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More than 60,000 people died when a 7.9 magnitude earthquake struck China’s Sichuan province. In the aftermath of rubble, dust, and carnage, health workers are struggling to treat thousands of injured survivors while trying to prevent outbreaks of disease. Jonathan Watts reports. The injured Sichuanese farmer was in agony. Fleeing the earthquake zone in an army speedboat, he grimaced each time the vessel bumped off the surface of the Min river. At the back of his skull, blood had started to congeal on a wide, deep wound. Despite the pain, the man kept silent throughout the 1-hour journey, until the boat reached a military camp near Zipingpu dam, where he screamed as he—and every other passenger—was sprayed with disinfectant. He collapsed and had to be carried to an ambulance, which sped him to the nearest hospital. Scenes like this have become commonplace in Sichuan since the 7.9 magnitude earthquake struck this southwestern Chinese province on the afternoon of May 12, 2008. Slopes were sliced off mountains, slipping down on to villages, towns, and factories in the valleys. More than 60,000 people died as 5 million homes were buried or shaken to the ground, along with factories, hospitals, and schools.


A coalition of dedicated health-care providers is bringing medical care to homeless people in the USA in the nooks and crannies where they live and, when necessary, helping them to navigate an almost impenetrable bureaucracy in order to obtain care. Norra MacReady reports. In the heart of downtown Los Angeles lies a 50-block enclave of cheap hotels, parking lots, liquor stores, and dumpsters. This pocket of the city also happens to be the centre of the largest population of homeless people in the USA. Welcome to Skid Row. It is hard to know exactly how many people in the USA are homeless. Most find some kind of housing after a few months on the street, while others, the really hard core, try to avoid attention. One of the best estimates comes from a 2007 study conducted by the National Law Center on Homelessness and Poverty, which found that approximately 3.5 million people experience an episode of homelessness in a given year. Of those, about 73,000 reside in Los Angeles, nearly double the number in the runner-up city, New York, which has a homeless population of about 39,000. The average duration of an episode of homelessness is 8 months.


Unlike any other natural disaster before it, the devastation caused by Cyclone Nargis has been worsened by the military government’s hesitancy to let relief operations into the country. 2 weeks on, aid agencies warn that a large-scale health crisis is looming. Justin McCurry reports. More than 2 weeks after Cyclone Nargis devastated huge swaths of Burma, aid workers say as many as 2.4 million people left homeless by the disaster face disease and starvation as international aid agencies struggle to get vital medical supplies, clean water, and food into the country. After refusing to accept large-scale aid from outside, Burma’s military regime said on Monday that it would allow fellow members of the Association of East Asian Nations [ASEAN] to oversee the distribution of foreign relief. The UN secretary general, Ban Ki-moon, was also preparing to fly to the capital Rangoon to chair a donor conference at the weekend. As the country began 3 days of mourning for victims of the May 2–3 cyclone, the UN said that only 500,000 of the estimated 2.4 million survivors had received international assistance.


The availability of home DNA test kits that promise to reveal disease risks has mushroomed in recent years. But concern about the predictive value of such tests and their use outside of clinical settings have led to their ban in some European countries. Priya Shetty investigates. In 2006, Steve Cross was on a mission. The then curator of the UK Wellcome Trust’s permanent collection wanted to investigate how much personal genetic information he could find out about himself armed with just a credit card. Cross was able to embark on this quest because of the plethora of home DNA testing kits that have mushroomed worldwide in the past few years, promising to reveal a variety of disease risks from stroke to obesity. Many of these “lifestyle” tests are unregulated, however, and several scientists say too little is known about the risks for complex diseases to offer meaningful information. The manufacturers counter that people have a right to know their own genetic information, however patchy that knowledge might be at this moment. Concern that the tests might provoke needless health concerns if done outside a clinical genetics setting have led to a ban on private tests in some European countries, and there is a simmering debate worldwide about whether the tests should be sold. A key factor in making these tests possible is the scientific behemoth of the Human Genome Project. The completion of the sequence in 2003 had major implications for finding disease genes. Many of the gene mutations behind single-gene disorders such as Huntington’s disease had already been pinpointed, but the genes that influenced more common complex diseases were largely a mystery.
ARTICLES


