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Dengue is spreading in the Americas. Incremental changes in climate could help explain the disease's expansion, according to environmental scientists. But some dengue experts have called the link with climate "alarmist" and scientifically unsound. Eliza Barclay investigates. Dengue fever was largely subdued in the Americas thanks to the widespread spraying of the insecticide dichloro-diphenyltrichloroethane in the mid-20th century. But the disease has made a comeback in the past 30 years, especially in South America, Central America, the Caribbean, and Mexico. According to the Pan American Health Organization (PAHO), 2007 was the worst year on record since 1985, with 918 cases of dengue and dengue haemorrhagic fever in the region. As scientists try to unravel the local and global factors that have contributed to its spread, the role of global climate change has emerged as an increasingly contentious issue. Countries like Paraguay, the Dominican Republic, and Mexico have had dengue epidemics and new cases have arisen in the past several years in surprising places, including the US state of Hawaii and the border region of Texas. Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases, recently published a commentary in the *Journal of the American Medical Association* to alert the public-health community to the potential threat of dengue in the region. "I was seeing a trend increasing more and more, and watching cases spill over to the Caribbean from South America", Fauci told The Lancet.


In an attempt to curb human trafficking, part of India's Government wants to make buying sex illegal. But public-health experts are worried that such a move would drive sex work underground and hamper efforts to control HIV/AIDS in the country. Patralekha Chatterjee reports. Last year, New Delhi's decision to introduce sex education in India's schools, aimed primarily at creating awareness about HIV/AIDS, evoked strident protests from many quarters. Many Indian states rejected the sex-education programmes supported by the federal government. In Kerala, India's most literate state, student organisations and church leaders argued that the proposed module would lead to "sexual anarchy". Now there is another tricky issue on the horizon for the Indian Government. Two federal ministries do not agree about proposed legal changes that would make buying sex a criminal offence. To try to curb human trafficking, the ministry for women and child development wants legislation on prostitution to change so that clients of sex workers, but not sex workers themselves, are punished. It also wants the punishment of human traffickers to be more severe. The current law—the Immoral Traffic (Prevention) Act 1956 (ITPA)—does not penalise sex workers. Instead, the legislation targets those who profit from or exploit prostitutes. Actively soliciting, running a brothel, and pimping are criminal offences under the legislation. The Act covers both women and men who are sex workers. The ITPA is not the perfect legal solution to the problems it seeks to address, but if Parliament passes the ITPA Amendment Bill, the situation will be worse, say critics.


Around 80% of all cardiovascular deaths occur in developing countries. Assessment of those patients at high risk is an important strategy for prevention. Since developing countries have limited resources for prevention strategies that require laboratory testing, we assessed if a risk prediction method that did not require any laboratory tests could be as accurate as one requiring laboratory information. The National Health and Nutrition Examination Survey (NHANES) was a prospective cohort study of 14,407 US participants aged between 25-74 years at the time they were first examined (between 1971 and 1975). Our follow-up study population included participants with complete information on these surveys who did not report a history of cardiovascular disease (myocardial infarction, heart failure, stroke, angina) or cancer, yielding an analysis dataset N=6186. We compared how well either method could predict first-time fatal and non-fatal cardiovascular disease events in this cohort. For the laboratory-based model, which required blood testing, we used standard risk factors to assess risk of cardiovascular disease: age, systolic blood pressure, smoking status, total cholesterol, reported diabetes status, and current treatment for hypertension. For the non-laboratory-based model, we substituted body-mass index for cholesterol. In the cohort of 6186, there were 1529 first-time cardiovascular events and 578 (38%) deaths due to cardiovascular disease over 21 years. In men, the laboratory-based model was useful for predicting events, with a c statistic of 0.829. The c statistic of the non-laboratory-based model was 0.831. In men, the results were similar (0.784 for the laboratory-based model and 0.783 for the non-laboratory-based model).


