bmj.39108.622535.59

Obituaries
This week’s obituaries

Roland Jacob Levinsky
Caroline Richmond
BMJ  2007;334:264, doi:10.1136/bmj.39108.594352.FA

Pamela June Alexander (née Tyson)
Rosemary Alexander

Peter MacDonald Crawford
Iain Broom

Thomas Goronwy ("T G") Evans
Sue Smith
BMJ  2007;334:265, doi:10.1136/bmj.39108.688646.FA

David Pratt
Roger Peel

Patricia Mary Qura'n (née Gilligan)
Alex Magee, Bronagh Bunting, Fiona Gibson

Francis James ("Jim") Zacharias
John Cunningham

Julian Thomas ("Tomi") Spenser
Shmuel Reis, Eva Alkon-Katz, Jim Shalom, Jonathan Spenser

Minerva
Minerva
Minerva
Andrew Sherley-Dale, Rod Hughes
BMJ 2007;334:266, doi:10.1136/bmj.39107.711655.47

Fillers
Are you addicted to your "crackberry"?
Mark Taylor

BMJ updates: Drug eluting stents don’t reduce mortality in the long term compared with bare metal stents

Medical folklore—the use of your stethoscope’s bell
Michael Reschen
BMJ 2007;334:253, doi:10.1136/bmj.39098.406852.BE

The God incarnate
Ajit Singh Kashyap, Kuldip Parkash Anand, Surekha Kashyap
BMJ 2007;334:256, doi:10.1136/bmj.39098.439016.BE

When I use a word: Geographic metals
Jeff Aronson
BMJ 2007;334:258, doi:10.1136/bmj.39113.728322.E0

Corrections
Minerva
BMJ 2007;334, doi:10.1136/bmj.39107.412465.BE

Obituary of William Ian McDonald
BMJ 2007;334, doi:10.1136/bmj.39107.418623.BE
Venlafaxine for major depression
More evidence that risks outweigh benefits for most patients?

In this week’s BMJ Rubino and colleagues provide new evidence that informs the debate about whether antidepressants increase the risk of suicide.1 The study, a retrospective observational analysis of the General Practice Research Database, found that patients prescribed venlafaxine were more likely to attempt or complete suicide than patients prescribed citalopram, fluoxetine, or dothiepin. Adjustment for possible confounders, however, greatly reduced the excess risk.

Venlafaxine is a serotonergic and noradrenergic reuptake inhibitor, and it may be more effective than selective serotonin inhibitors for major depression.2,3 However, patients often discontinue treatment because of side effects.4

The database analysed is the world’s largest computerised database of anonymised longitudinal medical records from primary care (more than 3.4 million active patients, about 13 million in total since 1987, from around 450 primary care practices throughout the United Kingdom; www.gprd.com). The database has been used extensively for pharmacoepidemiological research, including previous studies examining the possible association between death from suicide and the use of antidepressant drugs.5,6

The non-experimental nature of the database creates methodological problems that can make results difficult to interpret, as the study by Rubino and colleagues shows. Firstly, the patients treated with venlafaxine were probably selected clinically, and differed from those treated with other agents in several variables related to the risk for suicide. Although sophisticated statistical analyses were used to control for potential confounding, some variables—such as diagnosis, comorbidities, and pre-existing depression or suicidal ideation—may not have been effectively accounted for. Moreover, there may have been residual confounding by uncontrolled variables, such as treatment dosages and adherence to treatment.

Secondly, the choice of the primary outcome is important. Although some epidemiological studies have used the outcome of all deliberate self harm, Rubino and colleagues restricted the primary outcome to acts with a deliberate suicidal intent. Deliberate self harm, particularly suicide, is often thought to be a relatively “hard” outcome in studies of antidepressants, but enormous scope exists for ascertainment bias. For this reason, in a meta-analysis of randomised clinical trials of long term lithium therapy, we used all cause mortality as the primary outcome, and suicide and deliberate self harm as secondary outcomes, to limit ascertainment bias and make the findings more robust.7

Thirdly, differences in the drug being compared and sample populations may explain heterogeneity between the results of different observational analyses.5–8 For example, Rubino and colleagues selected only specific antidepressants as comparators (citalopram, fluoxetine, and dothiepin), excluded other agents, and did not include a reference group of patients not taking antidepressants.

Observational evidence offers insights into long term and real world outcomes for large groups of people, but it can rarely show a convincing causal relation between two events. It can be hypothesised that the drug itself can precipitate suicide, because of its potential mechanism of action. Randomised controlled trials are better able to establish causal relations, but they usually follow highly selected samples of patients for short periods.9 Systematic reviews of randomised controlled trials may increase statistical power, but absolute numbers of patients having rare adverse events such as completed or attempted suicide are low. Thus, reporting or not reporting a few cases can completely change the overall outcome.10 Even with these limitations, systematic reviews have consistently reported an excess risk of suicide in children and adolescents with major depression taking antidepressants, but not in adult patients.11–12

Despite these uncertainties, clinically useful conclusions for everyday clinical practice need to be formulated. Currently, UK guidelines recommend that treatment with venlafaxine should be started or managed only under the supervision of specialist mental health medical practitioners. The Medicines and Healthcare Products Regulatory Agency has recently changed this guidance, however, to apply only to severely depressed patients or those in hospital who need doses of 300 mg daily.

Recent observational evidence indicates that, in suicidal patients who have ever used antidepressants, current use of any antidepressant is associated with an increased risk of attempted suicide and with a decreased risk of completed suicide and death.8 In this analysis, venlafaxine was associated with the highest risk of suicide. A similar risk profile for venlafaxine was highlighted by reanalyses of data from clinical trials conducted in children.11 Finally, the Food and Drug Administration in the United States, the Medicines and Healthcare Products Regulatory Agency, and the manufacturer of venlafaxine have issued a warning about the risk of cardiotoxicity and toxicity associated with overdose of venlafaxine.
Venlafaxine therefore has a consistent but unexplained risk of increased suicide and toxicity. Despite evidence of its marginally greater efficacy compared with other antidepressants,2,3 current evidence suggests that venlafaxine should not be first line treatment for people with major depression.


Evidence increasingly suggests that intelligence is associated with health and survival,1,2,3 although the reasons for this are not fully understood. To varying degrees, intelligence could mediate the long term impact of early adverse circumstances (such as overcrowding), influence the acquisition of factors that protect health, and reflect underlying biological mechanisms that regulate health. A cohort study in this week’s BMJ by Gale and colleagues4 assesses whether intelligence can influence the acquisition of protective factors. In a large representative population study of more than 8000 British men and women, intelligence in childhood was associated with a vegetarian diet in mid-adulthood, and this was independent of educational attainment and social class.4

So what do the results say about the relation between intelligence and personal values, and whether intelligence influences lifestyle choices that protect health? An analysis of five prospective studies found that vegetarians had a mortality rate 76% lower than non-vegetarians, after adjusting for age, sex, and smoking.2 A randomised controlled trial found that higher intakes of vegetables, legumes, fruit, and bread (as well as more fish and chicken instead of red meat) were associated with reduced total mortality, death from heart disease, and incident cancer in men who had survived myocardial infarction.6

Like all good research, the study by Gale and colleagues raises provocative but testable questions. Firstly, given that childhood cognition is itself modified by nutrients, including iodine, iron, zinc, vitamin B-12, folate, and omega 3 fatty acids,1 do dietary patterns established in childhood influence food choice in adults? If so, might this long term influence in part explain the association between intelligence and vegetarianism? Little is known about how diet in childhood relates to that in adulthood, although preliminary evidence from the 1946 British birth cohort suggests that people from families who ate large amounts of fruit in childhood continued to do so in midlife, whereas those from families who ate little fruit in childhood also had low fruit consumption in midlife.8

Secondly, observational studies have reported positive associations between the intake of nutrients such as B complex vitamins, omega 3 fatty acids, and unsaturated unhydrogenated fats in adults and cognitive function in later life,9,10,11 although a randomised controlled trial found no effect of long term vitamin E supplementation in healthy women aged 65 years or more.12 Might the associations with cognitive aging reported in observational studies be explained to some extent by people choosing their dietary habits according to prior cognitive ability?

So to return to where we began, does diet mediate (or at least partly mediate) the effect of intelligence on other health outcomes—such as cardiovascular disease, colorectal cancer, diabetes, and Alzheimer’s disease—then public health interventions to encourage eating a consistently healthy diet may be beneficial. Such an approach should begin with parents encouraging children to eat healthily, with the aim that they continue to make

Childhood intelligence and being a vegetarian
Do bright children grow up to make healthy choices?


RESEARCH p 245

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KB
Leprosy after starting antiretroviral treatment

An increasingly reported clinical problem but not a serious public health risk

Recent media reports have highlighted a “startling and worrisome new link” between antiretroviral treatment and leprosy. Some people infected with HIV who have started such treatment in countries where leprosy is endemic have developed florid leprosy lesions in the initial months of treatment. What underlies these unusual manifestations and do they have implications for the control of leprosy?

The note of alarm is understandable—leprosy and HIV are both greatly feared diseases. The manifestations described, however, are a well recognised complication of antiretroviral treatment known as immune reconstitution disease or immune reconstitution inflammatory syndrome (IRIS). This presents with the manifestation (or “unmasking”) of a previously subclinical coinfection or the deterioration of an opportunistic infection that had been responding to treatment. These effects are due to antiretroviral treatment causing the rapid recovery of cell mediated immune responses, which trigger host immune responses to foreign antigen. Such reactions typically occur during the first four months of treatment—the most rapid phase of immune recovery.

The HIV pandemic has had surprisingly little effect on the epidemiology and clinical features of leprosy. However, immune reconstitution disease is a new and unexpected clinical interaction between these diseases in patients who have just started treatment. The first published case of leprosy associated immune reconstitution disease occurred in 2003 in a Ugandan living in London. More cases have been described since, mostly in patients living in South America. In most cases, immune reconstitution disease triggered the initial presentation of leprosy, often with a reactive state—acute inflammation within the leprosy lesions that may result in rapid loss of nerve function. Some reactions have been unusually severe with skin ulceration, protracted cutaneous inflammation, and neuropathy.

Antiretroviral treatment has been available since 1996 in countries with high average incomes. Immune reconstitution disease has been well characterised in this setting and is associated with a predictable range of opportunistic infections. Antiretroviral treatment is increasingly being used in resource poor countries where different coinfections exist; which of these infections have the potential to be associated with immune reconstitution disease is not yet clear. Immune reconstitution disease has, for example, recently been described in association with the parasitic infections leishmaniasis, strongyloidiasis, and schistosomiasis. Many of these cases were in immigrants receiving antiretroviral treatment in countries with higher incomes. Leprosy has joined this growing list of tropical infections associated with immune reconstitution disease.

Antiretroviral treatment is now more accessible in resource poor countries where leprosy is still endemic, such as South America, India, and Africa; not surprisingly, reports of leprosy associated with immune reconstitution disease are increasing. This disease is most likely to be seen in India, where the HIV epidemic is growing and where 161,457 new cases of leprosy were diagnosed in 2003 alone. From the patient’s perspective, HIV infection and leprosy are both highly stigmatising diseases, and having both is understandably distressing. This distress may be heightened by the patient’s perception that the leprosy was caused by

Emergency care in the first 48 hours

“Acute physicians” herald the new specialty of acute medicine

The importance of the first 48 hours in producing successful outcomes for acutely ill patients cannot be underestimated. The definition of a successful outcome depends on who is measuring it. Clinicians look for successful diagnosis and treatment, governance directors look for safety and use of pathways and guidelines, educators look for training opportunities, managers want to decrease length of stay, whereas patients (usually) just want to get better and go home. The problem is how to deliver on all of these fronts.¹

The traditional model of delivering acute care for medical patients, who make up the bulk of acute admissions to hospital, has been slowly changing. The older model of a hierarchal medical team has begun to disappear.² There have been many drivers to this change. In the United Kingdom changing patterns in the availability of junior doctors (such as the European Working Time Directive and the Modernising Medical Careers project (www.mmc.nhs.uk/pages/home)) has led to team fragmentation and multiple handovers of acutely ill patients.³ A growing deficit of primary care after normal working hours has meant an increase in hospital admissions at night. The imposition of a maximum stay of four hours in emergency departments in the UK has meant that many acutely ill medical patients have been rapidly moved to medical wards, perhaps before a full assessment.⁴

¹ Worrisome new link: AIDS drugs and leprosy. New York Times. 2006 October 24. http://query.nytimes.com/search/query?d=nytdsections%26kone%26ktwo%26r%26s%26t%26u%26w%26x%26y%26a%26b%26c%26query%3Dleprosy%26dialog selection=full


Some emergency departments have responded to the challenge by providing some acute inpatient care for up to 24-48 hours, but this is far from widespread.3

Specialty physicians are becoming less keen to participate in the acute medical take roster, which can lead to less input from consultants regarding the initial assessment and care of inpatients.4 This problem is much greater in Australia, where the specialty of internal medicine is facing an increasing shortage of recruits, as increasing numbers of trainees opt for the more remunerative procedural specialties (which provide invasive procedures such as endoscopy, angiography, and bronchoscopy).5 The increasing dearth of general physicians means that some hospitals have no general medical teams. In such hospitals, patients with several chronic diseases can no longer be treated by one team alone and require multiple consultations and longer stays in hospital.6

In the United States the rising role of the hospitalist, who is based entirely in the hospital and provides acute medical care, conflicts with the traditional role of the patient’s primary care doctor, who previously visited the hospital to provide inpatient care. The hospitalist model is becoming the benchmark for acute care for many medical patients in hospital in the US, although these clinicians are not recognised as internal medicine physicians in most places.8

The UK has seen the rise of the “acute physician,” who is dedicated to managing the first few days of all acute medical admissions. These individuals come mainly from the specialty of general medicine, but as the acute physician specialty develops its training model and approval for core training, it will soon have its own specialists.4 Individuals with core training in emergency medicine or critical care medicine will also join, so that a specialty dedicated to acute medical care will grow.9

Soon the Joint Committee on Higher Medical Training will implement the model for two years of common stem training in acute care to follow on from the two foundation years that new UK graduates now work. Thus, six months each of intensive care, emergency medicine, anaesthesia, and acute medicine will provide the robust platform for specialty training in acute medicine.

The question is whether this acute physician model is useful. Has it evolved only out of political change, or can it really make a difference? The expectation of the Royal College of Physicians is that with dedicated acute physicians undertaking ward rounds twice daily, seven days a week, the model should work.10

Acute physicians will initiate investigations and interventions from the moment the patient arrives in the emergency department or acute assessment unit. This will enable rapid assessment and management of patients with potentially complex comorbidities and multisystem disease from the outset. Acute physicians will coordinate allied health interventions and plan discharge from the outset. They will also liaise with specialist inpatient teams and where possible with domiciliary services and “hospital in the home” teams to avoid treating patients in hospital when they could be treated at home. The evidence to date on the effectiveness of the model is piecemeal. Better short term outcomes have been reported with the acute physician model than with traditional team based care in the UK, and the US hospitalist model has shown cost efficiencies without any robust long term outcome data as yet.11

The challenges are obvious if acute physicians are to succeed. The political drivers for change are strong, and hospital executives and commissioners will always favour a service that can deliver safe, effective, efficient, and fast care for inpatients. But what of the specialty of acute medicine itself? Respect from peers is hard to earn, and generalists are not so highly regarded as the superspecialist who may be seen (by colleagues and patients) as the master of a specific craft or skill set. To paraphrase Dame Carol Black (the last president of the Royal College of Physicians and an important figure in the development of this specialty) speaking at a meeting of the Society for Acute Medicine held in September 2006 in London: a specialty can exist only when a robust body of published work provides evidence of what the specialty does and why it should continue to exist. Thus will it earn the respect of its peers.

This is an exciting time to be in acute medicine; it should be the core specialty in the hospital of the future, around which other inpatient activity will flow.12 Acute physicians should be competent to manage medical emergencies and make complex multisystem medical diagnoses. But they should also be able to smooth the path of the increasingly truncated hospital journey. They should be the link between home treatment and brief but focused hospital based treatment, and they should also coordinate other specialist care whenever it is needed.

Allergy to hair dye
Its incidence is rising, as more and younger people dye their hair

For more than 100 years para-phenylenediamine (PPD) and other related members of the aromatic amine family have been the main agents used in permanent hair dyes, and more than two thirds of hair dyes currently contain PPD. This compound is an effective hair dye owing to its low molecular weight, its ability to penetrate the hair shaft and follicle, its strong protein binding capacity, and its rapid polymerisation in the presence of a coupler (a kind of catalyst) and an oxidising agent. However these properties also make PPD an ideal contact allergen and, indeed, it is among the most potent.

During the 20th century allergic reactions to PPD became such a serious problem that it was banned from hair dyes in Germany, France, and Sweden. Current European Union legislation allows PPD to comprise up to 6% of the constituents of hair dyes on the consumer market (3% when added to the oxidising solution required to develop the colour). No satisfactory or widely accepted alternatives to the aromatic amine agents are available for use in permanent hair dye.

A patient with contact allergy to a hair dye often presents with dermatitis on the face or around the hair line. Severe reactions also occur; some patients have had such gross facial swelling that they have been treated initially for angio-oedema and some have been admitted to hospital. Contact allergy to PPD and related aromatic amine dyes is detected by patch testing using 1% PPD in petroleum jelly. This is included in most standard series of patch tests used to screen for contact allergy in patients with eczema. Such screening may, however, fail to detect allergic reactions to other hair dyes.

Dermatologists report anecdotally that the frequency of positive reactions to PPD on patch testing is increasing. This was confirmed in a recent retrospective survey in London, with a doubling in frequency over six years to 7.1% in a clinic for adults with contact dermatitis. This rise could not be attributed to an increase in occupational PPD allergy — the use of temporary “henna” tattoos containing high concentrations of PPD (often when on holiday), or widely accepted alternatives to the aromatic amine and other related members of the aromatic amine family, and its rapid polymerisation in the presence of a coupler (a kind of catalyst) and an oxidising agent. However these properties also make PPD an ideal contact allergen and, indeed, it is among the most potent.1

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In the same London clinic from 1965 to 1975 between five and 11 patients with non-occupational PPD allergy were seen each year.8 More recently this figure has consistently exceeded 40 such patients annually. This increase is unlikely to be due to more consistent referral and diagnosis because only 15% of people with a history consistent with hair allergy seek medical attention, and of these only a minority are tested for allergy to hair dye.11

Data from patch testing in Belgian and Portuguese centres confirm the pattern seen in London (personal communication by A Goosens to the European and Environmental Contact Dermatitis Research Group in Leuven, 2005), as do studies from Denmark,9 Germany,10 and Singapore.11 12

In Bangkok screening of 2500 normal adult volunteers by patch testing showed a 2.7% prevalence of PPD allergy which, when extrapolated to the general population, suggests that more than one million Thai adults may be sensitive to PPD,13 while in Germany up to 1.3 million adults in the general population may be sensitive.12

Market research indicates that more people are dyeing their hair and are doing so at a younger age. In 1992 a survey by the Japan Soap and Detergent Association of young people in Tokyo, 13% of female high school students, 6% of women in their 20s, and 2% of men in their 20s reported using hair colouring products.14 15 By 2001 the proportions using hair colouring agents had increased in these three groups to 41%, 83%, and 33%, respectively. Furthermore, female high school students and young women were dyeing their hair at shorter intervals. In America the proportion of young men dyeing their hair increased by 25% in the five years after 1998.16 One leading Japanese company saw its hair dye sales more than double in the 10 years up to 2001, and according to data from the Japanese government total shipments of hair dye to Japan doubled in the 10 years up to 2001.17 In Denmark 75% of women and 18% of men have used hair dye,10 and the median age for first use of hair dye for both men and women is during the teenage years.18 Severe hair dye reactions among children have recently been reported.19 20

Wider debate on the safety and composition of hair dyes is overdue—among medical and scientific communities, the public, and legislators. Cultural and commercial pressures to dye hair and, perhaps, the widespread obsession with the “culture of youth” are putting people at risk and increasing the burden on health services. It may not be easy to reverse these trends, however, as some patients have continued to use such dyes even when advised that they are allergic to them and risk severe reactions.21

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Competing interests: None declared.

Systematic review addresses socioeconomic inequalities

We have grappled with social disadvantage and teenage pregnancy in our recent systematic reviews evaluating the effectiveness and appropriateness of interventions to reduce the social exclusion associated with teenage pregnancy.¹ As Henderson et al postulate,² we found that programmes aiming to change life opportunities for young people have a considerable positive effect on reducing pregnancy in this group. Our meta-analysis of high quality controlled trials indicated that pregnancy rates could be reduced by 39% in young people who themselves were recipients of day care as children or received youth development programmes in American studies. However, studies of young people’s views also showed important research gaps. These include the development and evaluation of policies to promote young people’s involvement in schooling, further education and training, and to support families experiencing problems linked with social disadvantage and poverty.

Happiness, enjoyment of school, and ambition can all help to delay parenthood in young people. The available research evidence also points both to day care and to youth development programmes as effective and appropriate ways of supporting children and young people. These findings imply a need for further research into the socioeconomic and cultural influences that shape young people’s choices about when they become parents, and what other options are open to them for a happy and satisfying life.

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Competing interests: None declared.


Schizophrenia can and should be renamed

Lieberman and First make the case against renaming schizophrenia on the grounds that changing the term would not change the stigma attached to the underlying condition.¹ Yet renaming is a key strategy used by marketing and public relations industries to improve image, alongside attitude change and education.

But what should it be replaced with? One of the conclusions emerging from the “Deconstructing psychosis” conference, part of the DSM-V Prelude project was for replacing the current categories with a general psychosis syndrome.² However, this would increase still further the heterogeneity that currently bedevils biological and psychosocial research, clinical practice, and resource management, when differentiation is really needed.

Trauma has recently been recognised as relevant to a significant group of patients with this diagnosis.³ Since the 1950s, a new group has also been included to broaden the diagnosis further: those in whom there is an association with hallucinogenic drugs.⁴ Renaming and differentiation of these two groups (“traumatic” and “drug precipitated”) psychosis is clinically possible from those patients who develop systematised delusions and those who seem to be particularly vulnerable to

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Competing interests: None declared.


TEENAGE PREGNANCY

Education programme has changed since study

Henderson et al studied sexual health and relationships education (SHARE) delivered between 1996 and 1999 in east Scotland.¹ They showed no statistically significant influence on conceptions or terminations by age 20 years.

In the article by Henderson et al, SHARE was delivered exclusively by school teachers,¹ but an earlier study on the same cohort highlighted the limitations of using such an approach.² Recent advice to local authorities and NHS organisations reinforces the need for a multidisciplinary approach in working to reduce teenage pregnancies.³ A review of the evidence in preparation for the second phase of the national health demonstration project, “Healthy Respect,” shows that a multifaceted approach combining education, information, and services has the best chance of improving sexual health outcomes.⁴ In Scotland, teachers now work alongside youth workers, school nurses, and voluntary organisations to deliver SHARE⁵ with improved access to services for young people.

B M | 3 FEBRUARY 2007 | VOLUME 334
An elderly patient had a hip fracture and a day or two later a cataract operation. The orthopaedic consultant in charge of the hip was unable to attend because he had to fly to a different hospital and the cataract surgeon was unable to see the patient. As this report confirms, 1 the lack of evidence of cost effectiveness of phase 1 of the ISTC programme is an expensive over-reaction in the independent sector treatment centre (ISTC) programme, further investment in cataract surgical facilities continues in phase 2. Meanwhile, for long term stability of the service, the best option for the public is to support local NHS units, which brought down cataract waiting times, which patients need to call on in an emergency or for chronic eye disease, and which train the next generation of surgeons while meeting waiting time targets. A constructive partnership of clinicians, managers, and commissioners is a surer way to achieve sustained improvements in access and quality of care, rather than centrally imposed targets. A constructive partnership of clinicians, managers, and commissioners is a surer way to achieve sustained improvements in access and quality of care, rather than centrally imposed initiatives and diktat, such as the needless cataract ISTCs.

The appeal court decision in the case of Burke makes clear that doctors are not obliged to offer treatment they believe will be ineffective, simply because a patient wishes to receive it. 2 If an arrest is foreseeable but prospects of CPR succeeding are very poor it should not be offered and a “do not attempt resuscitation” (DNAR) order should be made.

If the patient has capacity—which may be difficult to judge in the context of acute illness—then as part of the explanation of the treatment plan doctors should generally explain that CPR would not be offered because it would not succeed. If confusion or distress will probably result from such discussion then under common law 3 a doctor may decide it is not in a patient’s best interests to be told that an ineffective treatment will not be offered and a DNAR order is made without discussion. If the patient lacks capacity a relative may be told the reasons for a DNAR order when the treatment plan is explained.

Many elderly people would not wish to receive CPR. The principle of autonomy and the common law gives patients the right to refuse it. If an arrest is foreseeable and CPR has reasonable prospects of success patients should be asked if they wish to receive it. If they are not competent, relatives should be consulted to try and judge what the patient would have wished.

