abstract of
the Lancet

Volume 369, Number 9557 & 9558 - January 20 & 27, 2007
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## VIEWPOINT

**HIV self-testing: a time to revise current policy**
Frith L.
WORLD REPORT
(Since these articles have no abstract, we just provided an extract of the first 100 words of the full text and any section headings)

Six medics remain sentenced to death in Libya, accused of deliberately infecting hundreds of children with HIV in a city hospital. Libya’s leader, Muammar Gaddafi, is attempting to trade their lives for one of the country’s agents, currently serving life in prison in the UK. Katy Duke reports. Five Bulgarian nurses and a Palestinian doctor were controversially convicted late last year of deliberately infecting hundreds of children with the HIV virus...

Many countries in Latin America and the Caribbean have too many specialists and too few primary care providers and community health workers. These countries need to overhaul their training and payment practices to address this imbalance, say human resources experts. Barbara Fraser reports. Until recently, Mauro Reyes’ hospital, a jumble of pale blue buildings on the north side of Lima, was a neighborhood health centre. Then the government added some wards and renamed the facility San Juan de Lurigancho Hospital...

The number of cancer deaths has declined in the USA for the second consecutive year, according to a new study. The 2-year trend, researchers say, suggests the decline reported last year, the first in 70 years, was real and not a statistical “fluke”. Michael McCarthy reports. US cancer deaths have fallen for the second year in a row, according to a report released on Jan 17 by the American Cancer Society (ACS)...

Many women choose to deliver with traditional birth attendants in Guatemala—a fact that can’t be ignored, argue local public-health officials. They hope a new, culturally sensitive approach to training TBAs will help improve their quality of care and save lives. Jill Reploge reports. Two dozen Mayan traditional midwives, or comadronas, watch intently as their colleagues demonstrate manual removal of a retained placenta. Febe Guarcas, an experienced comadrona from the local Vida Association of traditional midwives, leads the training...

Following an outbreak of severe acute respiratory syndrome (SARS) in a Toronto hospital in March, 2003, which killed 44 people, the Ontario government commissioned an investigation. Paul Webster reviews the findings of the third and final report from the SARS Commission. The final report of a government-commissioned investigation into the 2003 outbreak of SARS in Toronto that killed 44 blames hospital downswing...

ARTICLES
Large numbers of stroke patients arrive at hospital at a very early stage, and effective treatments for the acute phase of the disease are available. However, evidence that patients with acute stroke benefit from stroke-unit care is scarce. Our aim was to determine whether admission to a stroke unit, rather than a conventional ward, affected the outcome of patients with acute stroke. We did an observational follow-up study of 11,757 patients hospitalized within 48 h of the onset of symptoms either in a stroke unit (n=4936) or in a conventional ward (6636). Patients were identified retrospectively from discharge records from 260 Italian hospitals. The primary outcome was mortality or disability (Rankin score greater than two), assessed prospectively by independent, masked assessors 2 years after admission. Analyses were adjusted for patient characteristics and clustered at the hospital level. Overall, 1576 patients died in hospital; 2169 died during the follow-up period. 347 patients were lost to follow-up. Compared with conventional-ward care, stroke-unit care was associated with a reduced probability of death or being disabled at the end of follow-up (odds ratio 0.81, 95% CI 0.72–0.91; p=0.0001). The potential benefit was significant across all age ranges and clinical characteristics, except for unconsciousness. No specific elements of setting, organisation, or process of care were associated with outcome.

Although the use of magnetic resonance imaging (MRI) for the diagnosis of acute stroke is increasing, this method has not proved more effective than computed tomography (CT) in the emergency setting. We aimed to prospectively compare CT and MRI for emergency diagnosis of acute stroke. We did a single-centre, prospective, blind comparison of non-contrast CT and MRI (with diffusion-weighted and susceptibility weighted images) in a consecutive series of patients referred for emergency assessment of suspected acute stroke. Scans were independently interpreted by four experts, who were unaware of clinical information, MRI-CT pairings, and follow-up imaging. 356 patients, 217 of whom had a final clinical diagnosis of acute stroke, were assessed. MRI detected acute stroke (ischaemic or haemorrhagic), acute ischaemic stroke, and chronic haemorrhage more frequently than did CT (p<0.0001, for all comparisons). MRI was similar to CT for the detection of acute intracranial haemorrhage. MRI detected acute ischaemic stroke in 164 of 356 patients (46%; 95% CI 41–51%), compared with CT in 35 of 356 patients (10%; 7–14%). In the subset of patients scanned within 3 h of symptom onset, MRI detected acute ischaemic stroke in 41 of 90 patients (46%; 35–56%); CT in 6 of 90 (7%; 3–14%). Relative to the final clinical diagnosis, MRI had a sensitivity of 83% (181 of 217; 78–88%) and CT of 26% (56 of 217; 20–32%) for the diagnosis of any acute stroke. MRI is better than CT for detection of acute ischaemia, and can detect acute and chronic haemorrhage; therefore it should be the preferred test for accurate diagnosis of patients with suspected acute stroke.