Surgical resection alone is regarded as the standard of care for patients with liver metastases from colorectal cancer, but relapse is common. We assessed the combination of perioperative chemotherapy and surgery compared with surgery alone for patients with initially resectable liver metastases from colorectal cancer. This parallel-group study reports the trial's final data for progression-free survival for a protocol unspecified interim time-point, while overall survival is still being monitored. 364 patients with histologically proven colorectal cancer and up to four liver metastases were randomly assigned...
to either six cycles of FOLFOX4 before and six cycles after surgery or to surgery alone (182 in perioperative chemotherapy group vs 182 in surgery group). Patients were centrally randomised by minimisation, adjusting for centre and risk score. The primary objective was to detect a hazard ratio (HR) of 0.71 or less for progression-free survival. Primary analysis was by intention to treat. Analyses were repeated for all eligible (171 vs 171) and resected patients (151 vs 152). In the perioperative chemotherapy group, 151 (83%) patients were resected after a median of six (range 1–6) perioperative cycles and 115 (63%) patients received a median six (1–8) postoperative cycles. 152 (84%) patients were resected in the surgery group. The absolute increase in rate of progression-free survival at 3 years was 7.3% (from 28.1% [95% CI 21.3–35.5] to 35.4% [28.1–42.7]; HR 0.79 [0.62–1.02]; p=0.058) in randomised patients; 8.1% (from 28.1% [21.2–36.6] to 36.2% [28.7–43.8]; HR 0.77 [0.60–1.00]; p=0.041) in eligible patients; and 9.2% (from 33.2% [25.3–41.2] to 42.4% [34.0–50.5]; HR 0.73 [0.55–0.97]; p=0.025) in patients undergoing resection. 139 patients died (64 in perioperative chemotherapy group vs 75 in surgery group). Reversible postoperative complications occurred more often after chemotherapy than after surgery (40/159 [25%] vs 27/170 [16%]; p=0.04). After surgery we recorded two deaths in the surgery alone group and one in the perioperative chemotherapy group.


A fully bioabsorbable drug-eluting coronary stent that scaffolds the vessel wall when needed and then disappears once the acute recoil and constrictive remodelling processes have subsided has theoretical advantages. The bioabsorbable everolimus-eluting stent (BVS) has a backbone of poly-L-lactic acid that provides the support and a coating of poly-D,L-lactic acid that contains and controls the release of the antiproliferative agent everolimus. We assessed the feasibility and safety of this BVS stent. In this prospective, open-label study we enrolled 30 patients who had either stable, unstable, or silent ischaemia and a single de-novo lesion that was suitable for treatment with a single 3.0×12 mm or 3.0×18 mm stent. Patients were enrolled from four academic hospitals in Auckland, Rotterdam, Krakow, and Skejby. The composite endpoint was cardiac death, myocardial infarction, and ischaemia-driven target lesion revascularisation. Angiographic endpoints were available for 26 patients and intravascular-ultrasound endpoints for 24 patients. Clinical endpoints were assessed in all 30 patients at 6 and 12 months. In a subset of 13 patients, optical coherence tomography was undertaken at baseline and follow-up. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00300131. Procedural success was 100% (30/30 patients), and device success 94% (29/31 attempts at implantation of the stent). At 1 year, the rate of major adverse cardiac events was 3.3%, with only one patient having a non-Q wave myocardial infarction and no target lesion revascularisations. No late stent thromboses were recorded. At 6-month follow-up, the angiographic in-stent late loss was 0.44 (0.35) mm and was mainly due to a mild reduction of the stent area (-11.8%) as measured by intravascular ultrasound. The neointimal area was small (0.30 [SD 0.44] mm2), with a minimal area obstruction of 5.5%. This study shows the feasibility of implantation of the bioabsorbable everolimus-eluting stent, with an acceptable in-stent late loss, minimal intrainstent neointimal hyperplasia, and a low stent area obstruction.