Orthopaedic consultant is responsible in hip fracture

Anwar and Ahmed highlight the difficulties making cardiopulmonary resuscitation (CPR) decisions for elderly people with hip fracture. 1 Published guidance and the law are confusing, 2 3 but there is a logical approach to using them.

It is not practicable to make a resuscitation decision on everybody in hospital. If an arrest is “foreseeable,” guidelines supported by common law and common sense dictate that a decision needs to be made. If it is not foreseeable then, provided the option to refuse CPR is available, no decision need be made, leaving a patient “for CPR” by default.

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Industry funded trials often have ghost authorship

Sally Hargreaves LONDON

Ghost authorship, whereby someone who has made a major contribution to a scientific article as an author is not acknowledged, is a widespread practice, says a study published this week.

In the clinical trials investigated in the study, three quarters of individuals who had made significant contributions to the final paper were not listed as authors (PLoS Medicine 2007;4:e19). In most cases these were statisticians working for the company sponsoring the trial.

“Ghost authorship is a form of research misappropriation, and we believe that this practice serves commercial purposes,” said the lead author of the study, Peter Gøtzsche, of the Nordic Cochrane Centre in Copenhagen.

“Authorship establishes accountability, responsibility, and credit for scientific articles. If authorship is misappropriated, readers may be misled, and the potential for manipulated analyses and conclusions may increase,” he added.

The researchers assessed all published, industry initiated randomised trials approved in 1994-5 by the scientific and ethical committees for Copenhagen and Frederiksberg in Denmark. They compared the full trial protocols, written before the trial started, with the primary scientific report that resulted from these trials and that was published in a peer reviewed journal. A total of 44 trials were included, of which 43 were initiated by drug firms and one by a local company.

Ghost authorship was considered to be present if individuals who wrote the trial protocol, did statistical analyses, or wrote the manuscript were not listed as authors of the publication or members of a study group or writing committee or were not mentioned in an acknowledgment.

Researchers found evidence of ghost authorship in three quarters (33) of the 44 trials. In 31 trials the ghost authors were statisticians. Eight publications acknowledged the assistance of statisticians, and four acknowledged the assistance of medical writers.

Journal editors increasingly demand full transparency before publication in terms of who wrote, paid for, and carried out studies. Many medical journals have introduced new procedures to ensure this transparency.

Guidelines such as those drawn up by the International Committee on Medical Journal Editors have, however, been criticised for being ineffective, and they lack sufficient endorsement outside the largest journals.

Dr Gøtzsche said that “the prevalence of ghost writing could be considerably reduced, and transparency improved, if existing guidelines were followed.”

Award gives a voice to the unheard

Bryan Christie EDINBURGH

Seven years ago Abu Bakarr Kargbo had his hands hacked off by rebels during Sierra Leone’s brutal civil war. Today he still lives with his wife and three children in an abandoned camp for amputees, hoping for a better future.

A series of photographs about his life as an amputee has won this year’s Luis Valtueña International Humanitarian Photography Award, organised by Médecins du Monde UK. The series is the work of a Greek freelance photographer, Yannis Kontos.

The award was established 10 years ago as a tribute to four humanitarian workers who were murdered in conflicts in Rwanda and Bosnia-Hercegovina. The exhibition is at the Institut Français d’Écosse, 13 Randolph Crescent, Edinburgh, until 28 March.

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For the full versions of articles in this section see bmj.com

UK NEWS Kidney patients should have dialysis closer to home, p226
WORLD NEWS Bush proposes plan to expand health insurance coverage, p225
bmj.com Politicians should not be making healthcare decisions
IN BRIEF

UN complaints about police raid:
The United Nations secretary general, Ban Ki-moon, has complained to Sudan after a police raid on a relief compound in which five foreign staff were beaten with rifles and another was sexually assaulted. Last month several agencies withdrew from Sudan after an aid worker was raped, and others threatened to suspend operations if security didn’t improve.

Stop providing unproved treatments, says association:
Some non-essential treatments for which there is no proof of clinical benefit, such as tonsil removal, hysterectomy for heavy menstrual bleeding, and varicose vein surgery, should no longer be available free on the NHS, said the Association of Directors of Public Health. The savings to the NHS could be used to make most prescriptions free instead, it said. See www.aodph.org.uk

Unwanted pregnancies in United States cost $5bn:
Direct medical costs of unintended pregnancies in the United States cost $5bn (£2.6bn; €3.9bn) in 2002—made up of $3.9bn for births, $800m for induced abortions, and $270m for fetal losses, says a paper in Contraception (doi:10.1016/j.contraception.2006.11.009).

Israeli doctors resist HIV testing of surgeons:
The Israel Medical Association and health ministry have decided not to impose routine testing of surgeons for HIV, even though a senior heart surgeon at a major Tel Aviv medical centre discovered that he is a carrier. Thousands of patients he operated on in the past decade have received letters inviting them to be tested.

US university sets up unsponsored education site:
Doctors at Georgetown University in Washington, DC, have started a website offering 200 free continuing medical education courses, which are required if US doctors are to keep their licence. Most US continuing education is funded by drug firms, whereas www.PharmedOut.org is publicly funded.

More institutions tighten rules on industry gifts:
The Henry Ford Health System in Detroit has joined Stanford and Yale Universities and the Geffen School of Medicine at the University of California at Los Angeles in banning meals and gifts from drug companies.

Antibiotics in second trimester may reduce risk of preterm birth

Barbara Kermode-Scott ALBERTA

Giving macrolides or clindamycin during the second trimester of pregnancy to women at risk of preterm births can lower the risk, a new systematic review and meta-analysis by Canadian researchers indicates. But the study also found that giving metronidazole in the second trimester is linked with a greater risk of preterm birth in the high risk population.

The study’s authors, from the University of Montreal and Laval University, Quebec, say that delivery before 37 weeks’ gestation complicates between 7% and 11% of all pregnancies, is the leading cause of perinatal morbidity and mortality, and is responsible for high healthcare costs (Journal of Obstetrics and Gynaecology of Canada 2007;29:35-44).

Anne-Maude Morency and Emmanuel Bujold undertook a systematic review and meta-analysis of randomised controlled trials that evaluated the effects of antibiotics administered during the second trimester on the rate of preterm delivery. Of the 61 articles yielded by their search, three original papers, investigating a total of 1807 women, examined the use of macrolides.

Women whose data were included in the analysis were all considered to be at risk of preterm delivery (for example, they tested positive for vaginal fetal fibronectin, had a urogenital mycoplasmal infection, or had had a preterm delivery before).

Dr Morency and Dr Bujold found that, in comparison with placebo, macrolides were associated with a lower rate of preterm births (odds ratio 0.72 (95% confidence interval 0.56 to 0.93)), as was clindamycin (odds ratio 0.68 (0.49 to 0.95)).

However, metronidazole was not linked with significant changes in the rate of preterm births (odds ratio 1.1 (0.95 to 1.29)). In fact, women who were given only mid-trimester metronidazole showed a higher rate of preterm delivery (odds ratio 1.31 (1.08 to 1.58)).

“There have been a lot of conflicting results about the role of antibiotics in preventing preterm birth,” said Dr Bujold, an assistant professor in the department of obstetrics and gynaecology at Laval University.

“These findings will go a long way towards dispelling some of the confusion around the use of antibiotics during pregnancy and help open up new thinking about how certain antibiotics can be used to help prevent preterm birth,” she said.

As many as 50% of spontaneous preterm births are related to infections, with Mycoplasma species being the most common microbial isolates from the amniotic cavity, said Dr Bujold.

Dr Bujold and Dr Morency say that more research is needed regarding their finding—they point out that uncertainty remains about how erythromycin and clindamycin should be administered, because of the different dosing regimens, different drug preparations, and different timing of administration in their analysis.

In light of their findings the authors conclude that metronidazole should be avoided during the second trimester of pregnancy in women at a high risk of preterm birth.
Bush proposes plan to expand health insurance

Janice Hopkins Tanne  NEW YORK
In his state of the union address last week President George Bush proposed changes to the tax laws that would, he said, let more people buy individual health insurance policies. This would help to insure the 47 million Americans who now lack coverage, he said.

The president also proposed redirecting Medicaid funds away from hospitals that provide free care to uninsured patients to subsidies to help poor people buy health insurance. Big city hospitals that treat uninsured patients said that this proposal would result in their suffering financial cuts of $30bn (£15bn; €23bn), which would particularly affect their emergency and outpatient departments.

Critics said that the tax changes would benefit richer people, while poorer people would still not be able to afford health insurance. Furthermore, the proposed changes would undermine the existing system of health insurance through employers.

The secretary for health and human services, Mike Leavitt, asserted that the proposed policy would make health insurance more affordable for uninsured people and would help states expand their health insurance coverage for poor people and for children.

About half of Americans receive health insurance through their jobs. Typically they pay part of the cost (deducted from their pay), and their employers pay a part.

Bush’s proposal would consider money spent on health insurance as taxable income, but would offer each family a new $15000 deduction for health insurance premiums from its federal income tax. Single people would get $7500.

People who get their health insurance through their jobs would face a choice. If they could buy health insurance more cheaply than what their employer pays (typically around $11500 for a family) then they would benefit: they would be able to deduct $15000 from their taxes but buy the insurance for less. Such people would probably drop out of their employer’s health insurance plan.

If a generous employer provided a plan worth more than $15000, then people would pay tax on the amount over $15000.

However, older people and people with existing health problems would be likely to stay with their employer provided health insurance because they would be unable to buy health insurance in the marketplace or would face high premiums. That would leave employers with a pool of older, sicker workers. Health insurance companies would probably raise premiums paid by the workers and their employers. The upshot might well be that employers would stop offering health insurance as a job benefit—a trend that has been under way for years.

Comments on President Bush’s plan have varied. The Wall Street Journal said, “Overall, the plan is a step in the right direction” (http://online.wsj.com), 24 Jan, “Bush health-care plan finds business backers”).

Karen Davis, a health economist and head of the non-profit Commonwealth Fund, said that the plan “would fail to assist most of the uninsured.” (See Observations, p 238.)

$500m for poor countries’ health systems will boost vaccination

John Zarocostas  DAVOS, SWITZERLAND
Vaccination programmes prevented more than 2.3 million premature deaths between 2000 and the end of 2006, show figures released last week by the public-private Global Alliance for Vaccines and Immunisation (GAVI).

“The results show that the GAVI has proven concepts, and we’re delivering the vaccines, saving lives, and getting coverage in the poorest, and some of the toughest, environments in the world,” said Julian Lob-Levyt, executive secretary of the alliance.

Since its creation at the annual World Economic Forum meeting in Davos, Switzerland, in 2000, the alliance has committed over $2.6bn (£1.3bn; €2.3bn) to support national immunisation programmes in more than 70 countries.

New projections of data from the World Health Organization, a member of the alliance, show that GAVI funding has protected 28 million children against diphtheria, tetanus, and pertussis.

This has increased the overall immunisation rate for these diseases to 77% of children in 2006, up from 63% in 1999.

Similarly, 138 million children have received new and underused vaccines against hepatitis B, Haemophilus influenzae type b, and yellow fever, boosting greatly the coverage for these diseases, a spokesman for the alliance said. For example, the number of countries providing hepatitis B vaccine grew from just 15 in 1999 to 61 in 2006.

Mr Lob-Levyt said that key targets now were to get the rate of immunisation above 80% in most countries of the world, to introduce new vaccines, “and to get those prices down and affordable.”

To further increase the global immunisation coverage, the alliance announced at last week’s annual meeting of the World Economic Forum that it would invest a total of $500m over the next five years to strengthen basic health systems in poor nations.

The alliance singled out weak healthcare infrastructure as the main barrier to providing immunisation.

The new funds, which will come in the form of flexible grants, are to be earmarked for activities such as recruiting and training health workers, building and enhancing systems to distribute vaccines and drugs, transporting healthcare workers and equipment, and purchasing basic medical supplies.

“Vaccines are a miraculous thing … When you save lives, that has an incredible value in and of itself,” Bill Gates, chairman of the Bill and Melinda Gates Foundation, told reporters during the release of the new findings at the annual World Economic Forum. “No child should be denied access to life saving immunisations,” he said.
MPs criticise organisers of £0.9bn PFI scheme for failing to consult doctors

Lynn Eaton LONDON

Failure to consult doctors and nurses at an early stage was partly to blame for the demise of a plan for an £894m (£1.4bn; $1.7bn) privately funded hospital in west London, MPs have ruled.

The ambitious private finance initiative (PFI) plan to unite three hospitals—Royal Brompton Hospital, Harefield Hospital, and St Mary’s, Paddington—into one state of the art campus foundered when, five years into the project, capital costs were set to rise exponentially.

The plan originally submitted to the Department of Health in 2000 was for a £411m scheme (at 2005 prices). But the proposed final cost by 2005 was £894m. By then, when the department pulled the plug on the project, £15m had already been spent.

In a damning report Edward Leigh MP, chairman of the House of Commons Committee of Public Accounts, said, “The collapse of the ambitious Paddington Health Campus project after five years was the direct result of appalling planning and forecasting of costs by the NHS trust partners; rows between them over the way forward; and uncertainty over the Department of Health’s degree of support for the scheme, which was lukewarm at best.

“The department, in effect, left this £900m construction project to local NHS staff, who were rapidly out of their depth and floundering. Their amateurism and incompetence in this field compounded the consequences of bad decisions made at the outset.”

Among the report’s numerous criticisms was the project’s failure to consult with medical and nursing staff before submitting initial plans to the Department of Health. Once this consultation did take place it soon became apparent that not enough land was available to develop the campus on the St Mary’s site.

“There was also lack of agreement on the number of beds needed, which ranged between 835 and 1200 over the five year planning period. This should have been agreed at the outset, said the committee.

The campus partners were, says the report, “imprudent” in submitting their report in 2000, which was “manifestly ambitious.”

“Overall, the scheme was simply too ambitious for the capacities of those responsible for delivering it,” says the report.

The committee went on to criticise not just the Paddington scheme but other privately financed hospital building schemes that have gone over budget, and it hit out at the Department of Health for failing to monitor these schemes adequately.


Thousands ask Novartis to drop its drug patent case

Sally Hargreaves LONDON

As the Indian High Court this week postponed the hearing of the legal challenge by the Swiss drug company Novartis against the Indian government over its refusal to grant the company a patent on imatinib (Glivec), nearly a quarter of a million people from more than 150 countries signed an international petition calling for Novartis to back down.

Unni Karunakara, from the charity Médecins Sans Frontières, said at a press briefing this week in New Delhi: “Over 80% of the medicines we use to treat AIDS patients come from India, and access to affordable and new drugs for HIV is now becoming imperative as drug resistance grows . . . Sixty seven per cent of India’s generic drug exports go to the developing world. We cannot stand by and let Novartis turn off the tap.”

Leena Menghaney, a lawyer for the charity, said: “The court case was adjourned today until 15 February to give the Indian government more time to prepare its defence.

“This comes amid growing public and patient opposition to the Novartis challenge. Patient groups have written to the Indian government this week calling for the best legal defence, and the Indian government has taken this very seriously. Many patient groups feel that their right to health under the Constitution of India is now under attack.”

India has been able to produce cheap generic versions of drugs patented in other countries because until 2005 the country did not grant pharmaceutical patents.

Patients should be

Roger Dobson ABERGAVENNY

More kidney transplantations, care that is planned better, and more people having dialysis are among the priorities of England’s new national clinical director for renal services. Donal O’Donoghue, a consultant renal physician who takes up his three days a week post immediately, also wants to see more seamless care, so that patients with kidney disease do not have to see a range of different professionals for their problems in areas such as blood pressure, diabetes, and cholesterol concentrations.
Publishers hire PR heavyweight to defend themselves against threat of open access

Owen Dyer LONDON
A new public relations campaign to be launched by the American Association of Publishers will equate open access to scientific journal articles with government censorship.

Email messages leaked to the journal Nature describe a meeting last summer, arranged by the association’s professional and scholarly publishing division. The meeting was between employees of the publishing houses Elsevier and Wiley and the American Chemical Society and the public relations consultant Eric Dezenhall (Nature, www.nature.com, doi: 10.1038/445347a).

Mr Dezenhall, author of several novels and of Nail ’Em! Confronting High-Profile Attacks on Celebrities and Businesses, specialises in “marketplace defence” and has been described by an industry publication as the “pit bull of PR.”

Mr Dezenhall described his proposed public relations strategy in a memo. He advocated “bypassing mass ‘consumer’ audiences in favour of reaching a more elite group of decision makers,” arguing that “it’s hard to fight an adversary that manages to be both elusive and in possession of a better message: free information.”

He encouraged his clients to “develop simple messages,” such as “public access equals government censorship,” “scientific journals preserve the quality/pedigree of science,” and “government [is] seeking to nationalise science and be a publisher.” Mr Dezenhall suggested teaming up with groups opposed to the expanding roles of government, such as the Competitive Enterprise Institute.

A leaked email from Wiley’s director of corporate communications, Susan Spilka, said that Mr Dezenhall had criticised the publishers’ response to open access campaigns as too defensive and too nuanced. “Media messaging is not the same as intellectual debate,” she noted.

Ms Spilka declined to comment on the email but said that the industry needed to counter the “soundbites” of advocates of open access, which she described as appealing but simplistic.

Mr Dezenhall’s company, Dezenhall Resources, never comments on its clients or contracts, but the American Association of Publishers has confirmed that it has engaged Mr Dezenhall’s services. The leaked emails suggest that Mr Dezenhall estimated the campaign’s cost at between $300 000 (£150 000; €230 000) and $500 000.

The publishers’ move comes at a time when commercial scientific publishers are under pressure from Congress to provide free access to articles covering research that is funded by US taxpayers through the National Institutes of Health.

Mark Patterson, director of publishing at the open access Public Library of Science, said, “The AAP’s [American Association of Publishers] action is an indication of how strong the open access movement has become. There has been huge progress towards open access over the past year in particular,” he said, and he predicted that “comprehensive open access is now inevitable.”

Brian Crawford, a senior vice president at the American Chemical Society and a member of the association’s executive chair, showed the BMJ a letter he had sent to members of the association’s scholarly publishing division saying that the leaked news of Mr Dezenhall’s hiring had led to “gross misinterpretation of our motives and methods.”

The letter said, “Scholarly publishers have been slow to recognise that the misleading soundbite messages and aggressive lobbying tactics of those who wish to influence government and public policy have been orchestrated and funded by organisations wishing to advance their own agenda.”

More than 12 000 academics have signed a petition urging the European Commission to publish publicly funded research free of charge on the internet. The question of open access is to be debated at a commission conference next month.

Signatories include the Nobel laureates for medicine Harold Varmus and Rich Roberts. The UK Medical Research Council signed as an institution, as did the Wellcome Trust, which allows money for open access publication in its research grants.

able to have dialysis closer to home

Dr O’Donoghue, who retains his clinical appointment at Salford Royal NHS Foundation Trust, said that seamless care was a key priority.

“The vast majority of patients with kidney disease have stage three disease, and only a minority will benefit from secondary care. Even for those where secondary referral is appropriate, a lot of the care plan can be delivered in primary care,” he said.

“It is important to recognise that chronic kidney disease is one of the vascular diseases. We want to move to a situation where we don’t have patients going for diabetes care one week, blood pressure the next, kidney the week after, and lipids the next week. There is no reason why nurse practitioners in primary care—who already see people with high blood pressure and diabetes—may not acquire the skills to manage kidney aspects of patients they are already seeing.”

“I also want to increase haemodialysis capacity, so that people can get it locally without long travelling times. An increased transplant rate is also a key target.”

He is keen too on seeing more renal research in England.

Dr Donal O’Donoghue

NEWS
The World Health Organization has issued new guidance on the treatment of patients with extensively drug resistant tuberculosis (XDR-TB), after it was suggested that people may need to be involuntarily detained to prevent a virtually untreatable disease from emerging.

Writing in the latest edition of *PLoS Medicine* (2007;4:e50, doi: 10.1371/journal.pmed.0040050), Jerome Singh, from South Africa's Centre for the Aids Programme of Research, recommends that the South African government follow the example of New York state in the 1990s, where forced confinement was used to contain an outbreak of multiple drug resistant tuberculosis.

The outbreak of XDR-TB in South Africa (*BMJ* 2006;333:566, 16 Sep) has so far caused 74 deaths, predominantly among people with AIDS. Its virulent nature and mortality of nearly 100% is starting to cause panic in southern Africa. Doctors in the region fear that it threatens to overwhelm Africa's fragile health systems, which already face the world's highest AIDS burden.

Dr Singh writes: “XDR-TB represents a major threat to public health. If the only way to manage it is to forcibly confine then it needs to be done. Ultimately in such crises, the interests of public health must prevail over the rights of the individual.”

But Peter Davies, a cardiothoracic consultant at the Cardiothoracic Centre (NHS) Trust, Liverpool, and at University Hospital Aintree and secretary of the advocacy group TB Alert, disagreed. He said, “We’re not in the business of locking up patients,” and he emphasised that resistance to treatment was generally the fault of health systems rather than patients.

Professor Davies said, “Drug resistance is not unprecedented—there’s no need to get into a flap about it. The one good aspect of the scare is that it will hopefully kickstart finance for new TB drug research. With sufficient funding we could probably get a treatment for XDR-TB within five years, but at the rate we’re currently going we’re not going to be there in 20 [years].”

WHO insists that XDR-TB should be given the same priority as avian flu and severe acute respiratory syndrome, and it recommends that any form of involuntary confinement “must be viewed as a last resort, and justified only after all voluntary measures to isolate such a patient have failed.”

WHO recommends: “Governments must ensure, as their top priority, that every patient has access to high quality TB diagnosis and treatment for TB and drug-resistant forms of TB.”

However, it adds: “If a patient wilfully refuses treatment and, as a result, is a danger to the public, the serious threat posed by XDR-TB means that limiting that individual’s human rights may be necessary to protect the wider public. Therefore, interference with freedom of movement... could be considered legitimate.”

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**Doctors argue over detention of patients with XDR-TB**

**Peter Moszynski | LONDON**

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Writing in the latest edition of *PLoS Medicine* (2007;4:e50, doi: 10.1371/journal.pmed.0040050), Jerome Singh, from South Africa’s Centre for the Aids Programme of Research, recommends that the South African government follow the example of New York state in the 1990s, where forced confinement was used to contain an outbreak of multiple drug resistant tuberculosis.

The outbreak of XDR-TB in South Africa (*BMJ* 2006;333:566, 16 Sep) has so far caused 74 deaths, predominantly among people with AIDS. Its virulent nature and mortality of nearly 100% is starting to cause panic in southern Africa. Doctors in the region fear that it threatens to overwhelm Africa’s fragile health systems, which already face the world’s highest AIDS burden.

Dr Singh writes: “XDR-TB represents a major threat to public health. If the only way to manage it is to forcibly confine then it needs to be done. Ultimately in such crises, the interests of public health must prevail over the rights of the individual.”

But Peter Davies, a cardiothoracic consultant at the Cardiothoracic Centre (NHS) Trust, Liverpool, and at University Hospital Aintree and secretary of the advocacy group TB Alert, disagreed. He said, “We’re not in the business of locking up patients,” and he emphasised that resistance to treatment was generally the fault of health systems rather than patients.

Professor Davies said, “Drug resistance is not unprecedented—there’s no need to get into a flap about it. The one good aspect of the scare is that it will hopefully kickstart finance for new TB drug research. With sufficient funding we could probably get a treatment for XDR-TB within five years, but at the rate we’re currently going we’re not going to be there in 20 [years].”

WHO insists that XDR-TB should be given the same priority as avian flu and severe acute respiratory syndrome, and it recommends that any form of involuntary confinement “must be viewed as a last resort, and justified only after all voluntary measures to isolate such a patient have failed.”

WHO recommends: “Governments must ensure, as their top priority, that every patient has access to high quality TB diagnosis and treatment for TB and drug-resistant forms of TB.”

However, it adds: “If a patient wilfully refuses treatment and, as a result, is a danger to the public, the serious threat posed by XDR-TB means that limiting that individual’s human rights may be necessary to protect the wider public. Therefore, interference with freedom of movement... could be considered legitimate.”

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**Dutch court acquits suicide counsellor of breaking the law**

**Tony Sheldon | Utrecht**

In a controversial ruling a Dutch court has acquitted a “suicide counsellor” of helping a 54 year old woman kill herself, judging that he had not actively initiated or directed her death. The counsellor’s advice on the quantity of drugs to be taken to be certain of death was judged to be within legal boundaries.

Ton Vink, a 53 year old philosopher, is attached to the Horizon Foundation, an organisation that offers help to people who choose to commit suicide. The woman rang him first in August 2003, 10 months before she committed suicide. The two had several contacts, through letters and telephone, to discuss suicide. In January she faxed him a letter listing her “supply” of drugs, with which she intended to kill herself. He later wrote confirming her plans to use dextropropoxyphene, flurazepam, and temazepam. He pointed out that the doses she planned were significantly higher than was recommended by websites which advise people about suicide, adding that this would “increase your sense of security.”

The prosecution argued that this was not general information but amounted to offering concrete instructions to address the woman’s special situation. It demanded an eight month prison sentence, five conditional.

