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agreements will not be enough to protect Pincock, high-tech buoys and international early-warning systems. But, reports Stephen an unprecedented way to strengthen tsunami the international community mobilised itself in In the wake of the 2004 Indian Ocean tsunami, Pincock, S. (2007). Gaps exist in tsunami hygiene-promotion programmes. governmental organisations) have developed methods of human waste disposal, dumping it in hygiene is poor—people still follow traditional diseases, and malaria are here too.” Personal hygiene is poor—people still follow traditional conditions with inadequate living space, lighting, and ventilation, and poor hygiene. “Diarrhoea is prevalent”, said Floyd Burnaby, who is managing several construction projects for the Hong Kong Red Cross in Aceh. “Vector-borne diseases, dengue, and malaria are here too.” Personal hygiene is poor—people still follow traditional methods of human waste disposal, dumping it in the back yard, even though many NGOs (non-governmental organisations) have developed hygiene-promotion programmes. Pincock, S. (2007). Gaps exist in tsunami preparedness plans. The Lancet, 369(9579), 2065.

In the wake of the 2004 Indian Ocean tsunami, the international community mobilised itself in an unprecedented way to strengthen tsunami early-warning systems. But, reports Stephen Pincock, high-tech buoys and international agreements will not be enough to protect people. On April 2 this year—the day an earthquake and tsunami hit the Pacific nation of the Solomon Islands, killing 52 and displacing thousands—the beaches on Australia’s pacific coast were closed as a precautionary measure. Since early that morning, when the Pacific Tsunami Warning Centre in Hawaii issued its first alert, Australia’s radio stations had been broadcasting bulletins about the real, albeit minor, risk to the country’s coastal region. Those messages were interpreted quite differently along the country’s eastern seaboard. In the northern state of Queensland, schools were closed and some people fled to higher ground, but the surfers at Sydney’s Bondi Beach further south were unperturbed, riding their boards on a fairly flat sea. Whether or not they were hoping to ride a tsunami, they were taking a foolish risk, says Dale Dominey-Howes, a coastal geologist from Sydney’s Macquarie University, who has advised the Australian government on the issue of tsunami preparedness. “It’s really not necessary to be in the water during a tsunami event”, he points out. For Dominey-Howes and other tsunami experts, the episode illustrates some of the key challenges the world still needs to tackle 2 years after 280 people died in the Indian Ocean tsunami of Dec 26, 2004—education and communication of tsunami risk.

SPECIAL REPORT


Over 2 years after the 2004 Indian Ocean tsunami caused massive devastation in southeast Asia, people are still living in temporary shelters. Reconstruction projects are struggling to ensure that new housing has clean water supplies and good sanitation. Margaret Harris Cheng reports. At the sites in Sri Lanka recovering from the havoc wreaked by the December, 2004, tsunami, recovery is a questionable word. The conflict between the majority Sinhalese government and the separatist group the Liberation Tigers of Tamil Eelam (LTTE) has reignited with renewed vigour and is adding to the mix of problems caused by the tsunamis. The tsunamis killed over 35, people in Sri Lanka. The conflict between the government and LTTE, spanning over 20 years, is taking lives daily and seems, for many Sri Lankans, never-ending. Although the politics vary, in most of the areas hit by the tsunamis, housing reconstruction projects have not progressed as quickly as those implementing and funding them would have wished, leaving many people living in temporary shelters. In December, 2006, an Oxfam progress report noted that in Indonesia’s capital Aceh, public-health conditions in the “baraks”—long low buildings still housing more than 70 people—“are an area of increasing concern”. Another 20 households are still living in self-constructed shelters, usually tents. Many of the people living in temporary housing, whether in large camps for displaced people or tents in someone’s backyard, are living in cramped conditions with inadequate living space, lighting, and ventilation, and poor hygiene. “Diarrhoea is prevalent”, said Floyd Burnaby, who is managing several construction projects for the Hong Kong Red Cross in Aceh. “Vector-borne diseases, dengue, and malaria are here too.” Personal hygiene is poor—people still follow traditional methods of human waste disposal, dumping it in the back yard, even though many NGOs (non-governmental organisations) have developed hygiene-promotion programmes.

