abstract of
British Medical Journal

Volume 334, 31 March & 7 April, 2007, Number 7595 & 7596
## FEATURES

- **Human papillomavirus vaccine: life saving treatment or giant experiment?**
  Coombes, R.

- **Duplicate publication: a bitter dispute**
  Gornall, J.

- **Advertising prescription drugs: sweetening the pill**
  Hannah, B.

- **Biobanks: genes on ice**
  Watts, G

## OBSERVATIONS

- **The week in medicine: open all hour**
  Eaton, L.

- **Body politic: the royal colleges must up their game or die**
  Hawkes, N.

- **Life and death: the growing gap**
  Heath, I.

## ANALYSIS

- **Towards sustainable clinical trials**
  Jill, B., Mike Clarke, Janet Darbyshire, Andy Haines, Richard Lilford, Maria Ramos, Ian Roberts, Haleema Shakur, Nandi Siegfried, and Paul Wilkinson

- **Screening programmes for chlamydial infection: when will we ever learn?**
  Low, N.

## RESEARCH

- **Anticoagulation for three versus six months in patients with deep vein thrombosis or pulmonary embolism, or both: randomised trial**

- **Parenting programme for parents of children at risk of developing conduct disorder: cost effectiveness**
  Edwards, R.T., Alan Ceileachair, Tracey Bywater, Dyfrig A Hughes, and Judy Hutchings

- **Commentary: reaching a milestone in diagnosing coeliac disease**
  Graber, M.L., and Atul Kumar

- **Pre-endoscopy serological testing for coeliac disease: evaluation of a clinical decision tool**
  Hopper, A.D, Simon S Cross, David P hurlstone, mark E McAlindon, Alan J Lobo, Marios Hadjivassiliou, Marion ESloan, Simon Dixon, and David S Sanders

- **Parenting intervention in Sure Start services for children at risk of developing conduct disorder: pragmatic randomised controlled trial**
  Judy, H., Frances Gardner, Tracey Bywater, Dave Daley, Chris Whitaker, Karen Jones, Catrin Eames, and Rhiannon T Edwards

- **Operational implications of using 2006 World Health Organization growth standards in nutrition programmes: secondary data analysis**
  Seal, A., and Kerac Marko

## CLINICAL REVIEW

- **Managing the acute psychotic episode**
  Byrne, P

- **Managing the menopause**
  Roberts, H

## PRACTICE

- **Cases in primary care laboratory medicine: Spurious hyperkalaemia**
  Smellie, W.S.A.

- **Pregnancy plus: type 1 diabetes and pregnancy**
  Taylor, R.

A vaccine that promises protection against a common female cancer—what could possibly be controversial about that? Plenty, if the vaccine in question targets a sexually transmitted infection that causes 70% of cervical cancers and, to be most effective, should be given to girls as young as 10 before they become sexually active. The vaccine is Merck’s Gardasil, which protects against four strains of human papillomavirus: types 16 and 18, responsible for 70% of all cervical cancers, and types 6 and 11, which cause 90% of cases of genital warts. Three injections provide protection for at least five years, but the vaccine is expensive at about $360 a shot. The vaccine is undoubtedly set to be a blockbuster product for Merck. Twenty US states are considering bills that would make the immunisation a requirement for school attendance, which could net Merck billions of dollars.


A bitter dispute over the authorship of a twice published medical paper has pitted a 35 year old Korean doctor against one of the most powerful players in the country’s struggle for biotech supremacy. The battle is threatening to disrupt Korea’s efforts to recover scientific credibility in the wake of the recent scandal over Woo-Sok Hwang’s stem cell research. On one side is Jeong Hwan Kim, a Korean doctor now working in Singapore. On the other is Kwang Yul Cha, a fertility specialist with important medical business interests in Korea and the United States and an emerging front runner in the race to inherit the disgraced Hwang’s crown as Korea’s foremost stem cell research pioneer. Dr Kim claims a paper about premature ovarian failure that he originally published in the Korean Journal of Obstetrics and Gynaecology in January 2004 was translated and republished in the American journal *Fertility* …