But Mr Vink’s lawyer argued that this wording was a confirmation of the woman’s intention to use more drugs.

The court ruled that the woman had taken higher doses of drugs on her own initiative and that Mr Vink should be given the benefit of the doubt. It judged that he had not actively guided or
Ontario to screen for colorectal cancer

David Spurgeon QUEBEC

Ontario has announced that it will become the first Canadian province to set up a province-wide screening programme for the early detection of colorectal cancer. This type of cancer has the second highest death toll of cancers in Canada.

The Ontario government says its scheme is the first such screening programme in North America to use the faecal occult blood test. Other countries that already have such a programme are Australia, Italy, France, Finland, and Israel. The United Kingdom started rolling out its programme in selected areas last June.

The province, which calls this blood test “the only method of colorectal cancer screening that has been proven in randomised controlled trials to reduce deaths from colorectal cancer,” will make test kits widely available through doctors’ surgeries, walk-in clinics, the healthcare helpline Telehealth Ontario, and pharmacies. The test kits are used at home. Small amounts of faeces are applied to a cardboard slide. The test detects trace amounts of blood in the faeces that may indicate the presence of cancer.

About 2% of people who complete the test and who have an average risk for the disease will show positive results and will need to be referred for a colonoscopy for further investigation. Cancer organisations recommend that everyone aged 50 or older with no symptoms and no family history of the disease should be screened. Those with a family history have a higher risk and should speak to their doctor about screening.

Ontario’s health and long term care minister, George Smitherman, said that colorectal cancer that is detected in its early stages has a 90% chance of being successfully treated. In 2006 an estimated 7500 Ontarians were given a diagnosis of colorectal cancer, and 3100 died from the disease. Currently a fifth of people aged 50 or over are screened for it, by any method. The new screening programme, which will target Ontario residents with a family history of the disease and everyone aged 50 to 74, will cost the Ontario government C$194m (€84m; £127m; £164m) over the next five years.

The Ontario division of the Canadian Cancer Society has been advocating the adoption of a screening programme for years, said Peter Goodhand, its chief executive officer. He calls the new programme “a real success.”

And the Oscar goes to . . . Salvarsan

Roger Dobson ABERGAVENNY

At last, recognition for the unsung heroes of the movies. Film actors, directors, and producers have their Oscars, BAFTAs, and other awards, but until now no one has thought to applaud the roles of antibacterial drugs in cinema.

The authors of a new study list nearly 70 movies where antibacterial drugs are classed as playing major, supporting, or just rub-on roles (Revista Española de Quimioterapia 2006;19:397-402).

The authors, from the department of preventive medicine at the University of Salamanca, write, “There are movies in which antibacterial agents form part of the central plot, while in others they are merely an important part of the plot. In still others, [the agent’s] presence is isolated, and in these it plays an ambient or anecdotal role.”

In the study the authors identified the presence of antibacterials in the treatment and prevention of diseases in popular movies over the past century. They say that the greatest movie about drug treatment is Dr Ehrlich’s Magic Bullet (1940), a film about the life of the German scientist Paul Ehrlich and the discovery of arsphenamine, which was marketed under the trade name of Salvarsan from 1910 as a treatment for syphilis.

After its film debut Salvarsan made a number of other appearances, including in Out of Africa (1985), in which the novelist Karen Dinesen Blixen returns to her native Denmark to receive treatment for syphilis, and Miss Evers’ Boys (1997), about the 1932 Tuskegee syphilis study. Salvarsan’s replacement, Neosalvarsan, had a key role in Captain Corelli’s Mandolin (2001).

But although arsphenamine takes the Oscar, the award for lifetime achievement seems to have been won by the sulphonamides, which feature in a huge number of films.

“They were widely used during World War II and their use is also seen in many films. When watching them, one senses that tons of sulphonamides were distributed for prophylactic and therapeutic purposes,” say the authors.

Credits for the sulphonamides include Destination Tokyo (1943), Batas (1943), Saving Private Ryan (1998), Guns of Navarone (1961), The Story of Dr Wassell (1944), Merrill’s Marauders (1962), None but the Brave (1965), Exodus (1960), and Kelly’s Heroes (1970).

Penicillin is the other big player in films, directed the woman’s suicide and that his actions, therefore, remained within the permissible boundaries for helping suicide. These actions include talking, giving information, and offering moral support. Assisted suicide remains an offence in the Netherlands. Only doctors are allowed a defence if they act within closely defined criteria, including the specification that the patient must be competent and must have a medically classifiable condition.

Concerns have been expressed that the judgment loosens the law on assisted suicide by making it clear how people other than doctors could help someone commit suicide without breaking the law. Theo Boer, professor of ethics at Utrecht’s Protestant Theological University, said that the judge could not convict Mr Vink because in the letter of the law he had done nothing wrong.

He believed that the judge’s decision represented a loophole that should be closed: “The verdict may in effect mark a further liberalisation of the Dutch practice. The state should have the obligation to dissuade its citizens from choosing to commit suicide.”

Last year the founder of the Horizon Foundation, Jan Hilarius, was sent to prison for helping a 25 year old woman kill herself (BMJ 2006;333:514).
Drug safety is too important to leave to industry

There’s a fundamental tension in many drug trials between the sponsors, who want the trial to be a useful marketing tool, and the guardians of public health, who want it to answer key questions about whether a drug works and is safe. Ideally, a trial should do both, but when the design is left to industry sponsors, important public health questions are often forgotten, according to two US academics. Cyclo-oxygenase-2 (COX 2) inhibitors are a perfect example. A clinical trial of a new COX 2 inhibitor, etoricoxib, randomised more than 30,000 people but could not establish the safety of this drug because it was compared with diclofenac, a drug that is likely to have similar cardiovascular and gastrointestinal side effects to etoricoxib. No differences were seen between the two drugs. Naproxen is now the “preferred comparator” of the Food and Drugs Administration (FDA) for large trials of COX 2 inhibitors, and it would certainly have been a more informative choice in this trial.

Important issues about the safety of new drugs should not be left in the hands of the industry that sells them, they write. The stakes are simply too high. US citizens urgently need an independent national champion (possibly the FDA or the Institute of Medicine) with the commitment to identify, design, and fund large clinical trials. These phase 4 trials would focus entirely on pressing clinical questions, not the diversions of the market place. The drug industry might even be inspired to follow suit.

Citalopram lifts depression after heart disease

Patients with coronary artery disease are vulnerable to depression. Depression makes it harder for patients to follow lifestyle advice and stick to complex drug regimens; this increases the chance of further coronary events or even death. Some doctors aren’t sure if this “natural” response to a life threatening event should be treated, but there’s now reasonable evidence that selective serotonin reuptake inhibitors can help, at least in the short term.

In one recent trial, citalopram worked significantly better than placebo in 284 people with established stable heart disease and major depression. The drug reduced scores on various depression rating scales and increased the chance of a response to treatment. The psychotherapy arms of the same trial (which had a factorial design) were less successful. Controls who had weekly meetings to discuss symptoms and drugs did just as well, or even better on some measures, than patients who had weekly interpersonal psychotherapy. Neither treatment had serious cardiovascular side effects, but citalopram caused the usual problems with dizziness (49%), diarrhoea (49%), somnolence (43%), and sexual dysfunction (21%).

If selective serotonin reuptake inhibitors work for depressed people with heart disease they might also prolong survival or at least reduce the risk of further heart attacks, writes an editorial (pp 411-2). Much bigger trials are needed to find out.

One fracture predicts another, especially in men

Plenty of data are available on the risk of osteoporotic fractures in older women, but fewer are available on the risk for men. To redress the balance, researchers analysed data for all adults over 60 in the small city of Dubbo, a few hundred miles northwest of Sydney, Australia. During 15 years of follow-up, 903 of the 2245 women (32 per 1000 person-years), and 337 of the 1760 men (16 per 1000 person years) had a low impact fracture.

An initial fracture increased the risk of
another one in both sexes, but the increase was more dramatic for men. Men who broke a bone after falling from a standing height were 3.5 times more likely to do so again than men who had never had a fracture (relative risk 3.47, 95% CI 2.68 to 4.48). Put another way, they had about the same risk of fracture as men 20 years older. The relative risk of a second fracture for women was a more modest 1.97 (1.70 to 2.25).

The risks of a recurrence were highest in the first few years after a fracture, but lasted up to a decade. By this time, about half the survivors of both sexes had had a further fracture. Only a minority of women (less than 25%) and even fewer men (3-4%) had any treatment for osteoporosis after their first fracture. The researchers say we could and should do better.


**Surgery still the definitive treatment for fibroids**

Uterine artery embolisation is a quicker and simpler alternative to surgery for some women with symptomatic fibroids. But one in five women who choose embolisation will need further treatment later to control their symptoms, a trial has found.

Researchers randomised 157 premenopausal women. The 106 women who had uterine artery embolisation had less pain, had shorter hospital stays (one day v five days), and returned to work sooner (20 days v 62 days) than the 51 who had myomectomy or abdominal hysterectomy. One year after treatment symptoms were better in the surgical group, although both groups had improved clinically definite multiple sclerosis, regardless of their antibody status at baseline. The authors found no link between the antibodies and progression in any subgroup of patients, including those given steroids. These antibodies are unlikely to be useful diagnostic tests for patients with early disease, say the authors.


**Antibodies to myelin don’t predict progression to multiple sclerosis**

It’s hard to predict what will happen to patients who present with a first neurological episode suggestive of multiple sclerosis. Some will recover, whereas others will progress to the full blown clinical disease. An accurate prognostic test would be a real benefit to patients, and antemyelin antibodies looked like a good candidate because antibody mediated demyelination is thought to have a role in multiple sclerosis. The latest research has been disappointing, however. The presence or absence of two antemyelin antibodies failed to predict outcome for 462 patients taking part in a trial of interferon beta-1b.

All participants had experienced just one neurological episode. They also had clinically silent but suggestive changes on magnetic resonance imaging of the brain. The authors found no significant associations between the presence of the two antibodies (antibodies to myelin oligodendrocyte glycoprotein (MOG) and myelin based protein (MBP)) and patients’ progress over two years. Just under a third of patients developed clinically definite multiple sclerosis, regardless of their antibody status at baseline. The authors found no link between the antibodies and progression in any subgroup of patients, including those given steroids. These antibodies are unlikely to be useful diagnostic tests for patients with early disease, say the authors.


**High school linemen are too heavy for their health**

American footballers have to be big, but some young players are so heavy they are putting their future health at risk. A survey of high school linemen (defenders) from Iowa found that 45% (95% CI 43.6% to 46.8%) were overweight, and another 28% (26.8% to 29.8%) were almost there, with a body mass index between the 85th and 95th centiles for their age. Almost one in 10 had a body mass index above 35, the adult threshold for severe obesity.

The authors made use of publicly available rosters that included data on height and weight for 3683 high school linemen throughout the state. The survey included 69% of Iowa’s high school teams and should be generalisable to linemen elsewhere. Body mass index may not be the best way to measure obesity in adolescents, say the authors. But it correlates well enough with fat mass to hint at the problems that might lie ahead for these players. The mean body mass index for Iowa’s school linemen was above the 85th centile in all categories of school grade and in all classes of school team.

\[JAMA 2007;297:363-4\]
One for the album

Expectant parents’ desire to see images of their unborn children has led to private ultrasonography services. Geoff Watts considers whether this non-medical use of the technique can be justified.

The pictures tell the story. Baby’s first feed, first smile, first steps, first birthday, first everything. The record is there to be scrutinised and treasured. But why wait until birth? Why not start this pictorial history in utero?

Ultrasound imaging may have entered obstetrics as a medical tool, but it is now establishing itself as something much more. Go to the web and you can find scores of companies willing to exploit the powerful emotional impact of seeing your fetus by generating still pictures to grace the first page of the album or moving ones to play on the home computer. Not medically necessary, of course. An indulgence, certainly, but harmless. Or is it?

Not everyone takes a benign view of non-medical ultrasonography. The US Food and Drugs Administration, the American Institute of Ultrasound in Medicine, and the French Academy of Medicine are among several official bodies that have reservations about such use of the technology. In the United Kingdom, Dr Paul Sidhu, chairman of the scientific and education committee of the British Medical Ultrasound Society, detects what he describes as an “overall sense of disapproval” among his colleagues for this development.

What was once the casual offer of hazy black and white Polaroid images during a routine antenatal scan has become a slick business transaction. Driving this transformation has been the big improvement in ultrasound technology. The early two-dimensional black and white scans gave a succession of poor resolution slices through the womb and its contents. Better technology sharpened the images. Then machines arrived that could assemble the slices into a 3D picture of the whole fetus with improved resolution and added colour. With the advent of the fourth dimension time the unborn child can be seen moving. The images are without question startling and, to a parent, captivating.

Many of the companies offering 3D and 4D scans publish testimonials. The Babyview website, for example: “The experience was out of this world ... The most overwhelming feeling in the world to see baby smile ... Probably the best hour of our lives ... Thank you for the amazing experience.” The word “amazing” crops up again and again. Expectant parents seeking a CD-ROM or a DVD of their scan can expect to pay £150-£250 (£220-£380; $300-$490).

Some critics regard the advent of this “boutique ultrasonography” as yet another step towards the medicalisation of birth. But this view is hard to sustain. Keepsake imaging is, if anything, about the demystification of medical technology. And if people choose to pay a couple of hundred pounds to undergo a safe imaging technique, why shouldn’t they? No reason at all so long as it really is safe. This, of course, is the nub of the argument.

“Most doctors are embarrassed by the concept of bonding”

Medical concerns

The commercial providers are reassuring. “During the 30 years or so since the introduction of ultrasound in obstetrics,” according to Babyview (www.babyview.co.uk/faq.asp), “it has not been proven to cause harm.” In similar vein, Create Health (www.createhealth.org/dimensional.htm) says: “Despite extensive studies over 30 years ultrasound has not been shown to cause any harm to mother or baby.” The FDA is more cautious: “Although there is no evidence that these physical effects can harm the fetus, public health experts, clinicians and industry agree that casual exposure to ultrasound, especially during pregnancy, should be avoided.”

The important distinction here is the familiar one between “absence of evidence” and “evidence of absence.”

The argument is not confined to Britain. Guillaume Gorincoeur is a radiologist specialising in prenatal diagnosis at Timone University Hospital in Marseilles. He worries about the growth of commercial keepsake scanning companies operating in France without medical supervision. How, he wonders, do staff deal with the discovery of a fetal abnormality? “Will they announce the bad news to the parents? Or will they say nothing?” Some contracts, he adds, specifically rule out the delivery of any medical information. Also, the ill judged breaking of bad news can influence parents’ decisions on whether to continue with an affected pregnancy.

Unlike some doctors working with ultrasound, Dr Gorincoeur has no inherent objection to generating keepsake images. “After we have performed ultrasound for medical reasons, we try to provide a good 3D picture of the face for the parents, as an extra service. From the medical point of view, 3D or 4D doesn’t add any diagnostic information. But humans are not machines. People want to see their baby.”

In the US, the FDA has long been opposed to non-medical ultrasonography. In the mid-1990s its Center for Devices and Radiological Health began investigating several companies that were doing ultrasonography without medical authorisation or supervision. This, it points out, “may be in violation of State or local laws or regulations regarding use of a prescription medical device.” In 2002 it announced that anyone administering ultrasound without a prescription is breaking the law.

But what of non-medical keepsake scans that are taken with the authorisation of a doctor? The FDA clearly takes a dim view of this too but seems not to have decided precisely what, if any, action to take. The
American Institute of Ultrasound Medicine, by contrast, tackles the issue head on.

In a statement issued last August it acknowledged the pressure from patients for keepsake scans. It then distinguished between three different circumstances in which expectant mothers might be given a keepsake scan:

• As the byproduct of a medically indicated ultrasound examination
• Through a commercial fetal imaging organisation operating without medical supervision
• Through a medical facility operating beyond the medically necessary use of ultrasonography.

The institute concludes that only the first of these three scenarios is consistent with “the ethical principles of our professional organisations.” The second is unacceptable by virtue of the absence of medical supervision, while the third runs counter to the American Medical Association’s code of ethics. This states: “The sale of non-health-related goods by physicians presents a conflict of interest and threatens to erode the primary obligation of physicians to patients.”

The British Medical Ultrasound Society does not, at the moment, have a specific policy on keepsake ultrasound scans. What it does have, says Dr Sidhu, is a policy on safety. This follows the ALARA principle (as low as reasonably achievable). The society is currently updating its policy, and the new version will probably include a statement on non-medical imaging. This is unlikely to be more permissive than that of its US counterpart.

One of the leading exponents of ultrasound in the UK is Professor Stuart Campbell, now retired from the health service and working with Create Health. He is not impressed by the safety argument. He points out that doctors in training, who haven’t yet mastered an efficient ultrasound technique, subject pregnant women to much greater doses than would a skilled operator. “Nobody bats an eyelid about that,” he says. If people were seriously worried about scanning time they would develop computer simulations on which doctors could practise their technique. “If you are competent at what you’re doing, the extra five minutes [required to generate a keepsake scan] is absolutely negligible.”

Bonding

Beyond spreading a little happiness, the case for non-medical imaging relies principally on bonding: the sense of attachment between a mother and her unborn child. The evidence that ultrasound images can foster this comes from 2D scans. But what of the newer technology? “3D or 4D doesn’t add anything more than classical 2D ultrasound in creating the mother’s emotional attachment,” according to Dr Gorincour. Indeed, a recent study found no evidence that 3D was more effective in enhancing maternal-fetal attachment in scans performed at 12 and 18 weeks.

Professor Campbell is conscious of the lack of firm evidence, and accepts that his enthusiasm may put him in a minority. But he continues to speak with passion about “the excited response of parents,” especially fathers, when they see the image on the screen.

He would like an assessment of the effect of 4D imaging in the third trimester. This, he suspects, would show the full effect of the technology. At present, he believes, “most doctors are embarrassed by the concept of bonding. They just want to do their examination and move on.”

The controversy over 3D and 4D imaging would be partially resolved if genuine medical utility could be shown. As Dr Sidhu points out, research is currently under way to find out if seeing the fetus in 3D might help spot abnormalities such as cleft lip. “Early indications are that it probably is a little bit more useful.” But for the moment, he adds, it is by no means self evidently beneficial. “It produces pretty pictures. But people who’ve been using ultrasound for many years and can understand images in 2D can get very good results from just that.”

There is, of course, one group that’s anything but dismissive about “pretty pictures”: the pro-life movement. Many women and the partners, according to one Christian magazine, “change their minds about aborting their child when they see their child’s image on the sonogram screen.” The headline that appeared a few months ago on a (now defunct) US Catholic website said it all: “GE’s new 4D ultrasound technology: a wonderful tool for the pro-life fight.”

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References:

Self interest is an integral part of every human’s programming. The challenge is not to eradicate what is impossible to remove but how to channel these powerful forces to serve the individual and the public good. Economists regard self interest as the engine of economic development. As epitomised in the writing of the economics Nobel laureate Milton Friedman,¹ the challenge for society is how to use self interest as an engine not only for economic development but as the means to maximise individual freedom in decentralised, competitive markets.

For Friedman and his 18th century predecessor Adam Smith,² the “invisible hand” of self interest and the individual pursuit of improvement in a free market with minimal government regulation would ensure that society’s scarce resources were used efficiently and economic growth maximised. This, in theory, makes self interest good.

This simplistic view ignores the realities of most markets, and the healthcare market in particular. Health care internationally is characterised by government sanctioned cartels such as trade unions (like the BMA) and the patent protected drug industry. Drug companies use high prices to fund research and development, which in the past decade has been disappointingly ineffective in bringing novel cost effective products to market. And poor governance of trade unions has meant they have perpetuated the inefficient use of society’s resources while remaining successful in achieving the personal and professional goals of those they represent.

Doctors’ self interest manifests itself in two ways: enhancing personal income and fiercely protecting clinical autonomy—the right to do what they think is best for the patient in front of them. The first type of self interest has enhanced average UK earnings to over £100,000 for both general practitioners and consultants with little observable improved activity or patient outcomes.

The general practice quality and outcomes framework inflated earnings by 30%,³,⁴ but with a limited evidence base and little baseline data its benefits are uncertain.⁴,⁵ Furthermore, by moving away from traditional non-financial incentives to pay for results, the NHS may have undermined public service values that emphasise the importance of trusting professionals to behave efficiently and created a system whose transactions costs, in terms of policing, may be high.

The consultant contract was also expensive and its design paid scant attention to inefficient variations in clinical practice, substantiated in policy literature for decades,⁶,⁷ the continuing long term decline in clinical activity,⁸ and the absence of outcome measurement.⁹ The potential in the contract for improving productivity by collaborative management, particularly of the content of job plans and clinical excellence awards, remains largely unconnected to quantitative management of activity and outcomes. This pay increase has inflated NHS expenditure with all too little benefit to patients or taxpayers, while giving more general practitioners incentives to deliver what good practitioners were already providing.

**Clinical autonomy**

The second area of doctors’ self interest is the understandable desire to do the best for their patients. Rationing requires doctors to decline care even when patients would benefit from it and would like to have it. Doctors should not support patients’ demands for care of marginal cost effectiveness when that inevitably results in depriving other patients of care from which they would benefit more. Furthermore, they must resist lowering treatment thresholds without evidence of cost effectiveness. A doctor’s concern for the individual patient and their self interest can lead to inefficient practice that ignores the opportunity costs of decision making—a decision to give Jones a marginally cost effective treatment deprives Smith of cost effective care. Such inefficiency in the use of society’s scarce resources is surely unethical?

**Pay increases are undermining patient care**

Self interest and responding to financial incentives are an unavoidable and potentially beneficial aspect of human behaviour if they are channelled into improving the performance of the NHS. Recent reforms have ignored this potential to improve patient care, putting the pay rise cart before the productivity horse. These pay increases, together with workforce management which has led to unaffordable employment increases, are creating deficits and undermining patient care and the financial performance of the NHS.

An essential part of the mitigation of these failures is the linking of reward to performance, in terms of activity and the measurement of patient outcomes. Shifting the focus to whether care improves patients’ health will create “signals” for targeting cost effective investment. Without such signals inefficient governments that misspend taxpayers’ resources and powerful providers focused on short term gambling will continue to undermine the NHS. Instead of talking merely about money, we need to determine whether its use benefits patients or is merely a form of social security for providers.

**Competing interests:** AM has been chair of York NHS Hospitals Trust since 1997. He is a member of Department of Health committees on payment by results and information and a specialist adviser of the House of Commons’ Select Committee on Health for their workforce inquiry.

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Recent newspaper headlines have suggested that doctors’ pay is responsible for the financial crisis in the NHS. Alan Maynard argues that financial and other self interest is endangering the service, but Laurence Buckman believes the remuneration is justified.

The NHS is its staff. Europe’s largest employer spends the bulk of its money on those who deliver health care to UK patients. The small amount that is doctors’ pay could not undermine the NHS, when the total number of workers is so large.

Without adequate pay there is no morale. Demanding and receiving proper pay and conditions is everyone’s right, even in the public sector. This is not self interest. Self interested doctors would go and work elsewhere. Reward, including non-cash benefits, in the NHS is less than that in the private sector for equivalently weighted jobs, and NHS professional pay was less than that of almost all other Western health services for many years until 2004.

Doctors’ pay has been maintained irregularly since the Doctors’ and Dentists’ Pay Review Body was created to advise governments 46 years ago. Periods of small pay rises have been followed by sudden large catch-up increases. The review body’s reports have repeatedly been interfered with by the treasury and the government because they did not like the results. Effectively, doctors’ pay is being used as a partial regulator of inflation, which is specifically forbidden in the review body’s rules.

Today’s general practitioners, like their predecessors, have to fund their practices from their income. Until 2003, there was a “cost plus” contract that supported business expenses, but it had become inflexible and complicated. General practitioners were working long hours, including nights and weekends. Out of hours pay was low, and general practitioners were willing to give up £6000 each to pass the responsibility to someone else. That out of hours care has proved much more expensive to reprovide is no surprise to doctors.

General practitioners’ morale was low in 2000. The new contract was an attempt to correct that by placing contracts with practices rather than general practitioners, setting limits to what a practice could be asked to do, and creating a total budget for staff and expenses. General practitioners’ pay became the profit that was left after expenses. Despite dishonest government taunts to the contrary, practices must continually invest in their staff and premises and provide high quality service or else patients will leave.

Performance and pay
The main source of extra income into practices from the new contract is the quality and outcomes framework, which accounts for 40% of practice income. During the development of the framework, civil servants and ministers repeatedly taunted that general practitioners were rubbish and could never deliver any quality. We replied that practices were doing much of what was in the framework already and that we regarded this as pay for work already done hitherto unrewarded. We told the government exactly what the profession would achieve if given performance related pay—it would perform. The government believed that general practitioners would score only 350 points (out of 1000) and took much persuasion that practices would do better than 750 points as this could be reached by data cleaning alone. When we asked what would happen if the NHS did not have enough money to pay for this improved quality, we were told that “the NHS bank” would bear the cost. Ultimately, the evidence based practice defined by the framework will save lives by preventing and limiting disease, but it is too early to show this.