Early intensive insulin therapy in patients with newly diagnosed type 2 diabetes might improve 6-cell function and result in extended glycemic remissions. We did a multicentre, randomised trial to compare the effects of transient intensive insulin therapy (continuous subcutaneous insulin infusion [CSII] or multiple daily insulin injections [MDI]) with oral hypoglycaemic agents on 6-cell function and diabetes remission rate. 382 patients, aged 25–70 years, were enrolled from nine centres in China between September, 2004, and October, 2006. The patients, with fasting plasma glucose of 7·0–16·7 mmol/L, were randomly assigned to therapy with insulin (CSII or MDI) or oral hypoglycaemic agents for initial rapid correction of hyperglycaemia. Treatment was stopped after normoglycaemia was maintained for 2 weeks. Patients were then followed-up on diet and exercise alone. Intravenous glucose tolerance tests were done and blood glucose, insulin, and proinsulin were measured before and after therapy withdrawal and at 1-year follow-up. Primary endpoint was time of glycemic remission and remission rate at 1 year after short-term intensive therapy. Analysis was per protocol.


Oxidative stress and inflammation are involved in the pathophysiology of atherosclerosis. Our aim was to assess the effects of the antioxidant succinobucol (AGI-1067) on cardiovascular outcomes in patients with recent acute coronary syndromes already managed with conventional treatments. After an acute coronary syndrome occurring 14–365 days before recruitment, 6144 patients were randomly assigned with a computer-generated randomisation list, stratified by study site, to receive succinobucol (n=3078) or placebo (n=3066) in addition to standard of care. Enrolment began in July, 2003; this event-driven trial was stopped in August, 2006, after the prespecified number of primary outcome events had occurred. The composite primary endpoint was time to first occurrence of cardiovascular death, resuscitated cardiac arrest, myocardial infarction, stroke, unstable angina, or coronary revascularisation. Efficacy analyses were done by intention to treat. All randomised patients were included in the efficacy analyses. Succinobucol had no effect on the primary endpoint (530 events in succinobucol group vs 529 in placebo group; hazard ratio 1·00, 95% CI 0·89–1·13, p=0·96). The composite secondary endpoint of cardiovascular death, cardiac arrest, myocardial infarction, or stroke occurred in fewer patients in the succinobucol group than in the placebo group (207 vs 252 events; 0·81, 0·68–0·98, p=0·029). The tertiary endpoint of new-onset diabetes developed in fewer patients without diabetes at baseline in the succinobucol group than in such patients in the placebo group (30 of 1923 vs 82 of 1950 patients; 0·37, 0·24–0·56, p<0·0001). New-onset atrial fibrillation occurred more often in the succinobucol group than in the placebo group (107 of 2818 vs 55 of 2787 patients; 1·87, 1·67–2·09, p=0·0002). Although the number of patients who reported any treatment emergent adverse event was much the same in the two groups, more patients in the succinobucol group than in the placebo group reported bleeding episodes or anaemia (32 vs 18 and 37 vs ten, respectively) as serious adverse events. Relative to treatment with placebo, succinobucol increased LDL cholesterol and systolic blood pressure, and decreased HDL cholesterol and glycated haemoglobin (p≤0·0001 for all). Although succinobucol had no effect on the primary endpoint, changes in the rates of other clinical outcomes—both beneficial and harmful—will need to be further assessed before succinobucol is used in patients with atherosclerosis or as an antidiabetic agent.


Delivery of high-quality, evidence-based health care to deprived sectors of the community is a major goal for society. We investigated the effectiveness of a culturally sensitive, enhanced care package in UK general practices for improvement of cardiovascular risk factors in patients of south Asian origin with type 2 diabetes. In this cluster randomised controlled trial, 21 inner-city practices in the UK were assigned by simple randomisation to intervention (enhanced care including additional time with practice nurse and support from a link worker and diabetes-specialist nurse [nine practices; n=868]) or control (standard care [12 practices; n=618]) groups. All adult patients of south Asian origin with type 2 diabetes were eligible. Prescribing algorithms with clearly defined targets were provided for all practices. Primary outcomes were changes in blood pressure, total cholesterol, and glycaemic control (haemoglobin A1c) after 2 years. Analysis was by intention to treat. This trial is registered, number ISRCTN 38297969. We recorded significant differences between treatment groups in diastolic
blood pressure (1.91 [95% CI -2.88 to -0.94] mmHg, p=0.0001) and mean arterial pressure (1.36 [-2.49 to -0.23] mmHg, p=0.0180), after adjustment for confounders and clustering. We noted no significant differences between groups for total cholesterol (0.03 [-0.04 to 0.11] mmol/L), systolic blood pressure (-0.33 [-2.41 to 1.75] mmHg), or HbA1c (-0.15 [-0.33 to 0.03]). Economic analysis suggests that the nurse-led intervention was not cost effective (incremental cost-effectiveness ratio £2893 per QALY gained). Across the whole study population over the 2 years of the trial, systolic blood pressure, diastolic blood pressure, and cholesterol decreased significantly by 4.9 (95% CI 4.0–5.9) mmHg, 3.8 (3.2–4.4) mmHg, and 0.45 (0.40–0.51) mmol/L, respectively, and we recorded a small and non-significant increase for haemoglobin A1c (0.04% [-0.04 to 0.13], p=0.290). We recorded additional, although small, benefits from our culturally tailored care package that were greater than the secular changes achieved in the UK in recent years. Stricter targets in general practice and further measures to motivate patients are needed to achieve best possible health-care outcomes in south Asian patients with diabetes.