When, in 2002, the European parliament voted resoundingly against allowing drug companies to provide information about their products directly to patients, public health lobby groups thought that the matter had been firmly dismissed. However, five years on, the resurgence of intense discussions about the “liberalisation of patient information,” as the European Commission refers to it, suggests that parliament’s resolve is set to be challenged again. At issue is a set of proposals for relaxing the current laws that limit drug companies’ communication with patients to the fixed format safety summary contained inside drug packaging. For the commission, which drafts European Union legislation, this debate is a trade-off between nurturing the competitiveness of one of the EU’s biggest industries and respecting the concerns of public health organisations. What worries campaign groups most is that the commission seems to be ignoring them.


Some people call them genome databases; others prefer the term human genetic research databases. But if you want to raise their profile and catch public attention there is only one label that cuts the mustard: biobank. A more colourful word, it encompasses the notion of storage of biological samples for future reference. Along with biological samples—collected principally as a source of DNA—these banks compile detailed personal information about their donors: what they do, how they live, and the illnesses they have. Different banks have different aims. I Some are private, some public; some are large, some small; some try to reflect entire populations, while others concentrate on smaller subgroups. But the underlying intention in most cases is much the same: to reveal how genetic and non-genetic factors interact in determining health and disease, and then to exploit this knowledge.


The government announced proposals last week to open up the provision of GP services, particularly in under-doctored areas, to new providers—including, potentially, supermarkets and retail pharmacies. Health secretary Patricia Hewitt said the move was to ensure all patients would be able to gain access to health services. She wanted to attract a “broad range of providers, from existing entrepreneurial GPs to social enterprises and” —here’s the rub—“corporate independent providers.” Boots the Chemist, which has just opened a GP surgery at a store in Poole, Dorset, welcomed this as “good news.” “We know from the success in Poole, and our experience of offering a chlamydia screening service in London, that accessibility to health services, especially in the evenings and at the weekend, is important,” said Alex Gourley, its director of healthcare. “We will be exploring these new opportunities with the NHS both nationally and locally.” But Hamish Meldrum, chairman of the BMA’s General Practitioners Committee, was less happy: “What we don’t want to see is any attempt to use this announcement as a back door way of privatising the NHS.”

Hawkes, N. Body politic: the royal colleges must up their game or die. *British Medical Journal*, 334(7596), 724.

The debacle over medical training has left the Royal Colleges feeling bruised, but they are in no mood to blame themselves for what went wrong. Their response is one of injured innocence: they feel just as much victims as do the young doctors denied a fair chance of a training post. Your pain is our pain; and whatever went wrong with the Medical Training Application Service (MTAS) had nothing to do with us. Professor Neil Douglas, president of the Royal College of Physicians of Edinburgh and the man chairing the panel trying to clear up the mess, said that he personally was annoyed at the “negative spin” blaming the
colleges for the process. Let’s grant him this much. The colleges are deeply implicated in Modernising Medical Careers (MMC), but may perhaps escape a guilty verdict over MTAS. Since Professor Douglas hails from Edinburgh, we might opt for the excellent Scottish.


A teacher once told me that it was the experience of enduring the dying days of communism in Poland that enabled him to recognise the obsession with regulation and control within the New Labour state education system. Perhaps similar experiences explain the insights of another Polish exile, Zygmunt Bauman, the emeritus professor of sociology at Leeds, who has described “a growing gap, indeed a contradiction, between values promoted in public discussion and those whose cause is served by political practice.” It is not difficult to recognise this description within New Labour’s version of the National Health Service. Public discussion is directed towards the worthy aspiration of improving services for patients. Patients’ views are given a central place within official rhetoric. Glossy NHS publications are now routinely illustrated by pictures of contented and attractive patients being cared for in optimal surroundings. Professionals are told to provide both “choice” and “patient centred care.”