Low folate and raised homocysteine concentrations in blood are associated with poor cognitive performance in the general population. As part of the FACIT trial to assess the effect of folic acid on markers of atherosclerosis in men and women aged 50–70 years with raised plasma total homocysteine and normal serum vitamin B12 at screening, we report here the findings for the secondary endpoint: the effect of folic acid supplementation on cognitive performance.Our randomised, double blind, placebo controlled study took place between November, 1999, and December, 2004, in the Netherlands. We randomly assigned 818 participants 800 g daily oral folic acid or placebo for 3 years. The effect on cognitive performance was measured as the difference between the two groups in the 3-year change in performance for memory, sensorimotor speed, complex speed, information processing speed, and word fluency. Analysis was by intention-to-treat. Serum folate concentrations increased by 576% (95% CI 539 to 614) and plasma total homocysteine concentrations decreased by 26% (24 to 28) in participants taking folic acid compared with those taking placebo. The 3-year change in memory (difference in Z scores 0.132, 95% CI 0.032 to 0.233), information processing speed (0.016 to 0.158) and sensorimotor speed (0.064, -0.001 to 0.129) were significantly better in the folic acid group than in the placebo group.Folic acid supplementation for 3 years significantly improved domains of cognitive function that tend to decline with age.

The effect of different classes of antihypertensive drugs on incident diabetes mellitus is controversial because traditional meta-analyses are hindered by heterogeneity across trials and the absence of trials comparing angiotensin-converting-enzyme (ACE) inhibitors with angiotensin-receptor blockers (ARB). We therefore undertook a network meta-analysis, which accounts for both direct and indirect comparisons to assess the effects of antihypertensive agents on incident diabetes. We undertook a systematic review up to Sept 15, 2006, and identified 48 randomised groups of 22 clinical trials with 143153 participants who did not have diabetes at randomisation and so were eligible for inclusion in our analysis. 17 trials enrolled patients with hypertension, three enrolled high-risk patients, and one enrolled those with heart failure. The main outcome was the proportion of patients who developed diabetes. Initial drug therapy used in the trials (and the number of patients with diabetes of the total number at risk) included: an ARB (1189 of 147185, or 8·3%), ACE inhibitor (1618 of 227441, or 7·05%), calcium-channel blocker (CCB, 2791 of 387607, or 7·23%), placebo (1686 of 247767, or 6·81%), á blocker (2705 of 357745, or 7·57%), or diuretic (998 of 187699, or 5·34%). With an initial diuretic as the standard of comparison (eight groups), the degree of incoherence (a measure of how closely the entire network fits together) was small (i=0·000017, eight degrees of freedom). The odds ratios were: ARB (five groups) 0·57 (95% CI 0·46–0·72, p=0·0001); ACE inhibitor (eight groups) 0·67 (0·56–0·80, p<0·0001); CCB (nine groups): 0·75 (0·62–0·90, p=0·0002); placebo (nine groups) 0·77 (0·63–0·94, p = 0·009); á blocker (nine groups) 0·90 (0·75–1·09, p=0·30). These estimates changed little in many sensitivity analyses.


We aimed to validate two similar existing prognostic scores for early risk of stroke after transient ischaemic attack (TIA) and to derive and validate a unified score optimised for prediction of 2-day stroke risk to inform emergency management. The California and ABCD2 scores were validated in four independent groups of patients (n=2893) diagnosed with TIA in emergency departments and clinics in defined populations in the USA and UK. Prognostic value was quantified with c statistics. The two groups used to derive the original scores (n=1916) were used to derive a new unified score based on logistic regression. The two existing scores predicted the risk of stroke similarly in each of the four validation cohorts, for stroke risks at 2 days, 7 days, and 90 days (c statistics 0·60–0·81). In both derivation groups, c statistics were improved for a unified score based on five factors (age ≥60 years [1 point]; blood pressure ≥140/90 mmHg [1]; clinical features: unilateral weakness [2], speech impairment without weakness [1]; duration ≥60 min [2] or 10–59 min [1]; and diabetes [1]). This score (ABC2D2, validated with a cohort of 833; overall, 1012 (21%) of patients were classified as high risk (score 6–7, 8–11 2-day risk), 2169 (45%) as moderate risk (score 4–5, 4–1%), and 1628 (34%) as low risk (score 0–3, 1-0%). Existing prognostic scores for stroke risk after TIA validate well on multiple independent cohorts, but the unified ABC2D2 score is likely to be most predictive. Patients at high risk need immediate evaluation to optimize stroke prevention.