Intensive lifestyle interventions can reduce the incidence of type 2 diabetes in people with impaired glucose tolerance, but how long these benefits extend beyond the period of active intervention, and whether such interventions reduce the risk of cardiovascular disease (CVD) and mortality, is unclear. We aimed to assess whether intensive lifestyle interventions have a long-term effect on the risk of diabetes, diabetes-related macrovascular and microvascular complications, and mortality. In 1986, 577 adults with impaired glucose tolerance from 33 clinics in China were randomly assigned to either the control group or to one of three lifestyle intervention groups (diet, exercise, or diet plus exercise). Active intervention took place over 6 years until 1992. In 2006, study participants were followed-up to assess the long-term effect of the interventions. The primary outcomes were diabetes incidence, CVD incidence and mortality, and all-cause mortality. Compared with control participants, those in the combined lifestyle intervention groups had a 51% lower incidence of diabetes (hazard rate ratio [HRR] 0.49; 95% CI 0.33–0.73) during the active intervention period and a 43% lower incidence (0.57; 0.41–0.81) over the 20 year period, controlled for age and clustering by clinic. The average annual incidence of diabetes was 7% for intervention participants versus 11% in control participants, with 20-year cumulative incidence of 80% in the intervention groups and 93% in the control group. Participants in the intervention group spent an average of 3-6 fewer years with diabetes than those in the control group. There was no significant difference between the intervention and control groups in the rate of first CVD events (HRR 0.98; 95% CI 0.71–1.37), CVD mortality (0.83; 0.48–1.40), and all-cause mortality (0.96; 0.65–1.41), but our study had limited statistical power to detect differences for these outcomes.


Trials of ß blockers in patients undergoing non-cardiac surgery have reported conflicting results. This randomised controlled trial, done in 190 hospitals in 23 countries, was designed to investigate the effects of perioperative blockers. We randomly assigned 8351 patients with, or at risk of, atherosclerotic disease who were undergoing non-cardiac surgery to receive extended-release metoprolol succinate (n=4174) or pla-