ANALYSIS

(Since these articles has no abstract, we just provided an extract of the first 150 words of the full text and any section headings)


Greenhouse gases are changing the global climate, with serious implications for health and ecosystems. All sectors of the economy, including the health sector, must act to reduce greenhouse gas emissions. High income countries need to cut emissions by about 90% by 2030 to limit the global average temperature to 2°C, and thus reduce the risk of the most serious consequences. The Sustainable Trials Study Group was convened by the London School of Hygiene and Tropical Medicine to find ways of reducing greenhouse gas emissions from clinical trials. This international health research institution has an extensive research programme on the links between environment and health. A sustainability group was established to reduce the institution’s carbon footprint, and this study is a product of its work.


The notion that a programme of widespread screening for chlamydial infection and reduced morbidity of the female reproductive tract is commonly cited as fact.2 3 4 Unfortunately, this assertion and similar claims about screening in the United States5 6 and Canada6 8 are not supported by rigorous research or practice. Here, I will show how misinterpretation of what comprises a screening programme led to uncritical acceptance of the effectiveness of chlamydia screening, and the funding of a National Chlamydia Screening Programme in England,3 before the benefits and harms were evaluated.

RESEARCH


In 1960 Barritt and Jordan established that anticoagulation reduced the risk of death and of recurrent embolism in patients with pulmonary embolism, a conclusion subsequently supported by retrospective studies from Oxford and the United States. Treatment regimens now consist of heparin for four to five days, with anticoagulation maintained thereafter by warfarin. In the 1970s and 1980s three relatively small randomised trials suggested that there was no benefit in anticoagulation for more than three to six weeks but practice in United Kingdom and abroad continued to vary widely. In 1992, the British Thoracic Society published the results of a large multicentre prospective study, which indicated that because the outcome with three months’ anticoagulation was significantly better than with one month, three months’ anticoagulation should be given to patients with pulmonary venous thromboembolism (first episode or no episode for the previous three years). This recommendation has not been universally accepted, with authoritative sources in the UK, North America, and Europe continuing to recommend six months or more. To obtain further evidence, the British Thoracic Society designed and conducted another multicentre study to compare the outcomes of two durations of anticoagulation, three and six months, with warfarin after initial heparin therapy. For those centres not already routinely using low molecular weight heparin, an expanded design was used to compare low molecular weight heparin with unfractionated heparin in terms of outcome during treatment outcome after the end of anticoagulation, and duration of inpatient stay. Too few patients (n=22) were entered into this randomisation for meaningful comparisons of these outcomes and so we used their results solely in the comparisons of three months versus six months of anticoagulation.


Conduct disorder is estimated to affect 5–10% of children aged 5–15 years in the United Kingdom and the United States. For those children with early onset in preschool years, conduct disorder often persists into adulthood and predicts poor employment prospects, marriage breakdown, and self harming or antisocial criminal behaviour. The economic implications of
severe behavioural problems in childhood are serious. The costs of publicly resourced services for those aged 28 with conduct disorder in childhood were estimated to be times higher (£70 019; [Euro sign]104 416, $137 450) than for those with no behavioural problems (£7423; [Euro sign]11 069, $14 571). Parenting is a key determinant in child behaviour. Parents who encourage prosocial behaviour have children with fewer behaviour problems. Parenting training programmes are effective in helping families with children at risk of developing conduct disorders. The Incredible Years basic parenting programme is described in more detail elsewhere and in the accompanying paper. The programme strengthens parenting competencies and reduces the risk of developing conduct problems. It is delivered by two trained leaders in weekly sessions. The recent National Institute for Health and Clinical Excellence (NICE) appraisal on parent training programmes for conduct disorders highlighted the dearth of evidence on cost effectiveness. In a review of 1600 papers, Romeo et al found only two that qualified as true economic evaluations of treatments for behavioural disorders. Muntz et al found that an intervention with parents of children with conduct disorder could be cost effective under conditions of resource trade off. We carried out a full cost effectiveness analysis, alongside a pragmatic randomised controlled trial, of the Incredible Years basic parenting programme in the UK. We present the programme costs and consequences for public sector resources and child behaviour outcomes.