The aim of the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) was to assess the safety and efficacy of intravenous alteplase as thrombolytic therapy within the first 3 h of onset of acute ischaemic stroke. Under European Union regulations, SITS-MOST was required to assess the safety profile of alteplase in clinical practice by comparison with results in randomised controlled trials. 6483 patients were recruited from 285 centres (50% with little previous experience in stroke thrombolysis) in 14 countries between 2002 and 2006 for this prospective, open, monitored, observational study. Primary outcomes were symptomatic (a deterioration in National Institutes of Health stroke scale score of ≥4) intracerebral haemorrhage type 2 within 24 h and mortality at 3 months. We compared mortality, the proportion of patients with symptomatic intracerebral haemorrhage as per the Cochrane definition, and functional outcome at 3 months with relevant pooled results from randomised controlled trials. Baseline characteristics of patients in SITS-MOST were much more similar to those as the same in the pooled randomised controlled trials. At 24 h, the proportion of patients with symptomatic intracerebral haemorrhage (per the SITS-MOST protocol) was 1·7% (107/6444; 95% CI 1·4–2·0); at 7 days, the proportion with the same condition as per the Cochrane definition was 7·3% (468/6438; 6·7–7·9) compared with 8·6% (40/4653; 6·3–11·6) in the pooled randomised controlled trials. The mortality rate at 3 months in SITS-MOST was 11·3% (701/6218; 10·5–12·1) compared with 17·3% (83/479; 14·1–21·1) in the pooled randomised controlled trials. These data confirm that intravenous alteplase is safe and effective in routine clinical use when used within 3 h of stroke onset, even by centres with little previous experience of thrombolytic therapy for acute stroke. The findings should encourage wider use of thrombolytic therapy for suitable patients treated in stroke centres.


In 2002, the UN General Assembly Special Session on Children adopted a goal to reduce deaths owing to measles by half by the end of 2005, compared with 1999 estimates. We describe efforts and progress made towards this goal. We assessed trends in immunization against measles on the basis of national implementation of the WHO/UNICEF comprehensive strategy for measles mortality reduction, and the provision of a second opportunity for measles immunization. We used a natural history model to evaluate trends in mortality due to measles. Between 1999 and 2005, according to our model mortality owing to measles was reduced by 60%, from an estimated 873 000 deaths (uncertainty bounds 634 000–714 000) in 1999 to 345 000 deaths (247 000–458 000) in 2005. The largest percentage reduction in estimated measles mortality during this period was in the western Pacific region (81%), followed by Africa (75%) and the eastern Mediterranean region (62%). Africa achieved the largest total mortality reduction, contributing 72% of the global reduction in measles mortality. Nearly 7·5 million deaths from measles were prevented through immunization between 1999 and 2005, with supplemental immunization activities and improved routine immunization accounting for 2·3 million of these prevented deaths. The achievement of the 2005 global measles mortality reduction goal is evidence of what can be accomplished when child survival is high, and childhood mortality when safe, cost-effective, and affordable interventions are backed by country-level political commitment and an effective international partnership.

SEMINARS


Subarachnoid haemorrhage accounts for only 5% of strokes, but occurs at a fairly young age. Sudden headache is the cardinal feature, but patients might not report the mode of onset. CT brain scanning is normal in most patients with sudden headache, but to exclude subarachnoid haemorrhage or other serious disorders, a carefully planned lumbar puncture is also needed. Aneurysms are the cause of subarachnoid haemorrhage in 85% of cases. The case fatality of subarachnoid haemorrhage is 50%; one in eight patients with subarachnoid haemorrhage dies outside hospital. Rebleeding is the most imminent danger; a first aim is therefore occlusion of the aneurysm. Endovascular obliteration by means of platinum spirals (coiling) is the preferred mode of treatment, but some patients require a direct neurosurgical approach (clipping). Another complication is delayed cerebral ischaemia; the risk is reduced with oral nimodipine and probably by
maintaining circulatory volume. Hydrocephalus might cause gradual obtundation in the first few hours or days; it can be treated by lumbar puncture or ventricular drainage, dependent on the site of obstruction.