Children with newly diagnosed type 1 diabetes in Finland who were listed on the National Public Health Institute diabetes register, Central Drug Register, and Hospital Discharge Register in 1980–2005 were included in a cohort study. We excluded patients with type 2 diabetes and diabetes occurring secondary to other conditions, such as steroid use, Down’s syndrome, and congenital malformations of pancreas. 100737 children—5816 boys and 4921 girls—were diagnosed with type 1 diabetes before 15 years of age during 1980–2005. The average age-standardised incidence was 42·9 per 100 000 per year (95% CI 42·6–44·3) during this period, increasing from 31·4 per 100 000 per year in 1980 to 64·2 per 100 000 per year in 2005. The age-specific rates per 100 000 per year were 31·0, 50·5, and 50·6 at ages 0–4 years, 5–9 years, and 10–14 years, respectively. We noted a significant non-linear component to the time trend (p<0·0003). In children aged 0–4 years, the increase was largest, at 4·7% more affected every year. The overall boy-to-girl ratio of incidence was 1·1; at the age of 13 years, it was 1·7 (1·4–2·0). The predicted cumulative number of new cases with type 1 diabetes before 15 years of age between 2006 and 2020 was about 100 800. The incidence of type 1 diabetes in Finnish children is increasing even faster than before. The number of new cases diagnosed at or before 14 years of age will double in the next 15 years and the age of onset will be younger (0–4 years).
Infection (78/322, 24%) and from those whose death from infants whose deaths were explained by bacterial mixed growth. Significantly more isolates, 484 (32%) of which showed pure growth and were sterile. Positive cultures yielded 2871 separate bacteriological samples were taken, of which 571 (27%) were done in 470 (93%) of the remaining 507 autopsies. 2079 lapse and resuscitation. Bacteriological sampling was done in 470 (93%) of the remaining 507 autopsies. 2079 bacteriological samples were taken, of which 571 (27%) were sterile. Positive cultures yielded 2871 separate isolates, 484 (32%) of which showed pure growth and 1024 (68%) mixed growth. Significantly more isolates from infants whose deaths were explained by bacterial infection (78/322, 24%) and from those whose death was unexplained (440/2306, 19%) contained group 2 pathogens than did those from infants whose death was explained by non-infective cause (27/243, 11%; difference 13-1%, 95% CI 6-9–19-2, p<0-0001 vs bacterial infection; and 8-0%, 3-2–11-8, p=0-001 vs unexplained). Significantly more cultures from infants whose deaths were unexplained contained Staphylococcus aureus (262/1628, 16%) or Escherichia coli (93/1628, 6%) than did those from infants whose deaths were of non-infective cause (S aureus: 19/211, 9%; difference 7-1%, 95% CI 2-2–10-8, p=0-005; E coli: 3/211, 1%, difference 4-3%, 1-5–5-9, p=0-003). Although many post-mortem bacteriological cultures in SUDI yield organisms, most seem to be unrelated to the cause of death. The high rate of detection of group 2 pathogens, particularly S aureus and E coli, in otherwise unexplained cases of SUDI suggests that these bacteria could be associated with this condition.


The cause and mechanism of most cases of sudden unexpected death in infancy (SUDI) remain unknown, despite specialist autopsy examination. We reviewed autopsy results to determine whether infection was a cause of SUDI. We did a systematic retrospective case review of autopsies, done at one specialist centre between 1996 and 2005, of 546 infants (aged 7–365 days) who died suddenly and unexpectedly. Cases of SUDI were categorised as unexplained, explained with histological evidence of bacterial infection, or explained by non-infective causes. Microbial isolates gathered at autopsy were classified as non-pathogens, group 1 pathogens (organisms usually associated with an identifiable focus of infection), or group 2 pathogens (organisms known to cause sepsicaemia without an obvious focus of infection). Of 546 SUDI cases, 39 autopsies were excluded because of viral or pneumocystis infection or secondary bacterial infection after initial collapse and resuscitation. Bacteriological sampling was done in 470 (93%) of the remaining 507 autopsies. 2079 bacteriological samples were taken, of which 571 (27%) were sterile. Positive cultures yielded 2871 separate isolates, 484 (32%) of which showed pure growth and 1024 (68%) mixed growth. Significantly more isolates from infants whose deaths were explained by bacterial infection (78/322, 24%) and from those whose death was unexplained (440/2306, 19%) contained group 2 pathogens than did those from infants whose death was explained by non-infective cause (27/243, 11%; difference 13-1%, 95% CI 6-9–19-2, p<0-0001 vs bacterial infection; and 8-0%, 3-2–11-8, p=0-001 vs unexplained). Significantly more cultures from infants whose deaths were unexplained contained Staphylococcus aureus (262/1628, 16%) or Escherichia coli (93/1628, 6%) than did those from infants whose deaths were of non-infective cause (S aureus: 19/211, 9%; difference 7-1%, 95% CI 2-2–10-8, p=0-005; E coli: 3/211, 1%, difference 4-3%, 1-5–5-9, p=0-003). Although many post-mortem bacteriological cultures in SUDI yield organisms, most seem to be unrelated to the cause of death. The high rate of detection of group 2 pathogens, particularly S aureus and E coli, in otherwise unexplained cases of SUDI suggests that these bacteria could be associated with this condition.