The Heart of Soweto Study aims to increase our understanding of the characteristics and burden imposed by heart disease in an urban African community in probable epidemiological transition. We aimed to investigate the clinical range of disorders related to cardiovascular disease in patients presenting for the first time to a tertiary-care centre. From Jan 1 to Dec 31, 2006, we recorded data for 4162 patients with confirmed cases of cardiovascular disease (1593 newly diagnosed and 2569 previously diagnosed and under treatment) who attended the cardiology unit at the Chris Hani Baragwanath Hospital in Soweto, South Africa. We developed a prospectively designed registry and gathered detailed clinical data relating to the presentation, investigations, and treatment of all 1593 patients with newly diagnosed cardiovascular disease. Most patients were black Africans (n=1359 [85%]), and the study population contained more women (n=939 [59%]) than men. Women were slightly younger than were men (mean 53 [SD 16] years vs 55 [15] years; p=0.031), with 399 (25%) patients younger than 40 years. Heart failure was the most common primary diagnosis (704 cases, 44% of total). Moderate to severe systolic dysfunction was evident in 415 (53%) of 844 identified cases of heart failure, 577 (68%) of which were attributable to dilated cardiomyopathy or hypertensive heart disease, or both. Black Africans were more likely to be diagnosed with heart failure than were the rest of the cohort (739 [54%] vs 105 [45%]); odds ratio [OR] 1.46, 95% CI 1.11–1.94; p=0.009) but were less likely to be diagnosed with coronary artery disease (77 [6%] vs 88 [38%]; OR 0.10, 0.07–0.14; p<0.0001). Prevalence of cardiovascular risk factors was very high, with 897 (56%) patients diagnosed with hypertension (190 [44%] of whom were also obese). Only 209 (13%) patients had no identifiable risk factors, whereas 933 (59%) had several risk factors. We noted many threats to the present and future cardiac health of Soweto, including a high prevalence of modifiable risk factors for atherosclerotic disease and a combination of infectious and non-communicable forms of heart disease, with late clinical presentations. Overall, our findings provide strong evidence that epidemiological transition in Soweto, South Africa has broadened the complexity and spectrum of heart disease in this community. This registry will enable continued monitoring of the range of heart disease.
Systemic-onset juvenile idiopathic arthritis does not always respond to available treatments, including antitumour necrosis factor agents. We investigated the efficacy and safety of tocilizumab, an anti-interleukin-6-receptor monoclonal antibody, in children with this disorder. 56 children (aged 2–19 years) with disease refractory to conventional treatment were given three doses of tocilizumab 8 mg/kg every 2 weeks during a 6-week open-label lead-in phase. Patients achieving an American College of Rheumatology Pediatric (ACR Pedi) 30 response and a C-reactive protein concentration (CRP) of less than 5 mg/L were randomly assigned to receive placebo or to continue tocilizumab treatment for 12 weeks or until withdrawal for rescue medication in a double-blind phase. The primary endpoint of the double-blind phase was an ACR Pedi 30 response and CRP concentration of less than 15 mg/L. Patients responding to tocilizumab and needing further treatment were enrolled in an open-label extension phase for at least 48 weeks. The analysis was done by intention to treat. At the end of the open-label lead-in phase, ACR Pedi 30, 50, and 70 responses were achieved by 51 (91%), 48 (86%), and 38 (68%) patients, respectively. 43 patients continued to the double-blind phase and were included in the efficacy analysis. Four (17%) of 23 patients in the placebo group maintained an ACR Pedi 30 response and a CRP concentration of less than 15 mg/L. Patients responding to tocilizumab and needing further treatment were enrolled in an open-label extension phase for at least 48 weeks.

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Primary-care physicians continue to overprescribe antibiotics for acute rhinosinusitis because distinction between viral and bacterial sinus infection is difficult. We undertook a meta-analysis of randomised trials based on individual patients’ data to assess whether common signs and symptoms can be used to identify a subgroup of patients who benefit from antibiotics. We identified suitable trials—in which adult patients with rhinosinusitis-like complaints were randomly assigned to treatment with an antibiotic or a placebo—by searching the Cochrane Central Register of Controlled Trials, Medline, and Embase, and reference lists of reports describing such trials. Individual patients’ data from 2547 adults in nine trials were checked and re-analysed. We assessed the overall effect of antibiotic treatment and the prognostic value of common signs and symptoms by the number needed to treat (NNT) with antibiotics to cure one additional patient. 15 patients with rhinosinusitis-like complaints were randomly assigned to treatment with an antibiotic or a placebo—by searching the Cochrane Central Register of Controlled Trials, Medline, and Embase, and reference lists of reports describing such trials. Individual patients’ data from 2547 adults in nine trials were checked and re-analysed. We assessed the overall effect of antibiotic treatment and the prognostic value of common signs and symptoms by the number needed to treat (NNT) with antibiotics to cure one additional patient. Patients with purulent discharge in the pharynx took longer to cure than those without this sign; the NNT was 8 patients with this sign before one additional patient was cured (95% CI NNT[benefit] 7 to NNT[harm] 190). Patients who were older, reported symptoms for longer, or reported more severe symptoms also took longer to cure but were no more likely to benefit from antibiotics than other patients. Common clinical signs and symptoms cannot identify patients with rhinosinusitis for whom...
treatment is clearly justified. Antibiotics are not justified even if a patient reports symptoms for longer than 7–10 days.