In 2004 framework pay rose sharply, but that was an agreed part of the 2003 deal. Since then practice resources have increased by small amounts, if at all. Increases are paid only if the practice undertakes a variety of government inspired activities. This money has proved hard to earn, and most practices have seen profit fall in real terms as expenses have risen. To limit losses, many have regrettably resorted to replacing general practitioners with non-medical staff.

The government claims that general practitioners’ pay has risen unexpectedly, but this is not so. The BMA predicted the rise quite accurately. Despite the frequently quoted £300m overpayment,1 the sum is actually only £140m as the rest was given to other primary care staff.2 The £140m was the amount that general practitioners earned by doing better than the government thought they would. Total pay has been deliberately misquoted by adding the employers’ pension contribution that general practitioners have to pay for themselves—which makes pay seem 14% higher than it is.

If patients want a health service round the clock delivered to a high standard by sufficient doctors of acceptable calibre then they have to pay taxes for it. Government figures show a shortage of general practitioners. If self interest had been pandered to there would be a glut of doctors. That there isn’t is because of the dreadful way that the NHS is managed by a government bereft of ideas and the honesty and wit to tackle the problems that deter young people from joining us. Doctors are fed up with being told that the small percentage of the NHS that they cost is the reason why the NHS is in financial trouble. Most patients see us as part of the solution and are willing to pay.

Competing interests: LB is a member of the BMA GP negotiating committee and deputy chairman of the BMA’s GP Committee.

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THE WEEK IN MEDICINE

So how much do doctors really earn?

According to the media, some UK general practitioners are reputed to be earning around £250 000 a year, but what is the truth behind the headlines, and how does UK doctors’ pay here compare with elsewhere, asks Michael Day

The rumbling political row over debt in the NHS means that the vexed issue of doctors’ pay is not going to go away any time soon.

Are doctors in the United Kingdom overpaid? An obvious way to address the question is to compare the earnings of UK medics with those of their overseas colleagues. That is easier said than done, though: few if any direct comparisons exist, and any comparison is made difficult by different contractual agreements and working conditions. The UK Treasury has, however, made an attempt, in its latest 2007 comprehensive spending review for the NHS.

The report contains estimates of average earnings of GPs and hospital doctors in 2003-4 in 16 countries, including the UK’s major competitors. The figures are based on research gathered by British embassies. It should be emphasised that the figures are estimates.

A widening gap

Nevertheless, a few things leap out from the data, including the large (and, in the case of hospital salaries, huge) lead that US doctors enjoy in pay terms. The second is the very large advantage that UK doctors have over their continental colleagues.

GPs in Italy have remarkably low average earnings—the result of the marketplace being flooded with too many doctors.

Bear in mind that these are 2003 figures. The latest, very large pay rises given to UK doctors will almost certainly have widened the salary gap between British and continental doctors even further.

It’s not in doubt, however, that GP partners have enjoyed very large pay increases in the last three years. And inevitably the contract that has led to the “pay bonanza,” as the newspapers have called it, has come under fire. When reports of GPs earning £250 000 a year broke last year, the Sun newspaper, in an editorial entitled “Wads up doc,” said it made sense “to cap doctors’ salaries and stop patients being short changed.”

Some of the broadsheets joined in. The Daily Telegraph’s Simon Heffer said: “I do not doubt that many GPs work hard . . . However, equally I do not doubt that a few are royally ripping off the Government and the taxpayer thanks to the stupidity with which the Government settled its deal with their trade union.”

Renegotiations are under way

Some leading health economists, such as John Appleby of the think...
tank the King’s Fund, say that the recent contracts are “not set in stone.” Professor Appleby says that behind the scene renegotiations are already under way.

In terms of the consultants’ contract, ministers will be seeking to include new incentives to boost productivity rather than simply to reward the amount of time consultants spend in hospital. But the BMA says that initial predictions of the size of consultants’ pay rises under their new contract have proved wide of the mark.

Between 2003-4 and 2004-5 their earnings rose by around 20% as the number of work sessions they attended rose from 10 to 12. Since then, however, Mr Ford says that rises in their salaries have stalled.

As far as GPs are concerned, ministers are keen to make performance related targets tougher. The BMA insists that the new contract had radically improved the care of patients, particularly for those with chronic diseases.

Hamish Meldrum, head of the BMA’s GPs committee, said, “In the area of raised blood pressure alone, GP care under the new contract means that over a five year period 8700 patients in England will avoid having a heart attack, stroke, angina, or heart failure.”

Nevertheless, outside the BMA there is a groundswell of opinion that GPs are being too generously rewarded for providing some aspects of care that should already have been regarded as routine.

Also, other observers, such as Niall Dickson, chief executive of the King’s Fund, say that the contract may actually have cut GPs’ productivity by allowing the closure of Saturday morning surgeries and the ending of 24 hour cover.

The government believes that value for money and its own pride could be partially restored if family doctors were to invest more of their expanding profits back into their businesses to improve patients’ care. If that’s the case, say its critics, then ministers should have drawn up a contract that required this.

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“In the area of raised blood pressure alone, GP care under the new contract means that over a five year period 8700 patients in England will avoid having a heart attack, stroke, angina, or heart failure”

Head of the BMA’s GPs committee Hamish Meldrum

Left: how the London Evening Standard covered claims about high earning GPs last year, and, below, the front page of the tabloid Daily Mail earlier this week
Is the president’s plan dead before arrival?

Bush’s proposed health reforms would do little for the millions of low income, uninsured Americans

In his State of the Union address of 23 January, President Bush unveiled his much heralded health reform initiative to a perplexed nation. As is their wont, the television media swiftly unearthed staunch proponents and staunch opponents of the proposal, and unleashed the extremists upon one another, thus adding to the confusion. It did not help that the president delicately omitted from his speech an important but politically risqué feature of his proposal, most likely to enhance the public marketability of the policy (www.whitehouse.gov/stateoftheunion/2007/initiatives/fact sheet). The full proposal has three distinct facets.

Firstly, the president would make health insurance premiums paid by employers on behalf of employees—hitherto not included in the employees’ taxable compensation—fully taxable with effect from 1 January 2009. The total loss to the US Treasury from this time hallowed tax preference has been estimated to range currently from $200bn to $220bn (£102bn to £112bn; €154bn to €170bn) a year, more than twice the sum that would be needed to move the nation to full universal health insurance coverage.

By itself, then, this facet of the proposal amounts to a sizeable tax increase. It is this facet of the president’s proposal that he delicately omitted from his televised speech, although it is clearly set out in the associated fact sheet on the White House website (www.whitehouse.gov/stateoftheunion/2007/initiatives/healthcare.html). The huge tax savings

The huge tax savings... continue to accrue disproportionately to high income families least in need of public subsidies for their health care

Secondly, the president would allow Americans, regardless of insurance status, to deduct from taxable income $7500 for individual tax payers or $15 000 for a family. This is the felicitous facet of the proposal upon which Bush dwelt in his speech. On average, a standard health insurance policy for an American family now costs about $12 000, although by 2009, the onset of the president’s plan, that figure is bound to be closer to $14 000. Americans whose employer in 2009 spent more on health insurance premiums than the standard deductions would, of course, pay added taxes on the excess. Because the standard deductions would be indexed over time only to general price inflation and not the much higher rate of inflation for health care, more and more Americans would find themselves in that position as time goes on.

Thirdly, the president would redirect funds the federal government already spends on health care to the budgets of state governors, who could use these funds to help their citizens gain access to health insurance. Neither Bush nor the White House fact sheet identifies which money already being spent would be redirected towards state government budgets, nor what the total sum of those funds might be. Everyone’s best guess is that the president has in mind the so called disproportionate share (DSH) funds now paid to hospitals that treat a disproportionate share of uninsured patients or patients covered by the federal-state Medicaid programme for the poor. In many states these funds pay hospitals far less than it costs them to treat Medicaid patients. Mentioning such specifics in a televised speech would have triggered an immediate outcry from the hospital industry and the champions of the poor.

Economists of all political stripes have remarked favourably upon the proposed changes in the tax code. However, the president’s plan perpetuates the regressive nature of tax deductions. The huge tax savings triggered by the proposed standard tax deductions continue to accrue disproportionately to high income families least in need of public subsidies for their health care.

Worse still, in addition to these standard deductions, the president apparently would continue to allow individuals or families to deduct from their taxable incomes annual deposits into a personal health savings account, as long as the family chose a health insurance policy with a high deductible.

At the same time, Bush would do little for the millions of low income, uninsured Americans who would not much benefit from the standard tax deductions, especially if their income is so low that they do not pay federal income taxes and who lack the income to procure health insurance on their own. Simply to redirect federal funds from safety net hospitals catering disproportionately to the poor towards general state budgets, without any guarantee of full universal health Insurance coverage, is a morally dubious, empty gesture—especially in light of the unwarranted public subsidies the proposal would continue to steer towards high income families.

As it happens, all of these musings are moot. The Democratic Congress already has signalled that the president’s plan is not only “dead on arrival” but “dead even before arrival.” And thus, after all the fanfare over the president’s proposal has died down, American health policy continues to march according to Churchill’s dictum that “you can always count on Americans to do the right thing—after they’ve tried everything else.”

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Defining limits in care of terminally ill patients

Despite what they might say, people at the end of life rarely want everything or nothing. Ursula Braun and colleagues explain how to understand and meet their needs.

Invasive procedures in terminally ill patients often fail to change the course of disease.\(^1\) Interventions can become inappropriate overtreatment if they result only in disease related and iatrogenic harm to the patient. Untimely referral to a hospice, poor technical performance, overuse of interventions inconsistent with preferences and prognosis, and poor communication,\(^1\) increase the likelihood of inappropriate clinical intervention.

To facilitate appropriate care and avoid inappropriate interventions doctors need to anticipate discordance between their views and those of patients or surrogates, using the informed consent process to prevent potential discordance from becoming actual discordance and responding quickly when conflicts do occur.\(^1\) It is imperative for good end of life decision making to identify, explain, and negotiate consensus therapeutic goals to ensure that appropriate treatment occurs. This process requires effective communication skills and cultural sensitivity. The clinical scenario below (which is fictitious but based on experience) illustrates the need for a proactive approach.

**Clinical scenario**

A 78 year old recently widowed man with non-small cell lung cancer and chronic obstructive pulmonary disease is admitted with pneumonia and impending respiratory failure for the third time within 10 months. His medical history includes congestive heart failure with an ejection fraction of 20%, a cerebrovascular infarct with mild cognitive impairment, and coronary artery disease. He has previously been difficult to wean from the ventilator and required a tracheostomy. During his last admission, he was finally weaned after 8 weeks. Afterwards, the patient told his wife and the team several times he never wanted to be on a ventilator again, but he did not complete an advance directive.

The doctor starts bilevel positive airway pressure, but intubation seems impossible to avoid. Because the patient is confused, his care is discussed with his son, who has not previously been involved. The son, who has not previously been involved. The son wants “everything” done for his father. The respiratory therapist and the house officer who have cared for the patient at former admissions recommend against intubation and suggest a do not resuscitate order based on the patient’s previously stated wishes.

**Implementing the doctor’s role**

The first step in preventing overtreatment of terminally ill patients is for both sides to collect and share information. Before doctors try to explain medically reasonable choices, they must listen to and focus on what the patient or family already understands about the patient’s condition. Goold and colleagues have assembled some questions for doctors to use in this context, such as “Why have you decided to…?” “What are you hoping we can achieve?” “What do you think the patient would want us to accomplish for him/her?” They also encourage doctors to consider what words or phrases they may have used that might be contributing to the conflict—for example, “stopping treatment,” “withdrawing care.”

Doctors should focus on knowledge about the disease course and its responsiveness to treatment. It is important to clarify the patient’s and surrogate’s expectations regarding outcomes, resolve misunderstandings, and correct unfounded expectations. Additionally, the patient or surrogate needs to understand the potential side effects of treatment and their prevalence. For example, when discussing cardiopulmonary resuscitation, it is important to explain that ribs may be broken, burns can occur, success is inversely proportional to length of resuscitation, and the likelihood of returning to the former level of functioning may be small. Both short and long term outcomes must be explained. Doctors should make clear that good medical care does not always mean doing everything that is technically possible; in fact, sometimes what is technically possible is clinically inappropriate.

Doctors need to identify what is important to the patient, including any religious beliefs.\(^8\) If the patient cannot respond, the doctor must determine from the surrogate what the patient's values and goals might be—the substituted judgment standard.\(^9\) Doctors need to remind surrogates that their decisions should be based as much as possible on what the surrogate thinks the patient would want, rather than on what the surrogate wants.

Finally, doctors should, after acknowledging the situation’s difficulty, present their expert opinions and not shy away from making recommendations because of a misplaced fear of upsetting the patient or surrogate.\(^10\) A surrogate may appreciate such recommendations because they can reduce guilt and the feeling of being solely responsible for the outcome.

**A good death**

In the late 18th century, the Scottish physician-ethicist John Gregory called for doctors to “smoothe the avenues of death.”\(^11\) In contemporary terms, this means that doctors should focus care on securing
effective palliation and helping patients maintain their dignity. Doctors should clearly convey to patients and families that inappropriate treatment is not benign but almost always associated with appreciable burdens and little or no expected clinical benefit. The goal should be to convey that overtreatment can cause preventable suffering.

Responding to requests
Surrogates usually do not realise that a request for doing “everything” may lead to overtreatment. Simultaneously, doctors often do not take the time to clarify the nature of such requests. In the scenario described above, the son, having had no conversation with his father regarding his preferences for care, requests everything. To prevent a crisis in decision making, the doctor should immediately explore what “everything” means to the son and what he understands its consequences to be. The doctor should then provide an accurate, sensitively presented account of the predictable consequences of doing everything and follow up by exploring with the son how these consequences may not serve the shared goal of providing the best care.

Explaining that refusing to intubate is not equivalent to stopping treatment and detailing all the therapeutic options that will ensure his father’s comfort will help the son to understand that good medical care will continue. Families need to understand that not doing “everything” is not equivalent to doing “nothing,” which some might wrongly assume. The doctor should set realistic goals that focus on preventing inappropriate intervention, thereby ensuring comfort and maintaining dignity.12

Build consensus
The process of finding out what the patient or surrogate already knows or does not know, identifying expectations and misconceptions, and clarifying expectations should always return to what the patient’s values and goals would be and why inappropriate intervention might not support these values. Identifying the most and the least likely outcomes helps both sides. In our scenario, the son had no knowledge of the extent of his father’s disease, his prognosis, or the wishes made known to his mother and the care team. Occasionally, responding to a request for aggressive treatment with an offer of a limited trial of an intervention (such as, mechanical ventilation for a few days) may preserve control for the family, protect the patient from prolonged inappropriate intervention, and conserve the opportunity to reach consensus on ending such intervention.8 13

Document agreements
Once consensus has been reached, it is important to document the discussion in the patient’s notes and to write appropriate orders immediately. Failure to promptly document the decision in the record can lead to overtreatment by default and harmful treatment. For example, both the house officer and the respiratory therapist knew of the patient’s desire not to be put on the breathing machine again. However, they failed to document it. Since the patient’s wife knew of his preferences, the doctors also should have encouraged her to discuss his wishes with other family members.

Planned discharge
Many patients who have a do not resuscitate order leave the hospital alive. Discharge planning is a crucial but underused tool to prevent inappropriate treatment. After being weaned from mechanical ventilation on his last admission, the patient should have been asked if he wanted a do not resuscitate order for future admissions and given the opportunity to complete an advance directive.

Additionally, in some US states patients can opt for do not resuscitate orders out of hospital. Failure to discuss and write such an order may lead to inappropriate resuscitation attempts. Other patients may benefit from orders not to be admitted to hospital—for example, patients with severe dementia whose quality of life may be severely diminished by hospital admission. Proactively discussing such options with surrogates can prevent patients becoming agitated by the new environment, which could result in patients falling or danger to caregivers.

Discussion
When doctors offer all technically possible alternatives unedited by clinical judgment about which ones are clinically beneficial or simply acquiesce to requests to “do everything,” they yield their proper role in the informed consent process.10 This failure reflects a fundamental misunderstanding of the doctor’s professional role in the informed consent process. It does not violate the terminally ill patient’s or a surrogate’s autonomy to recommend against clinically inappropriate interventions and provide an evidence based explanation that justifies the recommendation. A
Patients should not have to forgo curative treatments to have access to palliative care, nor should they have to forgo palliative care just because they are still undergoing curative treatment.

**Steps to avoid inappropriate intervention**

- Listen, verify understanding, and offer choices with contextual risks and benefits.
- Focus care on maintaining the patient’s dignity and supplying effective palliation.
- Respond to requests for intervention.
- Build consensus.
- Document agreement on an effective strategy for care and incorporate it in the care plan immediately.
- Plan the discharge and document decisions.

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**Are you addicted to your “crackberry”?**

Hand held computers and portable email devices are routine in many walks of life, including medicine. These devices facilitate working from home or while in transit, allowing busy individuals never to be “out to lunch.” However, they can also make it harder to achieve a healthy work-life balance, intruding into one’s time away from work.

In view of concerns over behavioural addiction to these new technologies, with consequent negative impact on other aspects of life, I have devised a short screening test (based on the CAGE questionnaire for alcoholism) for pathological addiction to hand held devices:

- Do you get annoyed if you are asked to stop using your hand held device?
- Do you take your hand held device on holiday with you?
- Do you get anxious if you cannot find your hand held device?
- Do you ever misperceive a sound as the ring tone or call sign of your hand held device?

If you answer yes to all four of the SHAM questions, then you should consider taking a period of abstinence from your hand held device. Others around you may find a period of abstinence changes you for the better.

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**Contributors and sources:** UKB is director of the hospice and palliative care unit at the Michael E DeBakey VA Medical Center. RJB is a geriatrician and palliative care consultant, University of Florida. He is a long standing supporter of the palliative care approach. MEF is a sociologist with an interest in decision making for patients with chronic diseases and multiple diseases. She has a long standing interest in improving the outcomes of older patients. MEF is a sociologist with an interest in decision making for patients with chronic diseases and multiple diseases. She has a long standing interest in improving the outcomes of older patients.

Curative and palliative care should not be dichotomous. Doctors need training in palliative care and in integrating it into their practice. Patients should not have to forgo curative treatments to have access to palliative care, nor should they have to forgo palliative care just because they are still undergoing curative treatment.

Earlier involvement of a palliative care approach, such as enrolment into a hospice, can facilitate subsequent transition to purely palliative care. Recommending palliative and hospice care is a seriously underused strategy for dealing with overtreatment of terminally ill patients.

**Resolving conflict**

The outcome of our opening scenario was that the house officer and the respiratory therapist who previously cared for the patient met with the son and discussed the goals for treatment. The son was informed of his father's previously stated wishes to avoid further intubations. The son was upset by seeing his father in respiratory distress. All agreed that the patient's comfort was most important. Morphine was started and a scopolamine patch applied. The patient died two days later with his son present.

**Competing interests:** None declared.


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Risk of suicide during treatment with venlafaxine, citalopram, fluoxetine, and dothiepin: retrospective cohort study

Annalisa Rubino, Neil Roskell, Pat Tennis, Daniel Mines, Scott Weich, Elizabeth Andrews

Abstract

Objective To compare the risk of suicide in adults using the antidepressant venlafaxine compared with citalopram, fluoxetine, and dothiepin.

Design Retrospective cohort study.

Setting UK General Practice Research Database.

Participants 219,088 patients, aged 18-89 years, who were prescribed venlafaxine, citalopram, fluoxetine, or dothiepin from 1995 to 2005.

Main outcome measures Completed suicide and attempted suicide.

Results Venlafaxine users had a higher burden of risk factors for suicide, including previous suicide attempts and proxies for severe depression or depression that was difficult to treat. In the analysis for completed suicides, unadjusted and adjusted hazard ratios for venlafaxine compared with citalopram were 2.44 (95% confidence interval 1.12 to 5.31) and 1.70 (0.76 to 3.80), for venlafaxine compared with fluoxetine were 2.85 (1.37 to 5.94) and 1.63 (0.74 to 3.59), and for venlafaxine compared with dothiepin were 2.54 (1.07 to 6.02) and 1.31 (0.53 to 3.25). Compared with other study drugs, venlafaxine was also associated with an increased risk of attempted suicide, but adjustment for measured confounders substantially reduced the hazard ratios.

Conclusions Venlafaxine use was consistently associated with higher risk of suicide compared with citalopram, fluoxetine, and dothiepin. Venlafaxine users had a higher burden of suicide risk factors, however, and adjustment for measured confounders substantially reduced the excess risks. Since the secondary data used in this analysis allowed only indirect and partial measurements of potential confounders, it is possible that residual confounding explains much, if not all, of the observed excess risk.

Introduction

In late 2004 drug regulatory agencies in the United States and Europe warned that adults being treated with antidepressants should be monitored closely for worsening of depression and for increased suicidal thinking or behaviour, particularly at the start of treatment or when changing doses. This action was largely in response to meta-analyses of randomised controlled trials in patients younger than 19, which found that selective serotonin reuptake inhibitors and other newer antidepressants may increase the risk of suicidal thinking and self harm. Three meta-analyses of clinical trials in adults, however, found no increased risk of suicide associated with antidepressants compared with placebo. Observational studies have not found any substantial and consistent differences in suicide risk across commonly prescribed selective serotonin reuptake inhibitors and tricyclic antidepressants. No observational studies have, however, quantified a potential association between treatment with venlafaxine and risk of suicide.

Venlafaxine, a serotonin and noradrenaline reuptake inhibitor, is an antidepressant indicated for the treatment of depression and anxiety. In clinical practice it has often been prescribed for patients unresponsive to selective serotonin reuptake inhibitors or tricyclic antidepressants. A recent observational study showed that patients treated with venlafaxine had a higher prevalence of risk factors for suicide, including previous suicide attempt, admission to hospital for depression, and diagnoses of schizophrenia and bipolar disorder than patients prescribed selective serotonin reuptake inhibitors. We assessed whether the risk of completed and attempted suicide in patients prescribed venlafaxine differs from that in patients prescribed other antidepressants.

We carried out a retrospective cohort study in the general practice research database, which collects electronic medical records within UK primary care. To minimise confounding by severity of disease, we selected the selective serotonin reuptake inhibitor citalopram as a comparator antidepressant. As citalopram and venlafaxine were introduced in the same year, we assumed that doctors would preferentially prescribe both agents to patients who were unresponsive to previously available therapies and presumably had similar background risks of suicide. We also selected fluoxetine and dothiepin because they are the most commonly prescribed drugs within their respective classes.

Methods

We selected patients on the basis of an incident prescription (that is, first ever prescription in the patient's medical record) for venlafaxine, citalopram, fluoxetine, or dothiepin during the study period 1995 to 2005. After we applied the quality control criteria for the general practice research database, we restricted the study population to patients aged 18 to 89 years at the time of incident prescription for any study drug, and with a record of depression or anxiety. To characterise medical history, we selected patients who were unresponsive to previously available therapies and presumably had similar background risks of suicide.

Patients were followed from their incident prescription date until the earliest of completed suicide or first attempted suicide, the end of the study period, or the end of the patient's record. We
censored follow-up time during periods of no use of any study drug.

Outcome measures
We defined two end points: completed suicide and the first attempted suicide during the study period, including completed suicides.

Completed suicide was defined by any coding for death associated with mention of suicide in free text entries or by a code for suicide in the medical record accompanied by a statement of death in the administrative record (30 days either way). For the completed suicide analysis we included patients with records of attempted suicide during the study period.

Attempted suicides were identified by a code for suicide attempts. We excluded records that at the review of free text notes did not seem to represent attempted suicide—for example, unintentional overdose or self harm without suicidal intent (see bmj.com).

Exposure to study drugs
We assumed that exposure to any study drug began on the day after the prescription date and extended to 14 days after the imputed end of the prescription, based on number of pills supplied and dosing instructions. If there was no gap between the imputed end of a first prescription plus 14 days and the date of the subsequent prescription for the same drug, then we concatenated the two periods to represent a continuous episode of treatment. We concatenated subsequent prescriptions similarly. Each participant could experience multiple episodes of treatment for one or more study drugs.

When prescription records indicated concomitant use of multiple antidepressants, including non-study antidepressants, we assumed there was a switch in therapy. When switching therapy participants could have been exposed to more than one antidepressant for a short period, and we accounted for this "overlap with other antidepressant" in the stratified and multivariable analyses. We also examined the effect of allocating usage time to more than one treatment. To avoid saturation of the model all the variables that modified the adjusted incidence rate ratios.