Clinical prediction rules for diagnosis seek to optimise the sensitivity and specificity of our diagnostic approach to a given problem. In this issue of the BMJ, Hopper and colleagues report a rare accomplishment in this regard—a decision rule that achieved 100% sensitivity in disease detection, in this case for coeliac disease. The rule is simple—a positive serological test for IgA antibody to tissue transglutaminase combined with being at “high risk” (having weight loss, diarrhoea, or anaemia). The rule identified every patient with the disease in a cohort of 2000 patients, all of whom underwent intestinal biopsy as the gold standard and the final diagnostic step. This is a welcome advance. As the authors emphasise, coeliac disease may affect up to one in a 100 people, only one case in seven is ever diagnosed, and an appreciable diagnostic delay of many years often occurs.


Adults with the classic (typical) form of celiac disease usually present with diarrhea, weight loss, or symptoms that suggest malabsorption or anaemia. Patients can also have the silent or atypical form, with non-specific abdominal pain, oesophageal reflux, osteoporosis, cryptogenic hypertransaminasaemia, insulin dependent diabetes mellitus, or neurological symptoms. A recent meta-analysis indicated that the ratio of known to undiagnosed cases of celiac disease was 1:7. The median delay in diagnosed ranges from 9 to 11 years. Serological markers are a cheap non-invasive method to identify patients with celiac disease. Th positive and negative predictive value of combining the measurement…


Antisocial behaviour in young people is a growing problem. In the United Kingdom and the United States about 5–10% of children aged 5–15 present with clinically important conduct disorders. Higher rates occur in single parent families and families with frequent changes of parental figures and parental substance misuse, psychopathology, marital problems, and poor parenting skills. Up to 20% of children in disadvantaged areas have conduct disorders. Early onset behavioural problems such as aggression and non-compliance are the best predictors of antisocial and criminal behaviour in adolescence and adulthood. Untreated, up to 40% of children with early difficulties develop subsequent conduct disorder, including drug misuse and criminal and violent behaviour. Early behavioural difficulties that predict long term problems are easily identifiable, and effective interventions prevent progression into more severe difficulties. There are severe financial costs if conduct disorder is not prevented. Use of health, social, education, and legal services is 10 times higher for this population, mostly borne by publicly funded services, especially in areas of social exclusion. Parenting behaviour contributes to the establishment of conduct disorder and many children learn, develop, or establish problem behaviours because parents lack, or inconsistently use, key parenting skills. When ineffective parenting is the problem, cognitive behaviourally based parenting programmes can provide an effective solution but are more effective with younger children. When problems are less well established parents can more easily influence their children’s behaviour. One UK government strategy is the Sure Start early preventive parenting support for families of preschool children living in identified high risk, disadvantaged areas. Since its launch in 2001, £3100m (€uro sign)4500m, $6000m) has been invested in the scheme. This funding was provided without direction from government about which services should be delivered. As a result, widely varying services were provided, many lacking evidence of effectiveness from randomised trials. The initial £20m (€uro sign)30m, $39m) non-randomised, area based evaluation of the first three years in England found no significant effect in preventing or reducing conduct disorder.