WORLD REPORTS


The Gaza Strip, already plunged into deep poverty by a western boycott, is recovering from a ferocious gun battle between the militant Hamas movement and rival Fatah faction, which left over 100 people dead and more than 600 injured. Sharmila Devi reports from Jerusalem. Days of fierce Palestinian factional fighting ended on June 15 after Hamas routed the secular, nationalist Fatah movement. The Islamists were left in control of Gaza while health professionals and aid workers tried to avert social collapse. The International Committee of the Red Cross (ICRC)—the only agency able to deliver assistance during the fighting—said on June 19 that by mid-June it was able to evacuate six people through Israel but said that another 50 people needed urgent treatment not available in Gaza. About 133 Palestinians were killed in the gun battle between the militant Hamas movement and rival Fatah faction, which left over 100 people dead and more than 600 injured. Sharmila Devi reports from Jerusalem. Days of fierce Palestinian factional fighting ended on June 15 after Hamas routed the secular, nationalist Fatah movement. The Islamists were left in control of Gaza while health professionals and aid workers tried to avert social collapse. The International Committee of the Red Cross (ICRC)—the only agency able to deliver assistance during the fighting—said on June 19 that by mid-June it was able to evacuate six people through Israel but said that another 50 people needed urgent treatment not available in Gaza. About 133 Palestinians were killed in the battles between forces loyal to Fatah, headed by President Mahmoud Abbas, and Hamas. About 630 more were injured, the ICRC said. “The hospitals are under a lot of stress simply because of the number of people injured during the fighting”, said Bernard Barrett, ICRC spokesman.

Little is known about the quality of life (QoL) of disabled children. We describe self-reported QoL of children with cerebral palsy, factors that influence it, and how it compares with QoL of the general population. 1174 children aged 8–12 years were randomly selected from eight population-based registers of children with cerebral palsy in six European countries and 743 (63%) agreed to participate; one further region recruited 75 children from multiple sources. Researchers visited these 818 children. 318 (39%) with severe intellectual impairment could not self-report; 500 (61%) reported their QoL using KIDSCREEN, an instrument with scores in ten domains, each with SD=10. Multivariable regression was used to relate QoL to impairments, pain, and sociodemographic characteristics. Comparisons were made with QoL data from the general population. Impairments were not significantly associated with six KIDSCREEN domains. Comparison of least and most able groups showed that severely limited self-mobility was significantly associated with reduced mean score for physical wellbeing (7·6, 95% CI 2·7–12·4); intellectual impairment with reduced mean for moods and emotions (3·7, 1·5–5·9) and autonomy (3·3, 0·9–5·7); and speech difficulties with reduced mean for relationships with parents (4·5, 1·9–7·1). Pain was common and associated with lower QoL on all domains. Impairments and pain explained up to 3% and 7%, respectively, of variation in QoL. Children with cerebral palsy had similar QoL to children in the general population in all domains except schooling, in which evidence was equivocal, and physical wellbeing, in which comparison was not possible. Parents can be reassured that most children aged 8–12 years with cerebral palsy will have similar QoL to other children. This finding should guide social and educational policy to ensure that disabled children participate fully in society. Because of its association with QoL, children’s pain should be carefully assessed.


Josette Sheeran, a former Bush Administration official, is the new executive director of the World Food Programme. She joins at a time when many are debating whether the agency’s current primary role—dealing with emergencies—still makes sense. Samuel Loewenberg reports. In the spring of last year, the World Food Programme (WFP) made a big splash in the news. The headlines were not because WFP—the UN agency that provides food to more than 90 million people worldwide—was doing its job. It was because WFP announced that it no longer could. The agency had received only a third of the money it had requested to feed more than 3 million people in the Darfur region of Sudan, and as a result it was going to cut its distributions of grains, oil, sugar, salt, and the rest of the nutrients it was handing out to people in the war-torn region by half, to 1050 calories a day. Within a week, WFP had received more than US$100 million in donations, and the food pipeline was restored.