Analysis covariates
To account for potential confounders we identified known risk factors for suicide, including the severity of underlying disease. The confounders we considered were age, sex, diagnosis for study inclusion (depression or anxiety, or both), suicide attempts, major life events, lifestyle factors, family history of psychiatric morbidity, psychotropic comedications, and psychiatric comorbidities. Age was categorised into the groups 18-29, 30-59, and 60 or more years. We also evaluated chronic and disabling non-psychiatric morbidities that are known to be associated with onset or worsening of depression. We estimated severity of depression and depression that was resistant to treatment using proxies such as admission to hospital and referrals to specialist mental health services, history of antidepressant treatment, antidepressant therapy, overlap with other antidepressants, and the 10 confounders associated with the largest changes of the adjusted incidence rate ratio of venlafaxine with each comparator. This resulted in 24 analysis covariates because we introduced those confounders identified in more than one paired comparison (for example, venlafaxine versus citalopram, venlafaxine versus fluoxetine, and venlafaxine versus dothiepin) only once in the model. The larger number of outcomes in the attempted suicide analysis allowed us to include in the model all the variables that modified the adjusted incidence rate ratios. We estimated hazard ratios (95% confidence intervals) for each treatment comparison and for each potential confounder in the model. All analyses were carried out using SAS for UNIX software (version 9.1).

Results
Overall, 219 088 patients aged 18-89 years who were prescribed venlafaxine, citalopram, fluoxetine, or dothiepin from 1995 to 2005 were identified from the general practice research database. The distribution of the population characteristics across drug groups and analysis covariates used in the completed and the attempted suicide analyses were similar. Table 1 provides data from the completed suicide analysis only.

Distributions of age and sex were consistent across drug groups (table 1). Most patients (90.5%, n=198 251) had a diagnosis of depression as opposed to anxiety. About 25% of patients had both diagnoses, and this proportion was higher among patients treated with venlafaxine (35.4%, n=7 725) than among those treated with fluoxetine (22.0%, n=20 893), citalopram (27.3%, n=16 073), or dothiepin (23.9%, n=10 387). Patients prescribed venlafaxine also showed signs of more severe or difficult to treat depression. For instance, history of other antidepressant therapy, history of antidepressant mutitherapy, and history of treatment with three or more antidepressants were more common among patients treated with venlafaxine (table 1). Furthermore, proxies of depression severity, such as admission to hospital for psychiatric disorders and referral to specialist mental health care, were more common among those prescribed venlafaxine than those prescribed comparator drugs (table 1). Previous attempted suicide was twice as common among venlafaxine users than among citalopram or fluoxetine users. Other suicide risk factors, including psychotropic therapy and family history of psychiatric disorders, were also more common among venlafaxine users (table 1). Distribution of chronic or incapacitating morbidities known to be associated with depression did not differ across drug groups. Similarly, bereavement or marital problems were equally distributed across groups (table 1).

Incidence rate and hazard ratio
The completed suicide analysis encompassed 54 events over 173 432 person years for use of any study drug, and the first
therapy, including antidepressant multitherapy and psychotropic therapy, and previous suicide attempts had the strongest confounding effect on the association between venlafaxine and completed or attempted suicide.

Unadjusted and adjusted hazard ratios were calculated for venlafaxine compared with each study drug. The unadjusted risk of completed suicide was more than twice as high during venlafaxine treatment. Adjustment for the measured confounders in the completed suicide models, however, reduced the excess risk by at least 50% in each paired comparison (table 3). The unadjusted risk of attempted suicide was also higher during venlafaxine treatment compared with citalopram, fluoxetine, and dothiepin treatments. The hazard ratio was substantially reduced after adjustment for measured confounders (table 4).

When the extended time at risk was reduced from 14 to seven days after the imputed end of a prescription, the adjusted hazard ratio of venlafaxine compared with citalopram increased from 1.70 (95% confidence interval 0.76 to 3.80) to 1.87 (0.81 to 4.29) in the completed suicide analysis and from 1.20 (1.07 to 1.34) to 1.29 (1.10 to 1.37) in the attempted suicide analysis, but such an increase was inconsistent across comparisons (table 5).

Discussion

The antidepressant venlafaxine was associated with a higher risk of suicide compared with citalopram, fluoxetine, and dothiepin. Venlafaxine users had a higher burden of risk factors for suicide, however, and adjustment for measured confounders substantially reduced the excess risks. While these data may reflect a causal association between venlafaxine use and suicide, given the substantial attenuation of this association after adjustment for confounding and the nature of the data, it is possible that residual confounding could explain much or all of the remaining risk.

Venlafaxine use in this study population of adults was associated with markers of severe and difficult to treat depression, with psychiatric comorbidities, and with previous treatment with psychotropic agents such as antidepressants and mood stabilizers. Admission to hospital for a psychiatric disorder and specialist care, family history of psychiatric morbidity, and a history of suicide attempts were also more prevalent in venlafaxine users. Furthermore, venlafaxine users were twice as likely to have an overlap prescription for another antidepressant, suggesting more frequent switching of drugs. Patients may switch antidepressant drugs owing to failure to achieve the desired therapeutic effect, suggesting that venlafaxine users had severe or treatment resistant depression.

Table 1 Frequency distribution of population characteristics by antidepressant use in completed suicide analysis. Values are percentages (numbers) unless stated otherwise

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Venlafaxine</th>
<th>Citalopram</th>
<th>Fluoxetine</th>
<th>Dothiepin</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of participants</td>
<td>37 857</td>
<td>75 749</td>
<td>108 934</td>
<td>54 035</td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>46.2 (16.4)</td>
<td>47.1 (18.0)</td>
<td>43.9 (16.7)</td>
<td>48.6 (7.3)</td>
</tr>
<tr>
<td>Men</td>
<td>33.5 (12)</td>
<td>30.5 (23)</td>
<td>30.6 (33)</td>
<td>30.0 (16)</td>
</tr>
<tr>
<td>No of treatment episodes</td>
<td>69 796</td>
<td>160 189</td>
<td>283 865</td>
<td>125 123</td>
</tr>
<tr>
<td>First prescription ≤ 14 days</td>
<td>9.9 (887)</td>
<td>7.3 (11 622)</td>
<td>19.7 (55 960)</td>
<td>10.2 (12 751)</td>
</tr>
<tr>
<td>Overlap with other antidepressants</td>
<td>22.4 (19 977)</td>
<td>11.6 (18 977)</td>
<td>8.7 (24 705)</td>
<td>13.4 (16 755)</td>
</tr>
<tr>
<td>Exposure during first 30 days of treatment</td>
<td>53.8 (48 036)</td>
<td>58.9 (99 019)</td>
<td>54.8 (155 571)</td>
<td>39.5 (74 468)</td>
</tr>
</tbody>
</table>

Table 2 Unadjusted incidence rate (95% confidence interval) of completed and first attempted suicides in adults according to antidepressant

<table>
<thead>
<tr>
<th>Event and antidepressant</th>
<th>No of patients*</th>
<th>Person years at risk</th>
<th>No of events</th>
<th>Incidence rate (95% CI) per 1000 person years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed suicide:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37 857</td>
<td>28 087</td>
<td>18</td>
<td>0.84 (0.40 to 1.92)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>75 749</td>
<td>45 839</td>
<td>12</td>
<td>0.28 (0.15 to 0.48)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>108 934</td>
<td>66 636</td>
<td>15</td>
<td>0.23 (0.14 to 0.37)</td>
</tr>
<tr>
<td>Dothiepin</td>
<td>54 035</td>
<td>33 090</td>
<td>9</td>
<td>0.27 (0.14 to 0.52)</td>
</tr>
<tr>
<td>First attempted suicide:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37 132</td>
<td>26 854</td>
<td>715</td>
<td>28.6 (24.7 to 28.7)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>75 103</td>
<td>44 796</td>
<td>781</td>
<td>17.4 (16.3 to 18.7)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>108 474</td>
<td>65 416</td>
<td>1138</td>
<td>17.4 (16.4 to 18.4)</td>
</tr>
<tr>
<td>Dothiepin</td>
<td>53 816</td>
<td>32 677</td>
<td>426</td>
<td>13.0 (11.9 to 14.3)</td>
</tr>
</tbody>
</table>

*Patients could contribute person years at risk to more than one antidepressant.

[1] Mood stabilisers, including carbamazepine, clonazepam, gabapentin, lamotrigine, lithium, topiramate, valproic acid, antipsychotics, and benzodiazepines.
[2] Depression, including dysthymia and chronic fatigue syndrome; somatoform disorders (for example, somatisation disorder and hypochondriasis); eating disorders (anorexia and bulimia nervosa); anxiety disorders, including phobias (social phobia, agoraphobia, simple phobias), obsessive–compulsive disorder, panic disorder, and post-traumatic stress disorder; mixed anxiety depressive disorder; bipolar affective disorder; schizophrenia; substance abuse disorder and alcohol abuse syndrome; dementia; and personality disorders, including schizoid, borderline, and antisocial behaviour.

Table 2 provides a summary of the unadjusted incidence rates of completed suicide and first attempted suicides in adults according to antidepressant use.
In our study, suicide rates were consistently higher across study drugs during the first 30 days of a treatment episode, confirming that starting antidepressants is associated with a higher risk of suicide. The study also confirmed that markers for severity of psychiatric morbidity were associated with an increased risk of suicide and suicide attempt in each drug group.

### Confounding

Pharmacoepidemiological studies are potentially confounded by indication; factors associated with choice of therapy may also be risk factors for the study outcome. Although a randomised clinical trial can eliminate such confounding, this design is not feasible to evaluate such rare outcomes as suicide. The richness of longitudinal records in the UK general practice research database allowed us to adjust for many factors associated with the risk of suicide and with the selection of antidepressant treatment, but it is possible that our adjustment was incomplete. The ability to control for confounding depends on the accurate measurement of potential confounders. Even when the sensitivity and specificity of the confounder measures are 90%, more than 50% of confounding remains uncontrolled. Adjustment for misclassification of this magnitude would move the point estimate for the risk of completed suicide for venlafaxine compared with citalopram from 1.70 to 1.39, and for attempted suicide from 1.20 to 1.07. We anticipated that data for defining referrals to mental health care and admission to hospital, as well as data on prescriptions, were appropriate and comprehensive. Psychiatric diagnoses, however, may be undiagnosed or misclassified to a noticeable extent. Most notably, severity of disease, a strong determinant of suicide risk, could only be measured indirectly. Furthermore, recognised risk factors for suicide, such as hopelessness, impulsivity, and abuse (child, domestic, or sexual), unemployment, poverty, social isolation, and suicidal
Table 5: Unadjusted and adjusted hazard ratios (95% CI) for completed and attempted suicides for venlafaxine treatment compared with citalopram, fluoxetine and dothiepin treatment when time at risk included seven or 14 days at imputed end of prescription

<table>
<thead>
<tr>
<th>Event and antidepressants</th>
<th>14 days</th>
<th>7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Completed suicide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine vs citalopram</td>
<td>2.44/1.12 to 2.74/1.68</td>
<td>1.70/1.29 to 2.07/1.62</td>
</tr>
<tr>
<td>Venlafaxine vs fluoxetine</td>
<td>2.85/2.17 to 3.52/2.78</td>
<td>1.63/1.23 to 2.04/1.61</td>
</tr>
<tr>
<td>Venlafaxine vs dothiepin</td>
<td>2.54/1.88 to 3.17/2.38</td>
<td>1.31/1.10 to 1.71/1.37</td>
</tr>
<tr>
<td><strong>Attempted suicide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine vs citalopram</td>
<td>1.49/1.34 to 1.66/1.72</td>
<td>1.20/1.15 to 1.34/1.42</td>
</tr>
<tr>
<td>Venlafaxine vs fluoxetine</td>
<td>1.68/1.52 to 1.86/1.68</td>
<td>1.28/1.15 to 1.52/1.42</td>
</tr>
<tr>
<td>Venlafaxine vs dothiepin</td>
<td>2.41/2.11 to 2.74/1.68</td>
<td>1.47/1.29 to 2.38/1.68</td>
</tr>
</tbody>
</table>

What this study adds

Venlafaxine users were more likely to commit or attempt suicide than patients using citalopram, fluoxetine, or dothiepin. Venlafaxine users had a higher burden of suicide risk factors at start of treatment; adjustment for measured confounders reduced the excess risk.

What is already known on this topic

The risk of suicide during treatment with commonly prescribed selective serotonin reuptake inhibitors and tricyclic antidepressants is similar.

The risk with venlafaxine, however, has not been evaluated in population based studies.

ideation, are not routinely recorded in the general practice research database and could not be accounted for in this analysis.

Adjustment for measured confounders substantially reduced the excess risk of suicide associated with venlafaxine. As the amount of residual confounding tends to reflect the overall confounding in the data, adjustment for measured confounding could not be accounted for in this analysis. We found a higher risk of suicide associated with venlafaxine compared with citalopram, fluoxetine, and dothiepin, which could reflect a causal association. However, because venlafaxine was channelled towards patients with more severe and treatment resistant depression, adjustment for measured risk factors could have left residual confounding that could explain some or all of the excess risk associated with venlafaxine.

Conclusions

We thank William Irish and Ken Rothman for their contribution to the analysis, interpretation of the results, and preparation of the manuscript.

Contributors: AR, NR, PT, EA were responsible for the study design, data analysis, and interpretation, with contributions from DM and SW. AR and NR developed the study protocol. NR was responsible for the statistical analysis. AR, PT, and SW reviewed notes for the definition of completed and attempted suicides. AR wrote the paper, with contributions from all authors. EA is the guarantor.

Funding: This study was sponsored by Wyeth, which produces and markets venlafaxine. The contract between RTI Health Solutions and Wyeth specified that the authors at RTI Health Solutions had ultimate control over all aspects of the study, including control over publication. During the course of the study, however, any differences about the presentation or interpretation of findings that arose between the company author and external investigators were resolved through honest scientific debate. All authors had access to the statistical reports and tables supporting the publication.

Competing interests: All other authors have no personal financial interest in the drug studies. RTI Health Solutions has received research funding from several companies, including Lilly, GlaxoSmithKline, and Pfizer, who market antidepressants and potentially gain or lose financially from the results of the study.

Ethical approval: This study was approved by the institutional review board at RTI International and the General Practice Research Database Scientific and Ethical Advisory Group.


Research

IQ in childhood and vegetarianism in adulthood: 1970 British cohort study

Catharine R Gale, Ian J Deary, Ingrid Schoon, G David Batty

Abstract

Objective To examine the relation between IQ in childhood and vegetarianism in adulthood.

Design Prospective cohort study in which IQ was assessed by tests of mental ability at age 10 years and vegetarianism by self-report at age 30 years.

Setting Great Britain.

Participants 8170 men and women aged 30 years participating in the 1970 British cohort study, a national birth cohort.

Main outcome measures Self-reported vegetarianism and type of diet followed.

Results 366 (4.5%) participants said they were vegetarian, although 123 (13.8%) admitted eating fish or chicken. Vegetarians were more likely to be female, to be of higher social class (both in childhood and currently), and to have attained higher academic or vocational qualifications, although these socioeconomic advantages were not reflected in their income. Higher IQ at age 10 years was associated with an increased likelihood of being vegetarian at age 30 (odds ratio for one standard deviation increase in childhood IQ score 1.38, 95% confidence interval 1.24 to 1.53). IQ remained a statistically significant predictor of being vegetarian as an adult after adjustment for social class (both in childhood and currently), academic or vocational qualifications, and sex (1.20, 1.06 to 1.36). Exclusion of those who said they were vegetarian but ate fish or chicken had little effect on the strength of this association.

Conclusion Higher scores for IQ in childhood are associated with an increased likelihood of being a vegetarian as an adult.

Introduction

Children and adolescents who score higher on standard tests of intelligence have a lower risk of coronary heart disease in later life. The underlying mechanisms are still unclear. Findings that higher intelligence is linked with a lower likelihood of starting to smoke and a higher likelihood of giving up, suggest that the ability to learn, reason, and solve problems may be important in determining how people respond to information on risk and the extent to which they adopt behaviours considered conducive to health.

Vegetarianism, “the practice of living wholly on vegetable food, with or without dairy products, honey and eggs,” is a behaviour that has for centuries been adopted primarily because of ethical objections to the use of animals for food. Some vegetarians have claimed that not consuming meat has beneficial effects on brain function. According to Benjamin Franklin, the 18th century statesman and scientist, a vegetarian diet results in “greater clearness of head and quicker comprehension.” But in the early part of the 20th century medical opinion on the potential health benefits of a vegetarian diet—at least in Britain—tended to be unenthusiastic: “Vegetarianism is harmless enough, though it is apt to fill a man with wind and self-righteousness,” declared Robert Hutchison in an address to the BMA in 1930. In the past few years, however, growing epidemiological evidence, some from prospective studies, has suggested that the health benefits associated with vegetarianism may be considerable: lower serum cholesterol concentrations, lower blood pressure, and a reduced risk of obesity and coronary heart disease.

Might vegetarianism explain in part why children and adolescents who score higher on tests of intelligence have a lower risk of coronary heart disease in later life? In view of the evidence that vegetarians tend to have lower levels of cardiovascular risk, the decision to adopt a vegetarian diet might be viewed as a healthier option than the consumption of meat. Does a higher IQ make this decision more likely? This question could not be answered by a search of the biomedical and social science databases. We used the 1970 British cohort study to examine prospectively the effect of childhood IQ on the likelihood of being a vegetarian as an adult.

Methods

The 1970 British cohort study comprises 17 198 live births occurring to parents living in Great Britain between 5 and 11 April 1970. Mental ability was assessed at the age of 10 years using a modified version of the British ability scales. The four subscales were word definitions, word similarities, recall of digits, and matrices. We carried out a principal components analysis of the positively correlated scores from these four tests to establish the presence of a general cognitive ability factor (traditionally referred to as “g”). The first unrotated principal component accounted for 57% of the total variance among the four tests. We used this component to derive a g score for each participant. For ease of interpretation we transformed the g score to the widely used IQ equivalent: mean (SD) 100 (15). At age 30 years participants were interviewed at home, when they were asked about whether they were vegetarian and, if so, what diet they followed. Information on socioeconomic status was reported by the parents when the participants were aged 10 years (parental occupational social class) and by the participants at age 30 (current occupational social class, academic or vocational qualifications, and income). Overall 11 204 participants provided information on vegetarian status at the 30 year follow-up, of whom 8170 (72.9%) had data on IQ score at age 10 years and were therefore included in our analyses.
We used analysis of covariance and the \( \chi^2 \) test to examine the characteristics of the participants, and logistic regression to examine prospectively the relation between childhood IQ score and vegetarianism as an adult.

### Results

In total 366 (4.5%) of 8170 participants of the 1970 British cohort study with IQ scores at age 10 years said they were vegetarian; nine (2.5%) were vegan and 123 (33.6%) stated they were vegetarian but reported consuming fish or chicken. Vegetarians were more likely to be female, to be of a non-manual occupational social class (in childhood and currently), and to have higher academic or vocational qualifications (table 1[T1]): 8.5% of vegetarians \( (n = 31) \) had a higher degree or equivalent vocational qualification compared with 3.5% of non-vegetarians \( (n = 275) \). This evidence of higher socioeconomic status was not reflected in the vegetarians’ annual income, which was similar to that of non-vegetarians. When strict vegetarians (no fish or meat) were compared with those who said they were vegetarian but consumed fish or chicken, no differences were found between them in any of these characteristics (data not shown).

IQ in childhood was associated with all indicators of socioeconomic status. Mean childhood IQ was higher in participants from non-manual occupational backgrounds, both in childhood and currently; in those with higher academic or vocational qualifications; and in those with higher annual gross earnings (data not shown).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>No (%) of non-vegetarians in each category</th>
<th>No (%) of vegetarians in each category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>4222</td>
<td>3957 (93.6)</td>
<td>271 (74.0)</td>
</tr>
<tr>
<td>Men</td>
<td>3848</td>
<td>3853 (99.8)</td>
<td>95 (26.0)**</td>
</tr>
<tr>
<td>Parental social class†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professional or managerial</td>
<td>2244</td>
<td>2119 (95.1)</td>
<td>125 (56.2)**</td>
</tr>
<tr>
<td>Skilled non-manual</td>
<td>752</td>
<td>719 (95.4)</td>
<td>33 (4.6)</td>
</tr>
<tr>
<td>Semi-skilled</td>
<td>3081</td>
<td>2945 (95.8)</td>
<td>136 (44.3)</td>
</tr>
<tr>
<td>Unskilled</td>
<td>1205</td>
<td>1165 (96.7)</td>
<td>40 (32.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>888</td>
<td>856 (96.5)</td>
<td>32 (8.5)*</td>
</tr>
<tr>
<td>Current social class:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professional or managerial</td>
<td>2968</td>
<td>2798 (94.6)</td>
<td>170 (56.6)**</td>
</tr>
<tr>
<td>Skilled non-manual</td>
<td>2102</td>
<td>1996 (94.4)</td>
<td>111 (52.7)</td>
</tr>
<tr>
<td>Semi-skilled</td>
<td>1649</td>
<td>1511 (91.6)</td>
<td>38 (23.1)</td>
</tr>
<tr>
<td>Unskilled</td>
<td>1274</td>
<td>1235 (96.9)</td>
<td>39 (30.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>177</td>
<td>169 (96.1)</td>
<td>8 (2.2)**</td>
</tr>
<tr>
<td>Academic or vocational qualifications:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No qualifications</td>
<td>695</td>
<td>685 (98.8)</td>
<td>10 (2.7)</td>
</tr>
<tr>
<td>CSE equivalent NVQ 1</td>
<td>541</td>
<td>629 (93.4)</td>
<td>18 (4.8)</td>
</tr>
<tr>
<td>O level or equivalent NVQ 2</td>
<td>2220</td>
<td>2246 (99.9)</td>
<td>74 (32.0)</td>
</tr>
<tr>
<td>A level or equivalent NVQ 3</td>
<td>1708</td>
<td>1638 (95.8)</td>
<td>70 (41.1)</td>
</tr>
<tr>
<td>Degree, diploma, or equivalent NVQ 4</td>
<td>2494</td>
<td>2331 (92.9)</td>
<td>163 (44.5)</td>
</tr>
<tr>
<td>Higher degree or NVQ 5</td>
<td>306</td>
<td>275 (89.4)</td>
<td>31 (8.5)**</td>
</tr>
<tr>
<td>Annual gross earnings‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>£11.40 - £14.40</td>
<td>1494</td>
<td>1424 (94.9)</td>
<td>70 (26.6)</td>
</tr>
<tr>
<td>£14.41 - £16.80</td>
<td>1494</td>
<td>1432 (95.0)</td>
<td>64 (42.3)</td>
</tr>
<tr>
<td>£16.81 - £22.00</td>
<td>1518</td>
<td>1451 (95.6)</td>
<td>67 (25.5)</td>
</tr>
<tr>
<td>£22.01 - £32.00</td>
<td>1484</td>
<td>1422 (95.4)</td>
<td>62 (32.9)</td>
</tr>
</tbody>
</table>

Table 1 Characteristics of study participants in relation to self-reported vegetarianism at age 30 years \( (n = 8170) \)

On average, vegetarians had a higher childhood IQ score than non-vegetarians. According to sex, the mean (SD) childhood IQ score of vegetarians compared with non-vegetarians was 106.1 (14.7) and 100.6 (15.2) for men and 104.0 (14.1) and 99.0 (14.7) for women, differences of 5.5 and 5.0 points \( (P<0.001) \).

When vegetarians were divided into those who were strictly vegetarian (no fish or meat) and those who consumed fish or chicken, no difference was found in IQ score. Among those who had taken vegetarianism to its logical conclusion (“gone the whole hog”, as it were) and become vegan (no animal products), mean IQ scores were lower. On average, vegans had a childhood IQ score that was nearly 10 points lower than other vegetarians: mean (SD) IQ score 95.1 (14.8) in vegans compared with 104.8 (14.1) in other vegetarians \( (P = 0.04) \), although this estimate must be viewed with caution as only nine participants were vegan.

The odds ratio for being vegetarian at age 30 years for one standard deviation increase in childhood IQ score was 1.38 (95% confidence interval 1.24 to 1.53; table 2[T2]). After controlling for sex, the odds ratio increased to 1.42 (1.28 to 1.59). Separate adjustment for social class, both in childhood and currently, and academic or vocational qualifications, attenuated these relations, particularly when academic or vocational qualifications were added to the model—but the associations remained statistically significant. In multivariate analysis the odds ratio for being vegetarian was 1.20 (1.06 to 1.36) for one standard deviation increase in childhood IQ score. When the analysis was repeated after removing those who said that they were vegetarian but consumed fish or chicken, this result was essentially unchanged (1.19, 1.03 to 1.39). Additional adjustment for annual earnings had no effect on the strength of the relation between childhood IQ and later vegetarianism (data not shown).

### Discussion

Participants of the 1970 British cohort study with higher intelligence test scores in childhood were more likely to report being a vegetarian at age 30 years. This relation was partly accounted for by educational attainment and by occupational social class in adult life but remained statistically significant after adjustment for these factors.

Several investigators have examined the link between education (a strong correlate of mental ability) and vegetarianism. Findings are mixed. Pooled data from a meta-analysis of vegetarianism and mortality showed that of four studies reporting data on educational attainment two showed higher levels in vegetarians than in non-vegetarians, whereas in two other studies the opposite association was seen. In previous analyses of the 1970 British cohort study, a greater consumption of non-meat products, such as bread or fresh fruit, was apparent in people with high educational attainment.