Important differences exist in the weight for height cut-offs used for defining acute malnutrition obtained from the WHO standards and NHCS reference data. These vary according to a child’s height and according to whether z score or percentage of
the median cut-offs are used. If applied and used according to
current practice in nutrition programmes, the WHO standards
will result in a higher measured prevalence of severe acute
malnutrition during surveys but, paradoxically, a decrease in
the admission of children to emergency feeding programmes
and earlier discharge of recovering patients. The expected
impact on case fatality rates of applying the new standards in
conjunction with current diagnostic criteria is unknown…

CLINICAL REVIEW

(Since these articles has no abstract, we just provided an
extract of the first 150 words of the full text and any section
headings)

Byrne, P. (2007). Managing the acute psychotic episode. British
Medical Journal, 334(7595), 686-692.

People with a first or recurrent psychotic episode tend to present
late for medical attention, and many do not present at all.
Presentation is often initiated by others, not by patients
themselves. Psychosis can also become apparent during a manic
presentation, when patients act on their delusions in a public
forum, or when they have the complications of substance
misuse. Patients who experience intolerable symptoms
(distressing delusions or voices; box 1) often seek medical help.
In emergency settings, family members’ concerns contrast with
the patient’s apparent indifference. The highest risk of suicide
in people with schizophrenia occurs during the first five years
of illness (“the critical period”), and interventions are most
fruitful during this time. Importantly, patients experiencing their
first episode should quickly be given competent assessments
and access to appropriate services.

Journal, 334(7596), 721-723.

The transition into the menopause usually begins with
elongation of cycle length, the term postmenopausal being used
after one year with no periods. Most women experience
menopause between 40 and 58 years of age.1 No menopausal
symptom is universal. In Western society the commonest
symptoms are hot flushes, night sweats, vaginal dryness, and
sleep disturbance. Many women manage the menopause by
themselves, with only about 10% seeking help from healthcare
providers. Hormone replacement therapy is the most effective
treatment for symptoms and although opinions are still polarised
advice on its use has changed after the women’s health initiative
studies.

PRACTICE

(Since these articles has no abstract, we just provided an
extract of the first 150 words of the full text and any section
headings)

medicine: Spurious hyperkalaemia. British Medical
Journal, 334(7595), 693-695.

A doctor responsible for clinical governance in a primary care
practice contacted her local biochemistry laboratory to ask
whether the laboratory had been experiencing problems with
potassium measurement. Her practice partners had noticed
several unexpectedly raised potassium results and one patient
had recently been contacted urgently at 9 pm to be taken to
hospital because a potassium result of 7.2 mmol/l had been
telephoned to the out of hours service. This 72 year old man
was being treated with lisinopril for hypertension and his
previous potassium results had been in the region of 4.5–5.0
mmol/l. A repeat measurement in casualty had been 4.8 mmol/l
and he had returned home in some distress. The laboratory
found that the average serum potassium result for that practice
was 0.5 mmol/l above the laboratory’s average for samples from
general practice and that average results for the month were 0.3
mmol/l higher than in the previous three months. The practice
was located 28 miles from the laboratory and was the first to be
visited by the van on a circular collection run. During a recent
winter cold spell, temperatures during the early evening, when
the samples were being collected, had fallen to -3°C. Samples
were held in a metal box in the van. An insulated box was
introduced to transport specimens, and the average for the
practice fell to 0.1 mmol/l above the laboratory’s average.

pregnancy. British Medical Journal, 334(7596), 721-
723.

Pregnancy in women with type 1 diabetes remains a challenge
for the patient and healthcare team alike. The scenario box on
this page highlights some of the problems in achieving
satisfactory pregnancy outcomes in women with diabetes. We
discuss in the article the main areas of concern. Julie rang the
diabetes specialist nurse having confirmed pregnancy with a
home test kit. Her period was two weeks late. Although she
recalled being advised about the need for prepregnancy care,
she thought her glucose control was good enough (HbA1c
concentration 7.9% at last check) and she had been taking a 400
µg tablet of folic acid daily. She had developed type 1 diabetes
16 years before (at age 8) and at her last annual review had no
retinopathy or microalbuminuria. She controlled her diabetes
with bedtime insulin glargine, plus insulin lispro (a rapid acting
analogue) before meals.)