ARTICLES


Most developing countries have adopted a standard WHO dosing schedule for vitamin A supplementation. However, in 2002 the International Vitamin A Consultative Group (IVACG) Annecy Accord recommended a new high-dose regimen for mothers and infants. Our aim was to test whether the new high-dose regimen of vitamin A supplementation would increase maternal and infant plasma vitamin A, reduce infant Helicobacter pylori infection and nasopharyngeal pneumococcal carriage, and improve infant gut epithelial integrity. In an area of moderate vitamin A deficiency in rural Gambia, 220 mother–infant pairs were enrolled in a randomised double-blind trial between September, 2001, and October, 2004, that compared the IVACG high dose with the WHO dose. The primary endpoints were levels of maternal and infant plasma vitamin A, H pylori infection, pneumococcal carriage, and gut epithelial integrity. 197 infants completed follow-up to 12 months (99 high dose and 98 WHO dose). There were no adverse events at dosing. No differences were found in the primary outcomes for high-dose versus WHO schedule: maternal vitamin A concentration at 2 months +0·02 imol/L (95% CI 0·10 to 0·15); infant vitamin A at 5 months +0·01 imol/L (0·06 to 0·08); H pylori infection at 12 months -0·3% (-0·7 to 1·2);
maternal pneumococcal carriage at 12 months -2.0% (–13.7 to 9.7); infant pneumococcal carriage at 12 months -4.1% (–15.8 to 7.6); infant gut mucosal damage at 12 months 5.2% (–8.7 to 19.2). There were more clinic attendances by the high-dose group in the first 6 months of life (p=0.018). Our results do not lend support to the proposal to increase the existing WHO standard dosing schedule for vitamin A in areas of moderate vitamin A deficiency. Caution is urged for future studies because trials have shown possible adverse effects of higher doses of vitamin A, and potential negative interactions with the expanded programme on immunisation (EPI) vaccines.


Dopaminergic neuronal loss in Parkinson’s disease leads to changes in the circuitry of the basal ganglia, such as decreased inhibitory GABAergic input to the subthalamic nucleus. We aimed to measure the safety, tolerability, and potential efficacy of transfer of glutamic acid decarboxylase (GAD) gene with adeno-associated virus (AAV) into the subthalamic nucleus of patients with Parkinson’s disease. We did an open label, safety and tolerability trial of unilateral subthalamic viral vector (AAV-GAD) injection in 11 men and 1 woman with Parkinson’s disease. We did an open label, safety and tolerability trial of unilateral subthalamic viral vector (AAV-GAD) injection in 11 men and 1 woman with Parkinson’s disease (mean age 58.2, SD=5.7 years). Four patients received low-dose, four medium-dose, and four high-dose AAV-GAD at New York Presbyterian Hospital. Inclusion criteria consisted of Hoehn and Yahr stage 3 or greater, motor fluctuations with substantial off time, and age 70 years or less. Patients were assessed clinically both off and on medication at baseline and after 1, 3, 6, and 12 months at North Shore Hospital. Efficacy measures included the Unified Parkinson’s Disease Rating Scale (UPDRS), scales of activities of daily living (ADL), neuropsychological testing, and PET imaging with 18F-fluorodeoxyglucose. All patients who enrolled had surgery, and there were no dropouts or patients lost to follow-up. There were no adverse events related to gene therapy. Significant improvements in motor UPDRS scores (p=0.0015), predominantly on the side of the body that was contralateral to surgery, were seen 3 months after gene therapy and persisted up to 12 months. PET scans revealed a substantial reduction in thalamic metabolism that was restricted to the treated hemisphere, and a correlation between clinical motor scores and brain metabolism in the supplementary motor area. AAV-GAD gene therapy of the subthalamic nucleus is safe and well tolerated by patients with advanced Parkinson’s disease, suggesting that in-vivo gene therapy in the adult brain might be safe for various neurodegenerative diseases.


The aim of this interim analysis of a large, international phase III study was to assess the efficacy of an AS04 adjuvanted L1 virus-like-particle prophylactic candidate vaccine against infection with human papillomavirus (HPV) types 16 and 18 in young women. 18’644 women aged 15–25 years were randomly assigned to receive either HPV16/18 vaccine (n=9319) or hepatitis A vaccine (n=9325) at 0, 1, and 6 months. Of these women, 88 were excluded because of high-grade cytology and 31 for missing cytology results. Thus, 9258 women received the HPV16/18 vaccine and 9267 received the control vaccine in the total vaccinated cohort for efficacy, which included women who had prevalent oncogenic HPV infections, often with several HPV types, as well as low-grade cytological abnormalities at study entry and who received at least one vaccine dose. We assessed cervical cytology and subsequent biopsy for 14 oncogenic HPV types by PCR. The primary endpoint—vaccine efficacy against cervical intraepithelial neoplasia (CIN) 2+ associated with HPV16 or HPV18—was assessed in women who were seronegative and DNA negative for the corresponding vaccine type at baseline (month 0) and allowed inclusion of lesions with several oncogenic HPV types. This interim event-defined analysis was triggered when at least 23 cases of CIN2+ with HPV16 or HPV18 DNA in the lesion were detected in the total vaccinated cohort for efficacy. Analyses were done on a modified intention-to-treat basis. Mean length of follow-up for women in the primary analysis for efficacy at the time of the interim analysis was 14-8 (SD 4-9) months. Two cases of CIN2+ associated
with HPV16 or HPV18 DNA were seen in the HPV16/18 vaccine group; 21 were recorded in the control group. Of the 23 cases, 14 (two in the HPV16/18 vaccine group, 12 in the control group) contained several oncogenic HPV types. Vaccine efficacy against CIN2+ containing HPV16/18 DNA was 90·4% (97·9% CI 53·4–99·3; p<0·0001). No clinically meaningful differences were noted in safety outcomes between the study groups. The adjuvanted HPV16/18 vaccine showed prophylactic efficacy against CIN2+ associated with HPV16 or HPV18 and thus could be used for cervical cancer prevention.