Although the vegetarians in this cohort were, on average, more intelligent, better educated, and of higher occupational

<table>
<thead>
<tr>
<th>Adjustments</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>1.38 (1.24 to 1.53)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.42 (1.28 to 1.59)</td>
</tr>
<tr>
<td>Current social class</td>
<td>1.29 (1.15 to 1.45)</td>
</tr>
<tr>
<td>Academic or vocational qualifications</td>
<td>1.16 (1.03 to 1.36)</td>
</tr>
</tbody>
</table>

Table 2 Odds ratios (95% CI) for being vegetarian at age 30 years for a one standard deviation increase in childhood IQ score in 8170 participants of the 1970 British cohort study
social class than the non-vegetarians, these socioeconomic advantages were not reflected in their income. It may be that ethical considerations determined not just their diet but also their choice of employment. Compared with non-vegetarians, vegetarians were less likely to be working in the private sector and more likely to be working in charitable organisations, local government, or education: 17% of the vegetarians worked in education compared with 9% of non-vegetarians. When asked, as part of the follow-up survey, what they thought of the statement “The government should redistribute income,” 50% of vegetarians said they agreed compared with 41% of non-vegetarians, and this proportion was even higher among male vegetarians (61% vs 42%). Such views may not be compatible with a career in the more lucrative employment sectors.

Some of the participants who reported being vegetarian said they consumed fish or chicken. We found no difference in IQ scores, or any marker of socioeconomic status, between this group and the strict vegetarians. It may be that vegetarianism exists as a continuum, with those who describe themselves as vegetarian but who are prepared to eat white meat or fish (flesh that is paler and less obviously meaty than beef, pork, or lamb) having the same trait but less of it than those who avoid consuming any animal flesh.

The strengths of this study are its size, resulting in high statistical power; the representativeness of the sample, resulting in a high degree of generalisability for the British population born around the same time; and the breadth of data on socioeconomic status, allowing an examination of the role of potential confounding and mediating variables.

Our study also has some limitations. Firstly, some attrition has occurred in the cohort over time. The participants at the 30 year follow-up did gain significantly higher IQ scores at age 10 than those who did not take part, although the size of the differences was modest (0.3 of a standard deviation). Unless the relation between childhood mental ability and vegetarianism is in the opposite direction in non-participants, little bias will have been introduced in our study. Secondly, we had no information from the 30 year follow-up on how long our participants had been vegetarian. Evidence from a subset of 3795 participants (46.5%) who had taken part in a previous follow-up of the cohort when they were aged 16 years suggests that most of those who were vegetarian at age 30 had chosen that type of diet as adolescents or young adults, some years after their IQ was measured: among these 3795 participants, only 32% of those who were vegetarian at age 30 were already vegetarian at age 16, and of those already vegetarian at age 16 95% had become vegetarian between the ages of 11 and 16. The difference in childhood IQ scores between vegetarian and non-vegetarian participants at age 30 was also apparent at age 16; compared with non-vegetarians at this age, those who were vegetarian scored on average 4.1 points higher on the mental ability test at age 10.

Although our results suggest that children who are more intelligent may be more likely to become vegetarian as adolescents or as young adults, it does not rule out the possibility that such a diet might have some beneficial effect on subsequent cognitive performance. Might the nature of the vegetarians’ diet in this cohort have enhanced their apparently superior brain power? Was this the mechanism that helped them to achieve the disproportionate number of higher degrees? Benjamin Franklin and George Bernard Shaw, both ardent vegetarians, would have us believe so. According to Shaw in an article published in The Stay in 1890, “A mind of the calibre of mine cannot derive its nutriment from cows.” Even Shakespeare, not known for his vegetarian sensibilities, expressed through Sir Andrew Aguecheek in Twelfth Night (Act I, Scene 3) a belief in the deleterious effects of consuming meat; “I am a great eater of beef and I believe that does harm to my wit.” Further research may be needed to explore this hypothesis.

Our finding that children with greater intelligence are more likely to report being vegetarian as adults, coupled with the evidence on the potential benefits to cardiovascular health of a vegetarian diet, may help to explain why higher IQ in childhood or adolescence is linked with a reduced risk of coronary heart disease in adult life. Additional studies of older cohorts with data on cardiovascular risk factors will be needed to examine the extent to which vegetarianism mediates the association between childhood IQ and coronary heart disease.

Alternatively it is possible that the link between childhood IQ and vegetarianism in later life is not on a causal chain of mechanisms related to health. People with a higher IQ may well differ from those with less superior brain power in many of their lifestyle decisions: for instance, choice of newspaper, type of books read, preferred form of entertainment. The association between IQ and vegetarianism may be merely an example of many other lifestyle preferences that might be expected to vary with intelligence but which may or may not have implications for health.

The 10 year follow-up was carried out by the Department of Child Health, Bristol University. The 30 year follow-up was carried out under the auspices of the Joint Centre for Longitudinal Research (comprising the Centre for Longitudinal Studies, Institute of Education, University of London; the International Centre for Health and Society, University College Medical School, London; and the National Centre for Social Research). We thank the UK Data Archive, University of Essex, for providing the data. The original data creators, depositors, or copyright holders, the funding agencies, and the UK Data Archive bear no responsibility for the analyses and interpretation presented here. GDB is a Wellcome fellow. IJD is the recipient of a Royal Society-Wolfson Research merit award. Contributors: CRG and GDB conceived the idea for the present analyses, which were developed by the coauthors CRG carried out the data analyses and wrote the first draft of the manuscript to which the coauthors made substantial contributions. IJD advised on the psychometric analyses of the mental ability tests. CRG and GDB are guarantors. Competing interests: CRG and GDB are lapsed vegetarians, IS is a committed vegetarian, and IJD is an omnivore. The IQs of three of the authors have never been tested; IJD opts not to disclose.

Ethical approval: Not required.

What is already known on this topic

Vegetarianism may be viewed by those of higher intelligence as a healthier option than consuming meat.

What this study adds

Higher scores for IQ in childhood are associated with an increased likelihood of vegetarianism in adulthood.


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Endometriosis

Cynthia Farquhar

What is endometriosis?
Endometriosis is a chronic condition characterised by growth of endometrial tissue in sites other than the uterine cavity, most commonly in the pelvic cavity, including the ovaries, the uterosacral ligaments, and pouch of Douglas (fig 1). Common symptoms include dysmenorrhoea, dyspareunia, non-cyclic pelvic pain, and subfertility (table 1). The clinical presentation is variable, with some women experiencing several severe symptoms and others having no symptoms at all. The prevalence in women without symptoms is 2-50%, depending on the diagnostic criteria used and the populations studied.1 The incidence is 40-60% in women with dysmenorrhoea and 20-30% in women with subfertility.2 3 The severity of symptoms and the probability of diagnosis increase with age.4 5 The most common age of diagnosis is reported as around 40, although this figure came from a study in a cohort of women attending a family planning clinic.6 7 Symptoms and laparoscopic appearance do not always correlate.2 The American Society for Reproductive Medicine has published a classification of severity of endometriosis at laparoscopy.8 9

What are the causes of endometriosis?
Several factors are thought to be involved in the development of endometriosis. Retrograde menstruation remains the dominant theory for the development of pelvic endometriosis, though as this is almost universal it is unlikely to be the sole explanation.7 8 9 The quantity and quality of endometrial cells, failure of immunological mechanisms, angiogenesis, and the production of antibodies against endometrial cells may also have a role.10 11 Embryonic cells may give rise to deposits in distant sites such as the umbilicus, the pleural cavity, and even the brain.12 13

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Alternative diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent painful periods</td>
<td>Adenomyosis, physiological</td>
</tr>
<tr>
<td>Painful intercourse</td>
<td>Psychosexual problems, vaginal atrophy</td>
</tr>
<tr>
<td>Painful micturition</td>
<td>Cystitis</td>
</tr>
<tr>
<td>Painful defecation during menstruation</td>
<td>Constipation, anal fissures</td>
</tr>
<tr>
<td>Chronic lower abdominal pain</td>
<td>Irritable bowel syndrome, neuropathic pain, adhesions</td>
</tr>
<tr>
<td>Chronic lower back pain</td>
<td>Musculoskeletal strain</td>
</tr>
<tr>
<td>Adnexal masses</td>
<td>Benign and malignant ovarian cysts, hydrosalpinges</td>
</tr>
<tr>
<td>Infertility</td>
<td>Unexplained (assuming normal ovulation and semen parameters with patent tubes)</td>
</tr>
</tbody>
</table>

Recurrences
In the five years after surgery or medical treatment 20-50% of women will have a recurrence. Long term medical treatment (with or without surgery) has the potential to reduce recurrence but evidence based research is lacking.

Summary points
Medical treatment
Avoid prescribing medical treatment for women who are trying to conceive.

The simpler treatments—such as the combined oral contraceptive pill, oral or depot medroxyprogesterone acetate, and the levonorgestrel intrauterine system—are as effective as the gonadotrophin releasing hormone (GnRH) analogues and can be used long term.

Surgical treatment
Laparoscopic excision or ablation at time of diagnostic laparoscopy if possible.

Endometriomata (large cysts of endometriosis) are best stripped out instead of drainage and ablation.

What are the risk factors for endometriosis?
Risk factors generally relate to exposure to menstruation: early menarche and late menopause increase the risk whereas the use of oral contraceptives reduces.5 5

What is the natural course of endometriosis?
Studying the natural course is difficult because of the need for repeat laparoscopy. Two studies in which laparoscopy was repeated after treatment in women given placebo, however, reported that over 6-12 months, endometrial deposits resolved spontaneously in up to a third of women, deteriorated in nearly half, and were unchanged in the remainder.9 12 13

Sources and selection criteria
I searched the Cochrane Database of Systematic Reviews from the Cochrane Library (issue 3, 2006), Medline (1966 to April 2006), and citation lists of relevant publications and included randomised controlled trials and review articles. I used the following subject headings and keywords: endometriosis, menstrual pain, period pain, and pelvic pain. I did not look for non-randomised studies except for studies on diagnostic tests and prevalence or if I found no randomised controlled trials.
Diagnosis of endometriosis
What features of history and examination are important?
In women of reproductive age who present with recurrent dysmenorrhea or pelvic pain you should take a full history of reproduction and carry out a pelvic examination. The cyclical nature of the pain and the relation of the pain to menstruation points to the diagnosis of endometriosis. Painful micturition, defecation, and dyspareunia are also associated. In young women you should consider other diagnoses such as pelvic infection, problems in early pregnancy, ectopic pregnancy, ovarian cyst torsion, and appendicitis (table 1). During pelvic examination, tenderness in the posterior fornix or adnexa, nodules in the posterior fornix, or adnexal masses may indicate endometriosis. Adolescents presenting with dysmenorrhea do not require a pelvic examination as disease is uncommon.

How is endometriosis diagnosed?
Transvaginal ultrasonography can reliably detect endometriomata (cysts of endometriosis), but failure to reveal cystic structures does not exclude the diagnosis of endometriosis. Magnetic resonance imaging is increasingly used to identify subperitoneal deposits, although retroversion, endometriomata, and bowel structures may mask small nodules.

Although concentrations of the cancer antigen CA125 are slightly raised in some women with endometriosis, the test neither excludes nor diagnoses endometriosis and is not considered useful in establishing the diagnosis. The threshold for surgery is unlikely to be influenced by the CA125 concentration, and the guidelines from the Royal College of Obstetricians and Gynaecologists described CA125 as having only limited value as either a screening or a diagnostic test. Laparoscopy is the only diagnostic test that can reliably rule out endometriosis. It is also accurate in detecting endometriosis and is considered the standard investigation.

What are the indications for laparoscopy?
Many young women experience dysmenorrhea (about 60-70%), and unless there are other features to indicate endometriosis laparoscopy is not recommended. Some women will require further investigation to guide management. For adolescents who present with dysmenorrhea, the recommended approach is to first prescribe non-steroidal anti-inflammatory drugs (NSAIDs) and oral contraceptives. The lack of measurable pain relief with these drugs is usually an indication for further investigation. Other indications for laparoscopy include severe pain over several months, pain requiring systemic therapy, pain resulting in days off work or school, or pain requiring admission to hospital.

What are the effective medical treatments?
Treatment options for medical therapy include oral contraceptives, progestogens, androgenic agents, and gonadotrophin releasing hormone (GnRH) analogues. All suppress ovarian activity and menses and atrophy of endometriotic implants, although the extent to which they achieve this varies. There have been few randomised controlled trials of medical treatment versus placebo, although many trials have

Table 2 | Medical treatment* for endometriosis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Length of treatment recommended</th>
<th>Adverse events</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone acetate/progestagens</td>
<td>Ovarian suppression</td>
<td>Long term</td>
<td>Weight gain, bloating, acne, irregular bleeding</td>
<td>May be given orally or by intramuscular or subcutaneous depot injection</td>
</tr>
<tr>
<td>Danazol</td>
<td>Ovarian suppression</td>
<td>6-9 months</td>
<td>Weight gain, bloating, acne, hirsutism, skin rashes</td>
<td>Adverse effects on lipid profiles</td>
</tr>
<tr>
<td>Oral contraceptive</td>
<td>Ovarian suppression</td>
<td>Long term</td>
<td>Nausea, headaches</td>
<td>Can be used to avoid menstruation by skipping the placebo pills</td>
</tr>
<tr>
<td>GnRH analogue</td>
<td>Ovarian suppression by competitive inhibitor of GnRH analogue</td>
<td>6 months</td>
<td>Hot flushes, other symptoms of hypo-oestrogenism</td>
<td>By injection or nasal spray only</td>
</tr>
<tr>
<td>Levonorgestrel intrauterine system</td>
<td>Endometrial suppression; ovarian suppression in some women</td>
<td>Long term use but change every 5 years in women &lt;40 years</td>
<td>Irregular bleeding</td>
<td>Also reduces menstrual blood loss</td>
</tr>
</tbody>
</table>

GnRH=gonadotrophin releasing hormone.
*Decisions about medical therapy will depend on patient’s choice, available resources, plans for fertility, and ongoing symptoms. Side effect profile may influence choice.
TIPS FOR THE GENERAL PRACTITIONER

Suspecting endometriosis
- Pain before or during menstruation
- Poor response to non-steroidal anti-inflammatory drugs and combined contraceptive pill
- Days off school or work
- Dyspareunia

Recommended initial investigations
- Transvaginal ultrasound to detect endometriomata
- CA125 levels
- Magnetic resonance imaging or computed tomography

Refer patient with suspected endometriosis if
- Failed treatment of primary dysmenorrhea with contraceptive pill and non-steroidal anti-inflammatory drugs
- Severe pain requiring systemic medication, days off school or work
- Recurrence of symptoms in women with previously treated endometriosis
- Delayed fertility in association with endometriosis

compared different types of medical treatment.\textsuperscript{7,10} All medical treatments are similarly effective in relieving pain during treatment (table 2).

The side effect profiles are important in deciding treatment choices. Progestogens are associated with irregular menstrual bleeding, weight gain, mood swings, and decreased libido. The side effects associated with danazol include skin changes, weight gain, and occasionally deepening of the voice, and it is infrequently prescribed now. GnRH analogues dramatically lower oestrogen concentrations, and side effects include the development of menopausal symptoms and the loss of bone mineral density with long term use (both reversible). Oestrogen therapy in an add back regimen is useful for preventing side effects with GnRH analogues.\textsuperscript{10} In the randomised controlled trials comparing subcutaneous depot medroxyprogesterone acetate (SC-DMPA) with GnRH analogues the bone loss was less with the progestrone during treatment.\textsuperscript{w20, w21}

Recurrence of painful symptoms after six months of medical treatment may be as high as 50% in the 12-24 months after the treatment is stopped.\textsuperscript{w22, w23} Recurrence may in part be because large lesions respond poorly to medical treatment. It is generally accepted that endometriomata are not amenable to medical treatment, although temporary clinical relief may be achieved.

The levonorgestrel intrauterine system (LNG-IUS) is an established treatment for heavy menstrual bleeding but can also be used for dysmenorrhea and endometriosis.\textsuperscript{11, w24} In one study only 10% of women who had a levonorgestrel intrauterine system after surgery for endometriosis had moderate or severe dysmenorrhea compared with 45% of the women who had surgery only.\textsuperscript{12} In a trial of 82 women with endometriosis the levonorgestrel intrauterine system had similar effectiveness to GnRH analogues, but the potential for long term use of this system is advantageous if the woman does not want to conceive.\textsuperscript{13} It has also been used in women with rectovaginal disease.\textsuperscript{14}

In the future aromatase inhibitors may have a therapeutic role in endometriosis as they inhibit oestrogen production selectively in endometriotic lesions, without affecting ovarian function.\textsuperscript{w25}

Is surgery or medical treatment more effective?
There are no randomised controlled trials comparing medical versus surgical treatments for the management of endometriosis, and the decision about medical or surgical treatment at the time of diagnosis will depend on several factors including patient’s choice, the availability of laparoscopic surgery, the desire for fertility, and concerns about long term medical therapy.

What are the effective surgical strategies?
Surgery for endometriosis can be performed laparoscopically or as an open procedure. It entails excision or ablation (by laser or diathermy), and both, of the endometriotic tissue with or without adhesiolyis. There are few trials of laparoscopic treatment.\textsuperscript{14, 15} Surgical excision of endometriosis results in improved pain relief and improved quality of life after six months compared with diagnostic laparoscopy only.\textsuperscript{14} In one of the trials laparoscopic treatment also included uterine nerve ablation (LUNA),\textsuperscript{13} and pain improvement persisted for up to five years in more than half of the women.\textsuperscript{w26} About 20% of women do not report any improvement after surgery.\textsuperscript{14}

No randomised controlled trials have compared laser versus electrosurgical removal of endometriosis, and only one small trial, with inconclusive results, compared excision versus ablation.\textsuperscript{w27}

How often does endometriosis recur after surgery?
Recurrence of endometriosis after laparoscopic surgery is common.\textsuperscript{16, w28} Even with experienced laparoscopic surgeons, the cumulative rate of recurrence after five years is nearly 20%.\textsuperscript{17} Another study reported recurrence of dysmenorrhea in almost a third of women within one year of laparoscopic surgery in women who received no other treatment.\textsuperscript{10}

What is the role of uterine nerve ablation at the time of laparoscopy?
Randomised controlled trials of laparoscopic uterine nerve ablation at the time of laparoscopic excision...
of endometriosis compared with laparoscopic excision only showed no evidence of benefit, although there was limited evidence of benefit with presacral neurectomy. 18

What is the evidence for surgery in women with endometriomata?
Randomised controlled trials comparing excision or drainage and ablation for endometriomata ≥3 cm reported that recurrences were reduced and subsequent spontaneous pregnancy increased in the women who underwent excision (fig 2). 19 Although excisional surgery of the capsule could lead to removal of normal ovarian tissue and result in reduced ovarian reserve, 20 28 there is no evidence that this occurs, whereas a recurrence of the endometriomata will inevitably mean further surgery. 19

What is the best approach in women with rectovaginal disease?
Rectovaginal endometriosis presents surgical challenges because of difficult access and the possibility of injury to the bowel. Although reported long term outcomes are encouraging with advanced laparoscopic techniques, there are few prospective studies and no randomised controlled trials. 16–17 One small study of the levonorgestrel intrauterine system in women with rectovaginal endometriosis found improved dysmenorrhea, pelvic pain, and dyspareunia after one year. 29 A trial comparing oestrogen and progesterone combination with low dose progestogen in 90 women with rectovaginal disease reported substantial reductions at 12 months in all types of pain without major differences between groups. 21 Overall, two thirds of patients were satisfied with this approach.

Should women have hormonal treatment before surgery for endometriosis?
Only one study has examined this question. There was no evidence of a difference in the difficulty of surgery in the women who had received preoperative hormonal treatment. 20

Should women have hormonal treatment after conservative surgery?
There was no evidence of improved pain relief with postoperative hormonal treatment (including danazol, GnRH analogues, oral contraceptives, and medroxyprogesterone acetate) up to 24 months after surgery. 21 The studies to date are small, however, and there is insufficient follow-up to rule out a benefit.

What are the effects of hormonal treatment after oophorectomy (with or without hysterectomy)?
There was no evidence of increased rates of recurrence in women who had both ovaries removed and who were given nearly four years of combined hormone therapy, but the study was underpowered to detect clinically important differences. 22

What is the impact of endometriosis on fertility?
Although management of pain may be the more immediate issue, the long term outcome of fertility should not be overlooked. Few studies have examined this. A systematic review of medical treatment for women with infertility and endometriosis did not find evidence of benefit, 7 and it is not recommended for women trying to conceive. 19 23 A systematic review of laparoscopic treatment of endometriosis in women with subfertility suggested an improvement in pregnancy rate in the 9–12 months after surgery. 20 21 A second systematic review of laparoscopic excision compared with ablation endometriomata reported a fivefold increase in rate of pregnancy. 19 There is the ongoing concern about ovarian reserve in women who have laparoscopic excision. 20 28 The other concern is the impact of endometriomata on artificial reproductive techniques. 30 The European Society for Human Reproduction and Embryology recommends surgery if endometriomata are ≥4 cm. 23

Conclusion
Endometriosis should be suspected in any woman of reproductive age who presents with dysmenorrhea or chronic pelvic pain. Only laparoscopy can reliably identify endometriosis. If endometriosis is diagnosed at the time of laparoscopy, laparoscopic surgery should be the first choice of treatment, especially in women of reproductive age with an endometriomata. In women with endometriomata, the cys
Medical folklore—the use of your stethoscope’s bell

In my efforts to tease out medicine’s innermost secrets and succeed at the final hurdle to becoming a member of the Royal College of Physicians by passing the clinical examination (PACES), I have uncovered what I consider to be an interesting and neglected fact about the bell and diaphragm of most stethoscopes.

Like a migrating bird, I return each Christmas to my birthplace, a place I remember with a fondness that might be considered sentimental. In the quiet of the holidays, I would often find myself rummaging through old school uniforms and old school albums, opening the box as if for the first time. I prised the instruction booklet from its foamy surround and began flicking through.

A single word caught my interest—“historical.” Fascinated, I read that the bell of the stethoscope had been, like my old uniforms, mercilessly superseded. I was astonished to find that the diaphragm side was capable of eliciting both high and low frequency sounds depending on the examiner’s pressure. I suddenly realised that the diaphragm itself was brought into play only with firm pressure and that for the past seven years I had actually been listening to the lower frequencies rather than medical, treatment should be offered.

22 Mataras R, Etorriaga MA, Pijoan JJ, Ramon O, Rodriguez-Escudero FJ. Recurrence of endometriosis in women with bilateral adnexectomy (with or without total hysterectomy) who received hormone replacement therapy. Fertil Steril 2002;77:303-8.
Headaches are one of the commonest reasons for attending a general practice or a neurology clinic. Some 15% of the UK adult population have migraine, and 80% have episodic tension-type headache from time to time. The lifetime prevalence of headache is 96%, being higher in women than in men. Every day more than 100,000 people are absent from school or work because of migraine, with a cost to the economy that may exceed £1.5bn ($2.3bn; $2.9bn) a year.1

What should I already know about this condition?
Most headaches are benign, with tension-type headaches and migraines being the main sorts.

Tension-type headaches are the most common type of headache, with the lifetime prevalence ranging between 30% and 78% according to different studies. Migraine can occur with or without an aura. A typical aura lasts from five to 60 minutes before the headache starts. It consists of transient visual, sensory, and speech disturbances. Visual symptoms are the most common manifestation of an aura and consist of flickering lights, spots or lines, or blind spots.

Cluster headaches are unilateral severe headaches that occur in clusters over six to 12 weeks. They are more common in men, people who smoke, and adults older than 20 years. They tend to occur daily and wake the patient if they occur within a few hours of falling asleep. The pain of cluster headaches is severe, sometimes compared to the pain from renal colic. They are associated with ipsilateral watering of the eye, conjunctival redness, rhinorrhea, nasal blockage, and ptosis. Their prevalence in the UK adult population is 69/100,000, so they are much less common than migraine.

Dangerous headaches—A small proportion of patients have headaches that are dangerous (such as subarachnoid haemorrhage, meningitis, temporal arteritis, and raised intracranial pressure for whatever reason). Fewer than 1% of patients referred to outpatient clinics with headaches have an intracranial lesion. Dangerous headaches tend to be “first and worst,” single and of sudden onset, progressive, and with onset later in life. Consider temporal arteritis in any patient older than 50 who has a headache of new onset.1 Only a minority of patients with temporal arteritis have temporal pain, but jaw claudication (pain in the jaw during talking or chewing) is virtually diagnostic. Arrange for a patient to have a temporal artery biopsy to confirm the diagnosis.

What new evidence do I need to know about?
Features of medication overuse headache
This study2 found that:

- Patients who overused 5 HT1 agonists (“triptans”) experienced medication overuse headaches faster and with lower doses than did those who overused ergotamine and analgesics
- Clinical features of medication overuse headaches depended on the type of drug overused
- Patients who overused ergotamine and analgesics typically had a daily tension-type headache
- Patients who overused triptans typically had a daily migraine-type headache or an increase in frequency of their migraines.