Huntington’s disease is an autosomal-dominant, progressive neurodegenerative disorder with a distinct phenotype, including chorea and dystonia, incoordination, cognitive decline, and behavioural difficulties. Typically, onset of symptoms is in middle-age after affected individuals have had children, but the disorder can manifest at any time between infancy and senescence. The mutant protein in Huntington’s disease—huntingtin—results from an expanded CAG repeat leading to a polyglutamine strand of variable length at the N-terminus. Evidence suggests that this tail confers a toxic gain of function. The precise pathophysiological mechanisms of Huntington’s disease are poorly understood, but research in transgenic animal models of the disorder is providing insight into causative factors and potential treatments.

REVIEW


This article reviews the recommended management of patients presenting to accident and emergency departments with acute ischaemic stroke, and focuses on thrombolysis. The review includes initial management, recommended clinical, laboratory, and radiographic examinations. Appropriate general medical care, consisting of monitoring of oxygenation, fever, blood pressure, and blood glucose concentrations are examined. Criteria for thrombolysis with intravenous recombinant tissue plasminogen activator (rt-PA) are discussed. Complications of rt-PA therapy, such as haemorrhagic transformation and angio-oedema, are reviewed. An approach to management of rt-PA complications is outlined. Only a small percentage of acute ischaemic stroke patients meet criteria for rt-PA; therefore, alternative acute treatment strategies are also discussed. Acute medical and neurological complications in stroke patients are analysed, along with recommendations for treatment.


Treatments for acute ischaemic stroke continue to evolve. Experimental approaches to restore cerebral perfusion include techniques to augment recanalising therapies, including combination of antplatelet agents with intravenous thrombolysis, bridging therapy of combining intravenous with intra-arterial thrombolysis, and trials of new thrombolytic agents. Trials with MRI selection criteria are underway to expand the window of opportunity for thrombolysis. Sonothrombolysis and novel endovascular mechanical devices to retrieve or dissolve acute cerebral occlusions are being tested. Approaches to improve cerebral perfusion with other devices and induced hypertension are also being considered. Although numerous neuroprotective agents have not shown benefit, trials of hypothermia, magnesium, caffeine, high doses of statins, and albumin are continuing. The findings of these randomised trials are anticipated to allow improved treatment of patients with acute stroke.

SERIES


This paper is the third in the Child Development Series. The first paper showed that more than 200 million children under 5 years of age in developing countries do not reach their developmental potential. The second paper identified four well-documented risks: stunting, iodine deficiency, iron deficiency anaemia, and inadequate cognitive stimulation, plus four potential risks based on epidemiological evidence: maternal depression, violence exposure, environmental contamination, and malaria. This paper assesses strategies to promote child development and to prevent or ameliorate the loss of developmental potential. The most effective early child development programmes provide direct learning experiences to children and families, are targeted toward younger and disadvantaged children, are of longer duration, high quality, and high intensity, and are integrated with family support, health, nutrition, or educational systems and services. Despite convincing evidence, programme coverage is low. To achieve the Millennium Development Goals of reducing poverty and ensuring primary school completion for both girls and boys, governments and civil society should consider expanding high quality, cost-effective early child development programmes.

VIEW POINT


A review of government policy about self-testing for HIV is needed in the UK. Since 1992 to sell or otherwise provide a member of the public with any form of self-test for HIV has been illegal in that country. This policy, which was developed at a time when HIV was regarded as different from other diseases (ie, exceptionalism) in public health measures, is now outdated. New technologies that enable rapid and accurate HIV testing are now becoming available. To increase the uptake of HIV testing and truly respect patient autonomy we need to challenge this outmoded practice and remove the legal obstacles to self-testing for HIV. On Nov 3, 2005, the US Food and Drug Administration’s (FDA) blood products advisory committee met to debate the issues raised by a self-test for HIV based on oral fluids, after its manufacturers declared their intention to seek over-the-counter status. The committee’s meeting is the first stage in a long approval process, but it suggests that self-testing for HIV is being considered in the USA. Most of the experts who spoke at the meeting argued that the introduction of self-testing for HIV was long overdue.

The Lancet — Vol 369 (9557 & 9558) January 5