Diastolic dysfunction might represent an important pathophysiological intermediate between hypertension and heart failure. Our aim was to determine whether inhibitors of the renin-angiotensin-aldosterone system, which can reduce ventricular hypertrophy and myocardial fibrosis, can improve diastolic function to a greater extent than can other antihypertensive agents. Patients with hypertension and evidence of diastolic dysfunction were randomly assigned to receive either the angiotensin receptor blocker valsartan (titrated to 320 mg once daily) or matched placebo. Patients in both groups also received concomitant antihypertensive agents that did not inhibit the renin-angiotensin system to reach targets of under 135 mmHg systolic blood pressure and under 80 mmHg diastolic blood pressure. The primary endpoint was change in diastolic relaxation velocity between baseline and 38 weeks as determined by tissue doppler imaging. Analyses were done by intention to treat. 186 patients were randomly assigned to receive valsartan; 198 were randomly assigned to receive placebo. 43 patients were lost to follow-up or discontinued the assigned intervention. Over 38 weeks, there was a 12·8 (SD 7·2)/7·1 (9·9) mmHg reduction in blood pressure in the valsartan group and a 9·7 (17·0)/5·5 (10·2) mmHg reduction in the placebo group. The difference in blood pressure reduction between the two groups was not significant. Diastolic relaxation velocity increased by 0·60 (SD 1·4) cm/s from baseline in the valsartan group (p<0·0001) and 0·44 (1·4) cm/s from baseline in the placebo group (p<0·0001) by week 38. However, there was no significant difference in the change in diastolic relaxation velocity between the groups (p=0·29).

Lowering blood pressure improves diastolic function irrespective of the type of antihypertensive agent used.


Violence and rape are believed to fuel the HIV epidemic in countries affected by conflict. We compared HIV prevalence in populations directly affected by conflict with that in those not directly affected and in refugees versus the nearest surrounding host communities in sub-Saharan African countries. Seven countries affected by conflict (Democratic Republic of Congo, southern Sudan, Rwanda, Uganda, Sierra Leone, Somalia, and Burundi) were chosen since HIV prevalence surveys within the past 5 years had been done and data, including original antenatal-care sentinel surveillance data, were available. We did a systematic and comprehensive literature search using Medline and Embase. Only articles and reports that contained original data for prevalence of HIV infection were included. All survey reports were independently evaluated by two epidemiologists to assess internationally accepted guidelines for HIV sentinel surveillance and population-based surveys. Whenever possible, data from the nearest antenatal care and host country sentinel site of the neighbouring countries were presented. 95% CIs were provided when available. Of the 295 articles that met our search criteria, 88 had original prevalence data and 65 had data from the seven selected countries. Data from these countries did not show an increase in prevalence of HIV infection during periods of conflict, irrespective of prevalence when conflict began. Prevalence in urban areas affected by conflict decreased in Burundi, Rwanda, and Uganda at similar rates to urban areas unaffected by conflict in their respective countries. Prevalence in conflict-affected rural areas remained low and fairly stable in these countries. Of the 12 sets of refugee camps, nine had a lower prevalence of HIV infection, two a similar prevalence, and one a higher prevalence than their respective host communities. Despite wide-scale rape in many countries, there are no data to show that rape increased prevalence of HIV infection at the population level. We have shown that there is a need for mechanisms to provide time-sensitive information on the effect of conflict on incidence of HIV infection, since
we found insufficient data to support the assertions that conflict, forced displacement, and wide-scale rape increase prevalence or that refugees spread HIV infection in host communities.