Bottom line—Medication overuse headache is an important cause of headaches.

Topiramate in migraine prevention
Topiramate has recently been licensed for migraine prophylaxis.3 This study reviewed key randomised controlled trials of the drug. It confirmed that a dose of 100 mg a day was effective and well tolerated. Bottom line—Topiramate is an effective and well tolerated drug for the prevention of migraine.

What new guidelines have been produced over the past three years?
British Association for the Study of Headache (BASH) management guidelines (2004)
These guidelines1 provide essential information about different types of headache, how to take a history and examination, and treatment. The important points are:

PRACTICAL TIPS
- Headaches are a major cause of morbidity, but specific management can help
- Make a diagnosis by taking a clear history and conducting a good examination as recommended by the British Association for the Study of Headache
- Patients may have more than one type of headache
- Be alert for medication overuse headache (patients using analgesics or triptans for >17 days a month are at risk)
- For migraine, try to identify triggers and advise the patient to avoid them, make an acute treatment plan (analgesics with or without antiemetics or triptans), and consider prophylaxis (initially β blockers or amitriptyline)
Box 1 | Taking a headache history (from BASH management guidelines)

How many different headache types does the patient experience?
* Separate histories are necessary for each. It is reasonable to concentrate on the most bothersome to the patient, but always inquire about the others in case they are clinically important

Time questions
* Why consulting now?
* How recent in onset?
* How frequent, and what temporal pattern (especially distinguishing between episodic and daily or unremitting)?
* How long lasting?

Character questions
* Intensity of pain
* Nature and quality of pain
* Site and spread of pain
* Associated symptoms

Cause questions
* Predisposing or trigger factors
* Aggravating or relieving factors
* Family history of similar headache

Response questions
* What does the patient do during the headache?
* How much is activity (function) limited or prevented?
* What medication has been used, and in what manner?

State of health between attacks
* Completely well, or residual or persisting symptoms?
* Concerns, anxieties, fears about recurrent attacks or their cause

Diagnosis
Take a full history (see box 1).

Treatment of migraine
First, discuss non-drug treatment measures such as relaxation, acupuncture, and massage. All these non-drug measures have been shown to have a mild to moderate impact on symptoms.

Ask the patient to identify triggers using a diary. These can be factors related to food, stress, and lack of sleep. Patients should try to avoid them as far as possible.

Take a stepwise approach to increasing patients’ medication (see box 2).

Prophylaxis of migraine
Patients should continue taking drugs that they find effective for at least four to six months. They should then withdraw these over two to three weeks to see whether the drugs are still necessary.

For first line prophylaxis, use β blockers such as atenolol and bisoprolol if your patient has no contraindications, such as asthma, depression, heart failure, or peripheral vascular disease. Second line choices are sodium valproate and topiramate. Try agents such as gabapentin for third line prophylaxis.

European Federation of Neurological Societies guideline on the drug treatment of migraine
NSAIDs and triptans are recommended for the acute treatment of migraine attacks.\(^4\) Prescribe an antiemetic such as oral metoclopramide or domperidone to be taken before the NSAID or triptan. For severe attacks, intravenous aspirin or subcutaneous sumatriptan is the preferred treatment.\(^5\)

Box 2 | Treatment ladder for migraine

**Step 1: NSAIDs**
- Start with non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin or ibuprofen
- Give these with an antiemetic drug such as prochlorperazone as a buccal tablet for nausea
- Advise patients to take treatment as soon as possible after an attack starts

**Step 2: Parenteral analgesics**
- Consider parenteral analgesics, such as diclofenac given intramuscularly, with or without an antiemetic such as domperidone as a rectal suppository

**Step 3: Triptans**
- Do not prescribe triptans with other migraine drugs such as ergotamine. People with headaches respond differently to different triptans. Recommend that your patient takes them when the headache starts rather than at the time of the aura
- All triptans are associated with relapse of symptoms in 20–50% of patients after 48 hours
- Sumatriptan is the most commonly used triptan and has the most evidence about its effects
- Recommend that the patient starts with a 50 mg tablet (also available as a rapidly dispersing preparation)
- If necessary increase the dose to 100 mg or suggest the 20 mg nasal spray
- The nasal spray is not useful if vomiting prevents oral treatment as the drug’s bioavailability depends partly on ingestion
- If a rapid response is needed, subcutaneous sumatriptan relieves migraine in 80% of patients within one hour of injection
- If sumatriptan is ineffective recommend another triptan
- Triptans are contraindicated in children younger than 12 years old and in patients with ischaemic heart disease, uncontrolled hypertension, or risk factors for coronary heart disease and cerebrovascular disease
- If treatment fails, review the diagnosis and then consider steps 4 and 5

**Step 4: Combination treatment**
- There is no formal evidence for combination treatment, but you could try combining steps 1 and 3 followed by steps 2 and 3

**Step 5: Emergency treatment of patients at home**
- Try diclofenac with chlorpromazine, both given intramuscularly
The God incarnate

A middle aged man was admitted with type 2 diabetes and coronary artery disease. He was a Hindu religious teacher, well versed in the ancient Hindu religious texts and epics, and an ardent devotee of Hanuman, the Monkey God.

To explain world events and happenings, he quoted extensively from Hindu mythology. Within no time he had established a good rapport with the treating team, and many of the ward staff and patients became his disciples.

He was to undergo coronary angioplasty for coronary artery disease. Unfortunately the angioplasty was complicated by coronary dissection and was converted to coronary artery bypass graft. Postoperatively he had sternotomy infection and sternal wound dehiscence. He recovered after a stormy postoperative course.

During the ward round one day, he smiled and said in a matter of fact manner that he had been told before the operation that coronary angioplasty was a routine, safe, and quick procedure; he had not expected to be turned by doctors from a mere disciple and devotee of Hanuman into the God himself.

According to Ramayana, Hanuman is an ardent devotee of Lord Rama and Goddess Sita. To display and confirm his devotion to them, Hanuman split open his chest in the midline with his bare hands, and his heart showed images of Lord Rama and Goddess Sita.

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**COMMONLY ASKED QUESTION—ANSWERED**

Will my patient benefit from having a scan, even if I do not think he or she has intracranial pathology (a primary headache syndrome)?

Possibly. One study found that patients who were offered a scan were less anxious at three months, although not at one year.\(^1\) Management costs for patients with anxiety at their initial presentation were significantly less if they were offered a scan at the onset.

**FURTHER EDUCATIONAL RESOURCES**

- British Association for the Study of Headache (BASH): [www.bash.org.uk](http://www.bash.org.uk)
- www.clinicalevidence.co
- BM Learning: [www.bmjlearning.com](http://www.bmjlearning.com)
- Common migraine: how to treat an attack
- Migraine: diagnosis and prevention

Drug of first choice. Prescribe corticosteroids if your patient has status migrainosus. For prophylaxis of migraine, β blockers such as propranolol and metoprolol, flunarizine (not licensed in the UK), valproate, and topiramate are drugs of first choice. Second line choices are amitriptyline, naproxen, bisoprolol, and *Petasites* (butterbur, available over the counter).

**Practical management tips**

Make a diagnosis by taking a clear history and conducting a good examination as recommended by the BASH guidelines.\(^1\) Recognise that patients may have more than one type of headache.

Be alert for medication overuse headache. Patients are at risk if they use analgesics or triptans for more than 17 days a month. Codeine based drugs are common culprits.

Be aware that your patient may have a rare primary headache disorder (most commonly cluster headache), and that these respond to specific drug regimens.

**Managing migraine**

Try to identify triggers and suggest the patient avoids these.

Make an acute treatment plan—analgesics with or without antiemetics or triptans. Patients with migraine often vomit. If a patient vomits their tablets, consider subcutaneous injections or rectal administration.

Consider prophylaxis. The order that you prescribe drugs should depend on side effects and any comorbidities. For all drugs, start at low doses and slowly titrate up until they are effective, the patient experiences side effects, or you reach the maximum dose. Recommended treatments are as follows:

- First line—β blockers or amitriptyline
- Second line—valproate, topiramate, or pizotifen
- Other agents—feverfew.

**When should I refer my patient?**

Refer patients immediately if they have a sudden severe headache. Also refer patients with progressive headaches, if they have physical signs, if you are uncertain of the diagnosis, or if standard treatments do not work.

**Common pitfalls**

Beware of:

- Causing medication overuse headache by treating chronic headache with regular analgesia rather than suggesting prophylaxis
- Undertreating migraine
- Missing unusual primary headache variants
- Blaming headaches on stress.

**Competing interests:** None declared.

Diagnostic laparoscopy or thoracoscopy can improve diagnosis of occult injuries to the diaphragm and reduce the risk of serious late morbidity

Stabbing injuries are now common, and the number of haemodynamically stable patients with penetrating injuries of the chest and upper abdomen who are treated conservatively has increased. The case we present supports a more aggressive approach to penetrating thoracic injuries that occur between the horizontal planes bounded by nipple line and umbilicus (junctional zone).

No universally accepted strategy for managing this condition exists. Some doctors use advanced cross sectional imaging\(^1\) complemented by clinical acumen; others adopt a more invasive approach—laparoscopy or thoracoscopy.\(^2\) We present a case where a missed injury to the diaphragm caused by penetrating thoracic trauma resulted in serious morbidity. We conclude that conservative management of such injuries results in a considerable risk of occult hernia of the diaphragm with potentially life threatening sequelae.

Case

A 15 year old healthy boy was assaulted with a knife and sustained a penetrating injury to his left posterior chest wall at the level of the ninth rib. He was haemodynamically stable, but plain x ray showed a left sided haemopneumothorax, which we managed successfully with a chest drain. He remained stable and a contrast enhanced computed tomography scan showed no visceral injury. He was monitored closely and was sent home after seven days. He was asymptomatic at three months’ follow-up. Clinical examination and a chest x ray were normal at that point and the patient was discharged. One year later, he presented to the accident and emergency department with sudden severe epigastric pain, complete dysphagia, and blood stained vomiting. He was constitutionally unwell with tenderness in the left upper abdomen and decreased air entry at the left lung base.

A chest x ray showed collapse of the left lower lobe and blunting of the left costophrenic angle. An urgent double contrast computed tomography scan showed a defect in the diaphragm through which most of the stomach had herniated into the left hemithorax (figure).

An emergency laparotomy showed that all but the pylorus of the stomach had herniated through a 4 cm central defect and was incarcerated in the left chest with evidence of irreversible ischaemia. We performed a total gastrectomy with roux-en-Y reconstruction, and the patient made an uneventful recovery. Histology of the specimen confirmed an ischaemic stomach due to strangulation.

Discussion

Injuries to the diaphragm caused by penetrating trauma to the junctional zone are often missed.\(^3\) The management of such injuries in haemodynamically stable patients is contentious. The merits of conservative management versus early surgical exploration have been debated extensively with no universal consensus.

Intrathoracic pressure is negative during inspiration, and over time even a small defect in the diaphragm can result in abdominal viscera being drawn into the chest. Clinical sequelae are rare on the right side because of protection from the liver. The diaphragm is exposed on the left side, however, and it is more vulnerable to these pressure effects.\(^4\) The central diaphragm is tendinous and poorly vascularised; this can compound the problem by compromising healing.

A three phase model of the natural course of injuries to the diaphragm has been described.\(^5\) The acute phase extends from the time of original trauma to recovery from apparent acute injuries and is followed by a latent phase where abdominal viscera gradually herniate into the thorax. Finally, the obstructive phase begins when the herniated viscera become ischaemic and the patient experiences acute symptoms. Patients whose injury is missed in the acute phase usually re-present in the obstructive phase with serious effects. Adopting a conservative approach during the acute phase can be dangerous in this group of patients. The natural course of the condition is insidious and often obscure, and many patients default on follow-up.

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**LESION OF THE WEEK**

**Penetrating trauma to the junctional zone needs aggressive management**

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Radiological investigations such as focused ultrasound and double or triple contrast helical computed tomography scans have a sensitivity of up to 85% to detect injury to the diaphragm. The problem is the 5% of patients who are asymptomatic but have an occult injury.

Laparoscopy is a valuable tool to investigate suspected injuries to the diaphragm, with a sensitivity of 87.5% and a negative predictive value of 96.8%. Video assisted thoracoscopic surgery (VATS) provides an accurate assessment of intrathoracic injuries. It can be used for the definitive and effective management of diaphragmatic injuries caused by blunt or penetrating thoracic trauma. This technique requires expert single lung anaesthesia but permits fastidious examination of the diaphragm.

In conclusion, we report an adolescent boy who sustained a perforating injury of the diaphragm that was not detected on initial presentation, who subsequently needed a total gastrectomy because of this missed injury. This case supports a more proactive management strategy for penetrating injuries to the junctional zone. The addition of diagnostic laparoscopy or thoracoscopy to currently available imaging techniques can greatly improve diagnosis of occult injuries to the diaphragm and reduce the risk of serious late morbidity. Patients with a penetrating trauma to the junctional zone should be followed up for longer, and detailed clinical examination should be supported by good quality chest radiology.

JA is the primary author. JG, BC, RK, and WDBC all helped manage the patient and write the paper. JAK was the principal surgeon. JAK and WDBC were the consultants responsible for the patient and are guarantors.

Competing interests: None declared.

References

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When I use a word

Geographic metals

Alexander Litvinenko, the former KGB officer who was supposedly murdered by a Russian agent, was poisoned by polonium. But this highly radioactive element is Polish, not Russian. It was discovered in 1898 by Marie Curie, working in Paris—a discovery for which she won the Nobel prize for chemistry in 1911, having already shared the 1903 physics prize with her husband, Pierre Curie, and Antoine Henri Becquerel. She named the new element after her mother country, Poland (Latin Polonia).

Many other elements have been named after places, usually because they were discovered there or nearby. Various parts of Europe can claim one apiece: europium itself, copper (Cyprus), germanium (the river Rhine, Latin Rheus), ruthenium (Russia, Latin Rusitna), and strontium (the town of Strotian in Scotland). The district of Magnesia in Thessaly boasts two—magnesium and manganese. France has three—francium, gallium (Latin Gallia=France), and lutetium (Latin Lutetia=Paris). The United States also has three—amercurium, berkeliunum, and californium, all discovered at the University of Berkeley in California.

But Scandinavia wins the terrestrial nomenclature battle, with seven in all. There are scavadium (Latin Scandia), hafniium after Copenhagen (Latin Hafnia), and holmium after Stockholm (Latin Holmia). And the little village of Yterby in Sweden lays claim to four, all to be found in the nearby quarry. In 1796 Johann Gadolin discovered a silicate, which he called ytterbite (later called gadolinite), from which A G Ekeberg extracted the earths (elemental oxides) yttria, erbia, and terbia. In 1828 Friedrich Wohler extracted yttrium from yttria, and in 1843 Carl Gustav Mosander extracted ytterbium, terbium, and erbium.

To beat that we must search the skies, finding eight elements named after celestial bodies—cerium (after the asteroid Ceres), palladium (the asteroid Pallas), selenium (Selene, the moon), helium (Helios, the sun), tellurium (Tellus, the earth), uranium (Uranus), neptunium (Neptune), and plutonium (Pluto). (The last three are named after the planets (or whatever Pluto is nowadays), not the corresponding classical gods.) If one of the synthetic elements with temporary names, such as ununbium (number 112) or ununtrium (number 113), needs a non-systematic name, sednium (Sd), after Sedna, the recently discovered body that cirles the sun in a highly elliptical orbit outside that of Pluto, is available. Sedna is the food goddess of the Inuit, with power over whales, seals, and polar bears, which were created from the parts of her fingers that her father cut off. Her other name is Arnaknagsak; anyone for Arnaknagsakum?

There is even an element named after an imaginary place—thulium. Thule (Greek, of unknown meaning) was, says Pliny, a place six days’ sail north from the Orkeys, first mentioned by Polybius (circa 150 BC) in his description of a voyage made by Pytheas from Massilia (Marseilles) in the late fourth century BC. At midsummer at Thule the sun did not set. Its inhabitants ate berries, oats, herbs, fruits, roots, and honey. It was surrounded by freezing fog, and to the north the sea itself was frozen. Eratosthenes situated it on the Arctic circle, Ptolemy by freezing fog, and to the north the sea itself was frozen. It was surrounded by freezing fog, and to the north the sea itself was frozen. Thulium was extracted in 1886 by Paul Emile Lecoq de Boisbaudran from the mineral thulite (thulium oxide), discovered by the Swedish chemist Per Teodor Cleve in 1879. Perhaps there are enough connections for thulium to be counted among the Scandinavian elements.

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Sedna, food goddess of the Inuit, is said to have power over whales, seals, and polar bears.
10-MINUTE CONSULTATION

Newly diagnosed iron deficiency anaemia in a premenopausal woman

Tony Todd,1 Tim Caroe2

A 40 year old woman with persistent fatigue has come back to you for the results of blood tests. The results show a hypochromic, microcytic anaemia with a haemoglobin concentration of 100 g/l and a ferritin concentration of 5 μg/l, the classic features of iron deficiency anaemia (IDA).

What issues you should cover

Symptoms of anaemia

Fatigue and mild dyspnoea after exertion may be the only symptoms in otherwise healthy people with slow onset anaemia. More serious symptoms such as angina, marked ankle oedema, or dyspnoea at rest don’t generally occur unless the haemoglobin concentration is less than about 70 g/l. Presence of such symptoms in a case like this indicates additional cardiorespiratory pathology.

Causes of the anaemia

Blood loss—Seek any history of haemorrhage. In the 5-10% of premenopausal women who develop IDA the commonest cause is menorrhagia. For reliable assessment simple pictogram charts may be better than subjective reporting.

Coeliac disease—In younger patients coeliac disease often presents with IDA, especially in women aged 20-60. Pay attention to gastrointestinal symptoms, including unexplained weight loss, diarrhoea, and abdominal pain.

Drug use—Some drugs, such as anticoagulants, aspirin, and non-steroidal anti-inflammatory drugs, may cause or exacerbate blood loss. Warfarin may worsen menstrual bleeding but rarely causes other major chronic haemorrhage (such as gut or genitourinary bleeding) without additional pathology. Warfarin may, therefore, be unmasking another pathology, and you should still seek an underlying cause of IDA.

Other history—Consider recent pregnancy, breast feeding, and blood donation. Pregnancy induced IDA usually resolves rapidly after birth but may persist in women from low income groups who have a poor diet, especially if they are breast feeding. Frequency of blood donation is limited to prevent IDA, but it may still occur, as in premenopausal women each unit contains about a tenth of the average amount of body iron.

Diet—In the United Kingdom IDA unrelated to pregnancy is rarely caused by poor diet, as major deficiency would arise only after several years without any food that contains iron (meat, leafy green vegetables).

Features of iron deficiency

Some classic features of IDA—koilonychia, angular stomatitis, and glossitis—are rare but distressing. They resolve on treatment.

Key points

- Iron deficiency is not a final diagnosis—you must identify and treat the underlying causes
- In premenopausal women, particularly consider menorrhagia (a simple visual scoring system may help in assessment) and coeliac disease
- Poor diet and warfarin use are rarely sole causes
- A significant response should occur within three weeks of treatment starting

What you should do

- No degree of IDA should be ignored. Audits show that iron deficiency is undertreated and that serious illness can be missed. Even when a cause seems clear, failure to respond to treatment should raise suspicion of alternative causes.
- Refer appropriately in cases of abnormal blood loss. Referral to gastroenterology is indicated if she has gastrointestinal symptoms, obvious gastrointestinal blood loss, or a strong family history of colorectal carcinoma (such as two first degree relatives or one first degree relative aged 45 years). Gastrointestinal referral is not needed in asymptomatic women under 50 unless they don’t respond to adequate iron supplementation and treatment of other identified causes. In women 4% of cases of IDA are due to coeliac disease, which may otherwise be asymptomatic. Women with relevant symptoms, those whose IDA lacks an apparent cause, and those who don’t respond to iron treatment should be tested for anti-endomysial or anti-transglutaminase antibodies. Faecal occult blood testing is unpleasant and of little diagnostic value.
- Treat identified underlying causes. Start replacement treatment with ferrous sulphate 200 mg three times a day (ferrous gluconate and ferrous fumarate are alternatives). Continue for three months after the anaemia resolves to fully replenish stores. Avoid slow release preparations, as these release most of their iron after passing the small bowel absorption site.
- Warn her of side effects of taking iron (constipation and black stool) and stress the importance of adherence. Also explain that IDA is a consequence of something else that iron alone won’t treat and that this needs proper investigation and treatment.
- Arrange a follow-up full blood count and consultation in three weeks. A rise of haemoglobin by then of <20 g/l indicates a problem with adherence, malabsorption, or continuing blood loss.
Collecting feathers in the health service

PERSONAL VIEW Anonymous

I am a senior practitioner. I am passionate about my work and about the NHS, which is why I have much to say on racism within the organisation. Racism is a threat to any organisation. The police force was the first state body to be publicly exposed as having “institutional racism.” The NHS faces the same allegation. An accusation of racism leads to denial or the accuser being accused of playing the “race card.” It seems that consciously or not some people are blind to racism, at least that which is real for the visible minority.

When I proposed changing my name to give me a better chance of securing an interview to study medicine in the 1980s, I was considered naive; a London medical school proved me not so naive some years later. At my graduation ball the professor of surgery gave me some advice: “Even with your surgery medal you will have to work harder, be smarter, try and join the right clubs and it will still take you longer—if you are lucky.” Fortunately I was not interested in a surgical career. I did come across racism in my career path though. While I was in surgery as a houseman, the consultant surgeon said: “You’re from Africa. Do you think black people are genetically incapable of running nations?” Except for the rhythmic noises of the gas machine, the theatre was still. Everyone awaited my answer. My immediate thought was of the consultant being a potential referee, so I took a white feather; I suggested that his query was perhaps a little more complex than just genetics. Covert racism is more interesting. By definition it is subtle, yet more visible to the visible minority and invisible to others.

I was clear about my career and how to go about achieving it. I chose to sidestep racist language, behaviour, and views from colleagues. I could have treated them as potential barriers; I could even have taken a formal, perhaps legal, route. Sidestepping was safest for me, but in doing so I failed to deal with the issues and left exposed others that followed. I kept collecting feathers. Yet pull the race card and whatever the outcome, the complainant is damaged—career, livelihood. So people just keep collecting feathers.

Despite my European education, indistinguishable English, and confidence, each of my career choices included a wider assessment of the potential for racism. Consider the international medical graduate with an Asian education, accented English, and unquestioning respect for seniors and institutions, grateful for the opportunities in an economically rich system. It is no surprise that the graduate from Bangalore feels more able to access support and direction from senior colleagues also from Bangalore. I chose deliberately to keep away from race issues. I was determined to stand out and be “the doctor” not “the Asian doctor.”

As a trainee I presumed that prejudicial recruitment practice was likely wherever I applied for work. For every application I visited the unit, not to inform myself but to inform potential employers of my abilities over and above a foreign sounding name. Ironically I am now involved in recruitment. I am in a position to implement good recruitment practice, bringing transparency, questioning assumptions, and being critical about supposedly historical practices. If a colleague genuinely believes that applicants with parents in medicine make better doctors, what other prejudices exist? I work on the assumption that most people I encounter and work with are fair, but I know that it takes few to corrupt an institution and to damage its employees and reputation.

Institutional racism has always been, and always will be, in the NHS. The McPherson report attempted a definition of institutional racism: “the collective failure of an organisation to provide an appropriate and professional service to people because of their colour, culture or ethnic origin which can be seen or detected in processes; attitudes and behaviour which amount to discrimination through unwitting prejudice, ignorance, thoughtlessness and racist stereotyping which disadvantages minority ethnic people.”

Just as people resent the accusation of being racist because they are unable to see it in themselves, organisations resent accusations of institutional racism. Exposure of such racism lies in building transparent systems rooted robustly enough to fight off the few invisible professionals who are hardened to damage otherwise forward thinking institutions.

Covert racism is more insidious, more difficult to frame legally, and more damaging than overt racism. When a senior, white, colleague commented in 2005 that a national award bestowed to a colleague from the visible minorities was more to do with achieving ethnic balance, it shows we still have a long way to go.

We have not yet travelled far enough for me to reveal my name, so pass me another white feather. You may know me, but do you know yourself?

The author, who is based in the north of England, wishes to remain anonymous but can be contacted at m.nasrudin@hotmail.com
Telling the inside story?

A sacked drug company executive claims to spill the beans on the industry in a new book, writes Jeanne Lenzer

Peter Rost, erstwhile drug company executive, self proclaimed whistleblower, and now book author, first became a cause célèbre in August 2004 when he wrote an endorsement of The Truth about the Drug Companies, the book by former New England Journal of Medicine editor Marcia Angell (review BMJ 2004;329:862). He posted a commentary on Amazon.com, saying, “I should start with a disclaimer. I’m a vice president within one of the largest drug companies in the world and I have spent close to 20 years marketing drugs. So I guess I’m not supposed to like this book. But the truth is I thought it was fantastic.”