**SEMI NARS**


Mumps is a common childhood infection caused by the mumps virus. The hallmark of infection is swelling of the parotid gland. Aseptic meningitis and encephalitis are common complications of mumps together with orchitis and oophoritis, which can arise in adult men and women, respectively; other complications include deafness and pancreatitis. Clinical diagnosis can be based on the classic parotid swelling; however, this feature is not present in all cases of mumps and can also occur in various other disorders. Laboratory diagnosis is based on isolation of virus, detection of viral nucleic acid, or serological confirmation (generally presence of IgM mumps antibodies). Mumps is vaccine-preventable, and one dose of mumps vaccine is about 80% effective against the disease. Routine vaccination has proven highly effective in reducing the incidence of mumps, and is presently used by most developed countries; however, there have been outbreaks of disease in vaccinated populations. In 2005, a large epidemic peaked in the UK, and in 2006 the American midwest had several outbreaks. In both countries, the largest proportion of cases was in young adults. In the UK, susceptible cohorts too old to have been vaccinated and too young to have been exposed to natural infections were the primary cause of the mumps epidemic. In the USA, effectiveness and uptake in combination appear not to have been sufficient to obtain herd immunity for mumps in populations such as college students.


Chronic lymphocytic leukaemia is the commonest form of leukaemia in Europe and North America, and mainly, though not exclusively, affects older individuals. It has a very variable course, with survival ranging from months to decades. Major progress has been made in identification of molecular and cellular markers that could predict disease progression in patients with chronic lymphocytic leukaemia. In particular, the mutational profile of immunoglobulin genes and some cytogenetic abnormalities are important predictors of prognosis. However, these advances have raised new questions about the biology, prognosis, and management of chronic lymphocytic leukaemia, some of which are addressed here. In particular, we discuss how better understanding of the function of the B-cell receptor, the nature of genetic lesions, and the balance between proliferation and apoptosis have affected our ability to assess prognosis and to manage chronic lymphocytic leukaemia. Available treatments generally induce remission, although nearly all patients relapse, and chronic lymphocytic leukaemia remains an incurable disease. Advances in molecular biology have enhanced our understanding of the pathophysiology of the disease and, together with development of new therapeutic agents, have made management of chronic lymphocytic leukaemia more rational and more effective than previously. Unfortunately, we know of no way that chronic lymphocytic leukaemia can be prevented. Early detection is practised widely, but seemingly makes no difference to the patient’s eventual outcome.


Mycosis fungoides and Sézary syndrome are the most common of the cutaneous T-cell lymphomas, which are a heterogeneous group of neoplasms that affect the skin as a primary site. Although the aetiologies of mycosis fungoides and Sézary syndrome are unknown, important insights have been gained in the immunological and genetic perturbations that are associated with these diseases. Unlike some B-cell lymphomas, cutaneous T-cell lymphomas as a group are rarely if ever curable and hence need chronic-disease management. New approaches to treatments are being investigated and include biological and cytotoxic drugs, phototherapy, and monoclonal antibodies that are directed towards novel molecular targets. New molecular technologies such as complementary-DNA microarray have the potential to increase the accuracy of diagnosis and provide important prognostic information. Treatments can be combined to greatly improve clinical outcome without substantially increasing toxic effects in advanced disease that is otherwise difficult to treat. Although present treatment strategies are generally not curative, there is hope that experimental treatments, particularly immunotherapy, might eventually reverse or suppress the abnormalities of mycosis fungoides and Sézary syndrome to the point at which they become non-life-threatening, chronic diseases.


Acute lymphoblastic leukaemia, a malignant disorder of lymphoid progenitor cells, affects both children and adults, with peak prevalence between the ages of 2 and 5 years. Steady progress in development of effective treatments has led to a cure rate of more than 80% in children, creating opportunities for innovative approaches that would preserve past gains in leukaemia-free survival while reducing the toxic side-effects of current intensive regimens. Advances in our understanding of the pathobiology of acute lymphoblastic leukaemia, fuelled by emerging molecular technologies, suggest that drugs specifically targeting the genetic defects of leukaemic cells could revolutionise management of this disease. Meanwhile, studies are underway to ascertain the precise events that take place in the genesis of acute lymphoblastic leukaemia, to enhance the clinical application of known risk factors and antileukaemic agents, and to identify treatment regimens that might boost the generally low cure rates in adults and subgroups of children with high-risk leukaemia.