Preclinical studies have suggested that transurethral injections of autologous myoblasts can aid in regeneration of the rhabdosphincter, and fibroblasts in reconstruction of the urethral submucosa. We aimed to compare the effectiveness and tolerability of ultrasonography-guided injections of autologous cells with those of endoscopic injections of collagen for stress incontinence. Between 2002 and 2004, we recruited 63 eligible women with urinary stress incontinence. 42 of these women were randomly assigned to receive transurethral ultrasonography-guided injections of autologous myoblasts and fibroblasts, and 21 to receive conventional endoscopic injections of collagen. The first primary outcome measure was an incontinence score (range 0–6) based on a 24-hour voiding diary, a 24-hour pad test, and a patient questionnaire. The other primary outcome measures were contractility of the rhabdosphincter and thickness of both the urethra and rhabdosphincter. Analysis was by intention to treat. At 12-months’ follow-up, 38 of the 42 women injected with autologous cells were completely continent, compared with two of the 21 patients given conventional treatment with collagen. The median incontinence score decreased from a baseline of 6·0 (IQR 6·0–6·0; where 6 represents complete incontinence), to 0 (0–0) for patients treated with autologous cells, and 6·0 (3·5–6·0) for patients treated with collagen (p<0·0001). Ultrasonographic measurements showed that the mean thickness of the rhabdosphincter increased from a baseline of 2·13 mm (SD 0·39) for all patients to 3·38 mm (SD 0·26) for patients treated with collagen (p<0·0001). Contractility of the rhabdosphincter increased from a baseline of 0·58 mm (SD 0·32) to 1·56 mm (SD 0·28) for patients treated with autologous cells and 0·67 mm (SD 0·51) for controls (p<0·0001). The change in the thickness of the urethra after treatment was not significantly different between treatment groups. No adverse effects were recorded in any of the 63 patients. Long-term postoperative results and data from multicentre trials with larger numbers of patients are needed to assess whether injection of autologous cells into the rhabdosphincter and the urethra could become a standard treatment for urinary incontinence.

SEMINAR


The clinical hallmark of neuroblastoma is heterogeneity, with the likelihood of cure varying widely according to age at diagnosis, extent of disease, and tumour biology. A subset of tumours will undergo spontaneous regression while others show relentless progression. Around half of all cases are currently classified as high-risk for disease relapse, with overall survival rates less than 40% despite intensive multimodal therapy. This Seminar focuses on recent advances in our understanding of the biology of this complex paediatric solid tumour. We outline plans for the development of a uniform International Neuroblastoma Risk Group (INRG) classification system, and summarise strategies for risk-based therapies. We also update readers on new discoveries related to the underlying molecular pathogenesis of this tumour, with special emphasis on advances that are translatable to the clinic. Finally, we discuss new approaches to treatment, including recently discovered molecular targets that might provide more effective treatment strategies with the potential for less toxicity.


Meningococcus, an obligate human bacterial pathogen, remains a worldwide and devastating cause of epidemic meningitis and sepsis. However, advances have been made in our understanding of meningococcal biology and pathogenesis, global epidemiology, transmission and carriage, host susceptibility, pathophysiology, and clinical presentations. Approaches to diagnosis, treatment, and chemoprophylaxis are now in use on the basis of these advances. Importantly, the next generation of meningococcal conjugate vaccines for serogroups A, C, Y, W-135, and broadly effective serogroup B vaccines are on the horizon, which could eliminate the organism as a major threat to human health in industrialised countries in the next decade. The crucial challenge will be effective introduction of
new meningococcal vaccines into developing countries, especially in sub-Saharan Africa, where they are urgently needed.

REVIEW


There is renewed interest in the potential contribution of community health workers to child survival. Community health workers can undertake various tasks, including case management of childhood illnesses (eg, pneumonia, malaria, and neonatal sepsis) and delivery of preventive interventions such as immunisation, promotion of healthy behaviour, and mobilisation of communities. Several trials show substantial reductions in child mortality, particularly through case management of ill children by these types of community interventions. However, community health workers are not a panacea for weak health systems and will need focussed tasks, adequate remuneration, training, supervision, and the active involvement of the communities in which they work. The introduction of large-scale programmes for community health workers requires evaluation to document the impact on child survival and cost effectiveness and to elucidate factors associated with success and sustainability.