Rost’s posting was picked up by the media and he became a much sought after guest on television and radio shows. He took up the cause of drug reimportation, a practice that would allow foreign drug companies to sell drugs in the United States. Reimportation, argued Rost, is widely practised in Europe and could drastically reduce drug prices in the US. His position was in sharp contrast with that of his employer, Pfizer, and to virtually all major US drug companies, which vehemently argued that reimportation would allow unsafe drugs to enter the US and would threaten the health and safety of its citizens.

But Rost began to run into trouble long before he became a public advocate of reimportation. In 2001, as the new head of the endocrine care division of Pharmacia, he learnt, according to his account, that the division’s flagship drug, Genotropin, a synthetic form of human growth hormone, was being promoted for off-label uses. Off-label promotion of growth hormone is a felony under federal anti-doping laws. Pfizer, which bought out Pharmacia in April 2003, failed to put a stop to the off-label promotions, says Rost.

Rost alleges that it was his complaints about the marketing of Genotropin that led Pfizer executives to fire him. He was first informed in an email message on 3 February 2003 that he was to be sacked, but he managed to hold on to his job for two and a half years, until 30 November 2005, when he was finally let go. Rost filed a qui tam, or whistleblower, lawsuit against both Pharmacia and Pfizer in December 2005. In the suit and the book, Rost claims to describe some of the inventive marketing techniques used by the companies to promote sales of Genotropin to “anti-aging” clinics and for the treatment of short children who did not have growth hormone deficiency.

Rost, who paints himself as a regular guy in his book, is the quintessential marketer. Along with the publication of The Whistleblower, he has a Hollywood agent looking for potential movie deals; he has written a fictional thriller about the drug industry entitled The Wolfpack; and he is scheduled to be interviewed for Sicko, Michael Moore’s documentary movie on the healthcare industry.

A nagging aspect of The Whistleblower is that Rost repeatedly wastes the reader’s time defending his motives for his various actions as he sought to hang on to his job. Some of his actions appear simply indefensible. Rost, who earned over $600 000 (€305 000; £460 000) annually (exclusive of benefits, annual bonus awards, and stock options) is hardly a man without warts. When Pfizer asked him to fire a number of his colleagues, Rost fired them—while bemoaning their fates in the book. He is at his worst, perhaps, when he spends an entire chapter on irrelevant speculation about the sexual activities of Pfizer’s bosses. Rost makes no bones about why he wants to pursue possible sexual improprieties, even though he has no first hand knowledge of the events. “If they feared what I knew about them,” he writes, “they would be less prone to take away the lifeline I had left—my salary.”

Rost’s book claims to chronicle problems in the way the drug industry manages to circumvent rules prohibiting off-label drug promotions. In addition, Rost’s endorsement of reimportation is perhaps one of the most articulate defences made in the US. The Whistleblower may also reach some lay readers who were not moved to pick up any one of a number of more academic books on the drug industry. Finally, his overview of serious violations by nine top drug companies in his chapter “How corrupt is the drug industry?” should make one thing crystal clear: fines simply don’t work. They are, as has often been said, simply the price of doing business.

“Working for a corporation,” writes Rost, “is like running with a wolf pack. Everyone helps out and is friendly as long as it benefits the group, but each wolf cares only about himself and will do anything to survive. Compassion, loyalty, caring … these are all buzzwords invented to control the masses.” Rost’s take on the nature of industry might leave one wondering whether Rost isn’t simply a very clever wolf himself.

The good news is that when the titans do battle—the fallout can be instructive.

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Flagging up a necessary division

In 1972 I holidayed in communist Bulgaria. My most vivid memory is of my communist father's cherry brandy fuelled rendition of the Red Flag on the bus. Back then the UK Communist party was the preserve of the private school intelligentsia, while many in the proletariat staunchly voted Tory. Despite the catchy drinking songs and natty uniforms, communism fell because its semi-religious dogma allowed its officials to rob their countries blind. So, unlike my father, I am a capitalist, recognising that people need incentives—sticks and carrots.

I do remain a socialist of sorts—perhaps the champagne kind, with my big house and skiing holidays. My kids attend a state school, but it operates a type of postcode selection. I have no need of private medical insurance, as I can be difficult enough to get the best out of the NHS. But I still see red when it comes to private medical practice. The idea that pain and suffering can be judged by a bank balance is unjustifiable, even to a capitalist. This isn’t merely misplaced ideology either. In humble general practice we hear hushed rumours of private medicine: absent consultants neglecting their NHS responsibilities and expressing rage at managers if challenged; consultants offering questionable investigations and charging questionable prices; a private sector that cynically cherry picks cases and dumps complex and chronic ones on the NHS.

Now much of this may just be medical myth, retold by each new generation of GPs. I know many consultants will also see red at such suggestions, and I have no doubt that the majority are fully committed to the NHS. But NHS and the private sector are two bitterly opposed teams. Private practice needs to operate, needs to investigate, and needs to churn patients through to make its money and so has huge financial incentive in seeing the NHS fail.

Perhaps it’s a throwback to Nye Bevan’s historical compromise, but why does the NHS allow its key consultants to play for both teams at the same time? The temptation to bend the system is simply too great. Is it time to make consultants choose a team? Private or public—but not both. NHS consultants should be able to earn extra income within the NHS, but this should be based on patients’ needs, not their income. But this is not communist dogma—the NHS doesn’t need red flags any more than it needs white flags.

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On the cheap

Like much else in health care in Britain, attempts to prescribe drugs by generic rather than brand names can be frustrating. This crucial contribution to containing the national drugs bill is sometimes disrupted by the tactics of the drug industry. And it must be rare to find patients who actively welcome being switched from a product with a familiar name and look.

Despite these negative aspects, the prescribing of generic drugs is a UK success story. That it isn’t celebrated (at least, not by patients) owes much to the downbeat way the topic is presented and discussed. Part of the problem is the low key nature of generic drugs and their producers. Few prescribers would struggle to name several major drug companies, yet how many could identify even a single producer of generics, let alone suggest how such outfits operate or relate to noisier, more powerful branches of the industry? This is a little odd, given how essential generic drugs are to the NHS.

Another issue is the language surrounding generics. In particular, unqualified use of “cheaper” and “cheap copies” in discussion of these products does not help. Such terms are too easily misinterpreted as “substandard.” Generics are not merely cheaper “copies” but equivalents that (with well documented exceptions) offer the same effectiveness, safety, and quality as their brand name versions and are, therefore, better value for money. Emphasising cheapness is a distraction.

So perhaps it’s time to learn from organisations that really know about championing value for money goods. Supermarkets are masters of this game. You won’t catch them presenting their “budget” or “value” products in ways that suggest “second rate” or “unfit for purpose.” Instead, their promotions carefully avoid making buyers feel mean, stupid, or inadequate for purchases that are made to minimise cost or maximise spending power. And somehow the shops achieve this while also marketing pricier items of undeniably higher class (a complication largely absent in comparisons of generic and brand name drugs).

A key difference between supermarket shopping and being prescribed generic drugs is the consumer’s lack of direct involvement in the NHS’s purchasing decisions. For patients and some prescribers this can mean that messages of value for money come a poor second to the higher profile trumpeting of brand names. So hearts and minds still need to be won on how generics benefit the nation without disadvantaging individuals.

In areas of expenditure where the public has much less day to day involvement than with drugs, such as defence or local government, the need for cost effective use of central funds goes without saying. Doesn’t generic prescribing deserve the same benign acceptance?

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Advice to travellers

I once took a job in the tropics, and my employer sent me for a medical examination to check that I was fit for hardship. My medical was just like the one that Marlowe underwent in Joseph Conrad’s Heart of Darkness, before he went out to the Belgian Congo.

Marlowe was in Brussels for his medical—a city, he says, that “always makes me think of a whitened sepulchre.” And then he adds, “Prejudice no doubt.” I confess to a similar prejudice. Brussels shows us our glorious future: bureaucracy and sex shows.

Marlowe is told that the medical is a simple formality, just as I was told it was. And so, indeed, it proves and proved.

Marlowe’s doctor—an old one, just as mine was—examines him in a perfunctory manner, just as I was examined. “The old doctor felt my pulse, evidently thinking of something else the while.”

Quite so: the old doctor in my case passed his stethoscope swiftly over my chest, the bell hovering just above the surface and never alighting anywhere. He would have heard anything only if I had had a tape recorder inside playing at full volume. It was more propitiation by a single ray of sunshine that fell on his negligently unprotected neck. The injunction to keep calm at all costs was therefore a very serious one.

My doctor advised that I should be careful of the water and not drink too much alcohol. Insects, he said, were to be avoided.

I didn’t altogether succeed in following his advice: I got malaria, jiggers, and myiasis.

As Marlowe leaves the consulting room the doctor says, with an admonitory wag of the finger, “Du calme, du calme. Adieu.”

This reminds me of another time I departed for an exotic destination: India. I was a student, and my trip meant that I would return late to medical school. I went to the dean to ask his permission to do so.

“India,” he said. “Ah …” He looked in the far distance, far beyond the walls of his office, extracting a rare insight from a point at infinity. “A land of people—and animals.”

He gave me his permission, even his blessing; and at the door, as I left him, he repeated, “Remember: people—and animals.”

I’ve never forgotten it. But what exactly did he mean? The same question has, of course, been asked of Conrad.

Theodore Dalrymple is a writer and retired doctor.

The medical was just like the one Marlowe underwent in Heart of Darkness

The ceremony nearly over, the doctor dispenses advice to Marlowe: “Avoid irritation more than exposure to the sun…In the tropics one must before everything keep calm.”

Of course, in those days the rays of the tropical sun were thought to be dangerous, if not fatal, to white people; even 30 years later Dr Schweitzer recounts in one of his books the case of a man driven stark mad by a single ray of sunshine that fell on his negligently unprotected neck. The injunction to keep calm at all costs was therefore a very serious one.

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BETWEEN THE LINES

Theodore Dalrymple

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MEDICAL CLASSICS

Tropical diseases By Patrick Manson

First published 1898

"Textbook knowledge" has a bad ring these days. Knowledge grows so quickly that textbooks are assumed to be purveyors of yesterday’s news. A century ago, medicine was also changing rapidly, and yet two textbooks, each published in 1898, transformed the medical landscape. William Osler’s Principles and Practice of Medicine elegantly brought the glad tidings of the new scientific medicine to students of medicine throughout the world. Patrick Manson’s Tropical Diseases spearheaded a new medical specialty, at a time of global imperialism.

Manson, a genial Scot with practical experience in China, Formosa, and Hong Kong, was then a tropical medicine consultant in London. He had demonstrated that filariasis was transmitted through mosquito bites. This clinical research alerted him to the importance of parasites in “tropical” diseases and to the role of insects in spreading them.

Before Manson, tropical diseases were generally assumed to be simply the diseases of warm climates, which emerged from the confluence of heat, humidity, vegetation, and decay that characterised these areas. Manson reversed the flow of causality: the conditions did not cause disease, but they permitted the existence of unique disease causing organisms. What Manson called the “cosmopolitan” diseases of the old world—diseases such as plague and leprosy—were ubiquitous because the germs could be found everywhere. They had largely disappeared from Europe.

In a sense, Tropical Diseases merely applied the germ theory to diseases of hot climates. Nevertheless, Manson argued, tropical medicine was not simply a branch of bacteriology.

Rather, the range of tropical organisms dangerous to human beings included many other biological groups: worms, protozoa, and plasmodia. Tropical medicine was thus really a branch of parasitology, and since many of the organisms had complicated extra corporeal developmental cycles, and complex means of spread, including via insects, special tools and modes of thought were required to understand the range of diseases found in the tropics.

Tropical Diseases appeared at an opportune time. Manson’s protégé Ronald Ross had discovered the malaria parasite in mosquitoes the year before and demonstrated its role in transmitting the disease in birds. Schools of tropical medicine in Liverpool, London, and several European countries established the discipline firmly. Manson oversaw a sixth ever expanding edition in 1917. One characteristic of a classic is that it stays available: the 21st edition of Manson’s textbook was published in 2003.

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Roland Jacob Levinsky

Pioneered the first successful bone marrow transplants in children with primary immunodeficiency and became a fearless university administrator

The dreadful death of Roland Levinsky has shocked the world of paediatric oncology and genetics. He was an immunologist of international renown who performed the UK's first successful bone marrow transplant in children with primary immunodeficiency in 1979 at Great Ormond Street children's hospital. He went on to perform the UK's first successful attempts at gene therapy in children with fatal inherited diseases. He transformed the Institute of Child Health in London into a topclass research institution. Later, he did a similar makeover at Plymouth University, sending it soaring up the league tables.

Levinsky was born in South Africa to a British-born mother and Polish/Lithuanian father. His father, died when Roland was 13. Two years later his mother returned to England with her three children.

He spent his sixth form years at William Ellis School in Camden. At University College London he was inspired by the great zoologist J Z Young, to take an intercalated degree in physical anthropology.

He gained the expertise that shaped his future during a year's postgraduate training and research on autoimmune kidney disease in Philadelphia. Returning to the Institute of Child Health, he did outstanding research with Professor John Soothill on circulating immune complexes and masterminded the successful bone marrow transplants for blood cancers and severe combined immune deficiency. With Professors Christine Kinnon and Adrian Thrasher, he initiated international collaborations that discovered the genetic basis of several primary immunodeficiency diseases. Because he understood the potential unleashed by the revolutions in molecular genetics since the late 1980s, he was one of the first UK scientists to obtain funding for gene therapy clinical trials. They were successful. He established a method for prenatal diagnosis of severe combined immune deficiency.

He rose to reader in and then professor of immunology, and then dean of the Institute of Child Health. It was clinician led when he took office and was, said Professor Andrew Copp, the current dean, “missing a trick.” He reorganised its structure and recruited young clinical and non-clinical researchers from a wide range of fields. This revved up the quality of the institute's research output and hence its ability to attract substantial research grants.

In 1992, two years after he was appointed, the research assessment exercise gave the institute a score of 3. At the next assessment four years later it scored 5, and later a starred 5, the highest possible. It was widely acknowledged that this was due to Levinsky's recruitment and reorganisation.

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He served on the editorial board of four medical journals and lectured internationally on immunodeficiency diseases and gene therapy. He coauthored over 200 research papers, many of them of landmark importance, and several books. He served on the Royal College of Physicians’ clinical immunology advisory board, the British Paediatric Association’s academic board, the Department of Health's joint committee on vaccination and immunisation, and was medical adviser on vaccines for the British National Formulary. He was president of the European Group for Immunodeficiency Diseases, a group member of the EC Concerted Action in Stem Cell Biology, and a founder member of the European BMT working party for immunodeficiency diseases.

In 2002 he left London and medicine to become a big fish in a smaller pond. As chief executive and vice chancellor of the University of Plymouth he moved its three colleges on to a single site in Plymouth. Moving Seale Hayne Agricultural College met with fierce opposition from a powerful farming lobby including the Prince of Wales and many of the landed aristocracy in the House of Lords, who had learnt estate management there. He received a nocturnal death threat, but magnanimously allowed the perpetrator to finish her course and graduate after she apologised and said it was a prank. Levinsky also aligned the university's research strategy with that of the regional development authority, investing in marine science and technology, biomedicine and health, and creative arts.

He did an MA in modern Russian history to rediscover the experience of being a student. He was an accomplished potter who sold his porcelain at craft galleries and crossed the Atlantic in his 13 metre yacht.

On New Year’s Day he and his wife were walking their dog in blustery weather when a high voltage power cable became detached from its pylon, whipped through the air, and hit him on the head. He died instantly. He is survived by his wife, two daughters, and a son.

Caroline Richmond

Roland Jacob Levinsky, lecturer, reader, then Hugh Greenwood professor of immunology (1972-99); dean, Institute of Child Health (1990-9); vice provost and head of graduate school, University College London (1999-2002); chief executive and vice chancellor, University of Plymouth (2002) (b 16 October 1943; q University College Hospital, London, 1968; BSc, MD, FRCP), d 1 January 2007.
**Pamela June Alexander**

(née Tyson)

Former general practitioner East Yorkshire (b 1924; q Liverpool 1947), d 25 May 2006.

Pamela June Alexander ("June") was involved in early trials of streptomycin for tuberculosis before being appointed lecturer in physiology. After marriage she moved to Yorkshire and was a single handed practitioner for 35 years, delivering her patients' babies at the local maternity unit. After compulsory retirement at 70 she worked part time, working two sessions a week up to her death. She was also a doctor for Victim Support for many years. June co-founded Riding for the Disabled. She built up the Okeden Arabian Stud and was elected president of the Arab Horse Society in her 81st year. Predeceased by her husband, Gordon, in 2004, she leaves three children and four grandchildren.

Rosemary Alexander

**Peter MacDonald Crawford**

Former general practitioner Ballater (b 1925; q Glasgow 1948; LVO, DoObst RCOG), d 3 December 2006.

After house jobs in Glasgow, Peter MacDonald Crawford proceeded to national service in the Royal Army Medical Corps, being stationed in Egypt. He then entered general practice in East Kilbride, starting his own practice there in 1957. In 1977 he gave up his town practice and medical politics as a member of the BMA’s General Medical Services Committee for single handed practice in Ballater, Royal Deeside. Here he was later appointed apothecary to the Queen in Scotland. On his retirement in 1981 he was made an LVO. After retirement he brought many projects to fruition in Upper Deeside and served on the community council. He leaves a wife, Margaret, and three children.

Iain Broom

**Thomas Goronwy (“T G”) Evans**

Former consultant surgeon Singleton and Llanelli Hospitals, Swansea (b 1920; q St Bartholomew’s Hospital, London, 1942; TD, FRCS), died from multiorgan failure on 25 November 2006.

Thomas Goronwy Evans ("Goronowy") left for London at the age of 16 to train at St Bartholomew’s Hospital. He was sent to the Middle East and worked as an army surgeon in Palestine and Egypt during 1946-8. From 1954 to 1990 he worked as a general surgeon in Swansea, retiring completely at the age of 75. He also worked in the Royal Army Medical Corps with the Territorial Army until he retired as lieutenant colonel. Predeceased by his first wife, Joan, in 1970, he leaves a second wife, Mary; three daughters from his first marriage; and eight grandchildren.

Sue Smith

**David Pratt**

Former consultant general and vascular surgeon St James’s University Hospital, Leeds (b 1930; q Leeds 1954; BSc (Anat), FRCS), died from acute coronary insufficiency on 23 May 2006.

After an outstanding undergraduate career culminating in a degree with first class honours and distinctions in surgery and forensic medicine, David Pratt undertook house appointments in Leeds. He did national service in the Royal Navy, serving as a surgeon lieutenant on HMS Eagle during the Suez Crisis. On returning to Leeds he trained in surgery before his appointment to St James’s University Hospital and Chapel Allerton Hospital. In retirement he pursued his fascination for all things French, excelling as a domestic chef and watercolour artist. He leaves a wife, Libby, and three sons.

Roger Peel

**Patricia Mary Qura’n**

(née Gilligan)

Former consultant obstetrician and gynaecologist Amman, Jordan (b 1953; q Queen’s University Belfast, 1978; DRCOG, JBOG), died from complications of ovarian cancer on 4 October 2006. At school Patricia Mary Gilligan was a star performer at the Patricia Mulholland Irish Ballet School. After her marriage to Ziad, whom she met at university, she went to Amman and quickly became fluent in Arabic, much to the surprise of many an unsuspecting motorist. She continued her training in obstetrics and gynaecology through the Jordanian army medical service, subsequently developing a successful practice in Amman. She introduced many young girls to the skills of Irish ballet. Diagnosed with ovarian cancer in 1999, she returned to her clinic as soon as possible. She leaves a husband, Ziad, and three children.

Alex Magee, Bronagh Bunting, Fiona Gibson

**Julian Thomas (“Tomi”) Spenser**


Julian Thomas Spenser ("Tomi") was evacuated to England in 1939 on a Kindertransport and after practising in the United Kingdom moved in 1966 to kibbutz Sasa, Israel. He worked for 30 years with his wife in Arab-Jewish rural clinics. His interest in the problem oriented medical record produced the record used for 80% of the country’s population. Tomi helped found the department of community and family health in Haifa, and the Israeli Balint Society, and chaired the Israel Family Medicine Association. He retired in 1996 and established the programme for the study of the Holocaust and medicine in Haifa and was a hospice director and volunteer consultant. Predeceased by his wife, Sheine, he leaves four children and 15 grandchildren.

Shmuel Reis, Eva Alkon-Katz, Jim Shalom, Jonathan Spenser

**Francis James (“Jim”) Zacharias**

Former consultant physician Clatterbridge Hospital, Wirral (b 1917; q Liverpool 1941; MD, FRCP), died from renal failure on 26 November 2006. Francis James Zacharias ("Jim") served with the Royal Air Force in the Gold Coast and RAF Halton during the later stages of the second world war, being discharged as a squadron leader. His appointment to Clatterbridge Hospital was the start of a distinguished career in the management of hypertension from its earliest days. His work on propranolol and then atenolol built the clinical database that helped to establish the use of β blockade as standard treatment. He loved sailing and the Scottish islands, and was a keen photographer and model railway enthusiast. He leaves a wife, Fran; four children; and nine grandchildren.

John Cunningham
After a cremation in Japan, it’s usual for a bereaved family to move to the “pick up bone room” and use chopsticks to pick out the bones from the movable hearth or cremation tray and put them into an urn. In western Japan they pick up only the bones they regard as important, while in eastern Japan they pick up all of them (Pharos International, 2006(Winter):3-12). [www.cremation.org.uk](http://www.cremation.org.uk).

The protein that facilitates the transfer of “good” HDL to “bad” LDL cholesterol in blood is a curved tunnel, say scientists. Cholesteryl ester transfer protein has been shown to transfer HDL cholesterol to LDL cholesterol. The boomerang shape of the protein allows HDL to bind onto its concave surface. Researchers successfully altered lipid transfer by blocking the tunnel’s mechanism, so drugs that interfere with this activity could theoretically be used to treat patients who have high LDL concentrations (Nature 21 January 2007 doi: 10.1038/nsmb1197).

Adults from a coastal fishing village in Tamil Nadu, India, which was severely affected by the December 2004 tsunami, were interviewed two months after the catastrophe. The prevalence of post-traumatic stress disorder was 12.7%, and the risk was higher in women, in people with no household income, and in those injured during the tsunami. These findings highlight the critical importance of social interventions that focused on income-generating activities and early return to work (American Journal of Public Health 2007;97:99-101 doi: 10.2105/AJPH.2005.071167).

Our minds automatically wander when we’re not sufficiently mentally challenged, according to psychologists. When the brain is not engaged in demanding thinking but is performing monotonous tasks, some cortical regions remain active. This “background” activity produces the images and feelings that constitute “stimulus-independent thought” (daydreaming). More challenging and novel tasks attenuate neuronal activity in the “default” cortical regions, indicating greater focus. Findings of functional brain imaging correlate with subjects’ own reports of daydreaming while performing boring tasks (Science 2007;315:393-5). [www.sciencemag.org](http://www.sciencemag.org).

The Nigerian Institute of Medical Research is the oldest health research facility in Nigeria, and it has just launched the “maiden” edition of its own journal—the Nigerian Journal of Clinical and Biomedical Research (2006;1). It will be published twice a year, and authors are invited to submit suitable material now, for the June 2007 issue. For more information email nijcb@nimr.nig.org.

Encouraging patients with functional dyspepsia to focus specifically on learning flexible coping strategies may help reduce their dyspeptic symptoms, more than offering them empathy and support, say researchers who conducted a randomised controlled trial in Hong Kong (Psychosomatic Medicine 2007;69:81-8 doi: 10.1097/01 psy.0000249734.99065.6f). Participants who received flexible coping psychotherapy rather than conventional counselling reported reduced dyspepsia symptoms comparable to the level in a healthy community sample, and also a reduction in anxiety symptoms.

An urban planning professor reckons there’s a connection between the shape of a city and the shape of our bodies (Science Online 2007;171 www.sciencenews.org/articles/20070112) b0b9.asp). Human-made landscapes described as “urban sprawl,” characterised by a low density of buildings, dependence on vehicles, and a separation of residential and commercial areas, are thought to discourage physical activity, leading to greater obesity and higher blood pressures. But others claim this is a phenomenon of “sorting” and personal preference rather than causation.

From 1950 to the 1970s Japan “enjoyed” the highest age adjusted mortality from stroke in the world. It started to fall dramatically after 1970, when blood pressure management improved—and the average height of Japanese people increased. Formal analysis found that height was significantly inversely correlated with age and with crude stroke mortality in Japanese men. Increased height has been thought to discourage physical activity, leading to greater obesity and higher blood pressures. But other theories claim this is a phenomenon of “sorting” and personal preference rather than causation.

A little-known risk for haemorrhagic strokes in particular seems to be the phenylpropanolamine (PPA) contained in over the counter cold remedies in some countries. A Korean study reports that in Korean people, exposure to this agent significantly increased the risk of a cerebral bleed, especially in women. The trends were dose related and also related to recent use and duration of use (Neurology 2007;68:146-9 doi: 10.1212/01.wnl.0000250351.38999.f2).