Non-steroidal anti-inflammatory drugs and colchicine used to treat gout arthritis have gastrointestinal, renal, and cardiovascular adverse effects. Systemic corticosteroids might be a beneficial alternative. We investigated equivalence of naproxen and prednisolone in primary care. We did a randomised clinical trial to test equivalence of prednisolone and naproxen for the treatment of monoarticular gout. Primary-care patients with gout confirmed by presence of monosodium urate crystals were eligible. 120 patients were randomly assigned with computer-generated randomisation to receive either prednisolone (35 mg once a day; n=60) or naproxen (500 mg twice a day; n=60), for 5 days. Treatment was masked for both patients and physicians. The primary outcome was pain measured on a 100 mm visual analogue scale and the a priori margin for equivalence set at 10%. Analyses were done per protocol and by intention to treat. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN14648181. Data were incomplete for one patient in each treatment group, so per-protocol analyses included 59 patients in each group. After 90 h the reduction in the pain score was 44-7 mm and 46-0 mm for prednisolone and naproxen, respectively (difference 1-3 mm: 95% CI -9-8 to 7-1), suggesting equivalence. The difference in the size of change in pain was 1-57 mm (95% CI -8-65 to 11-78). Adverse effects were similar between groups, minor, and resolved by 3 week follow-up. Oral prednisolone and naproxen are equally effective in the initial treatment of gout arthritis over 4 days.
SEMINAR


Type 1 diabetes is associated with a substantially increased risk of cardiovascular disease that might not always be appreciated in view of the fairly young age of patients with this condition. In fact, in type 1 diabetes, the heart is subject to a variety of pathological insults, including accelerated atherosclerosis, cardiac autonomic neuropathy, and possibly intrinsic cardiomyopathy. Although the relation between hyperglycaemia and microvascular complications has been well established, a direct effect of hyperglycaemia on cardiovascular disease in type 1 diabetes has long been debated. More recently, several studies, most notably the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications, have clarified this issue and provided conclusive evidence that hyperglycaemia is indeed a mediator of cardiovascular risk in type 1 diabetes and that intensive diabetes therapy can reduce cardiovascular disease outcomes.

REVIEW


We review the epidemiological and clinical characteristics of tick-borne encephalitis, and summarise biological and virological aspects that are important for understanding the life-cycle and transmission of the virus. Tick-borne encephalitis virus is a flavivirus that is transmitted by Ixodes spp ticks in a vast area from western Europe to the eastern coast of Japan. Tick-borne encephalitis causes acute meningoencephalitis with or without myelitis. Morbidity is age dependent, and is highest in adults of whom half develop encephalitis. A third of patients have longlasting sequelae, frequently with cognitive dysfunction and substantial impairment in quality of life. The disease arises in patchy endemic foci in Europe, with climatic and ecological conditions suitable for circulation of the virus. Climate change and leisure habits expose more people to tick-bites and have contributed to the increase in number of cases despite availability of effective vaccines. The serological diagnosis is usually straightforward. No specific treatment for the disease exists, and immunisation is the main preventive measure.


Individuals with type 2 diabetes mellitus have increased cardiovascular disease risk compared with those without diabetes. Treatment of the residual risk, other than blood pressure and LDL-cholesterol control, remains important as the rate of diabetes increases worldwide. The accelerated atherosclerosis and cardiovascular disease in diabetes is likely to be multifactorial and therefore several therapeutic approaches can be considered. Results of mechanistic studies done in vitro and in vivo—animals and people—can provide important insights with the potential to improve clinical management decisions and outcomes. In this Review, we focus on three areas in which pathophysiological considerations could be particularly informative—ie, the roles of hyperglycaemia, diabetic dyslipidaemia (other than the control of LDL-cholesterol concentrations), and inflammation (including that in adipose tissue) in the acceleration of vascular injury.


The use of doping agents, particularly anabolic androgenic steroids (AAS), has changed from being a problem restricted to sports to one of public-health concern. We review the prevalence of misuse, the evidence that some drugs improve performance in sport, their side-effects, and the long-term consequences of AAS misuse for society at large. There is substantial under-reporting of the side-effects of AAS to health authorities. We describe neuropsychiatric side-effects of AAS and their possible neurobiological correlates, with particular emphasis on violent behaviour. Analytical methods and laboratories accredited by the World Anti-Doping Agency can detect the misuse of all doping agents; although the analysis of testosterone requires special techniques, and recently discovered interethnic differences in testosterone excretion should be taken into account. The prevention of misuse of doping agents should include random doping analyses, medical follow-ups, pedagogic interventions, tougher legislation against possession of AAS, and longer disqualifications of athletes who use AAS.