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8-12 May 2004 Alice Springs Australia	Australian Society of Infectious Diseases Meeting 2004 Contact: Dart Associates – Christine Treasure / Shirley Corley, PO Box 781, Lane Cove, Australia 2006 Phone: 02 9418 9396/97 Fax: 02 9418 9398 E-mail: dartconv@mpx.com.au WWW: http://www.racp.edu.au/asid
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Important role of nosocomial surveillance in infection control

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Surveillance is defined as "the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. Surveillance of nosocomial infection is recognized as an essential component of infection control.

Fewer than 10% of all nosocomial infections occur as recognised outbreaks (1). It is the endemic infections which constitute the main bulk of ongoing surveillance. The purposes of setting up a nosocomial surveillance program include obtaining "baseline" data and identifying areas for improvement which in turn will help to modify infection control practices and eventually improving patient outcomes.

There are seven essential elements to a successful nosocomial surveillance program (2). First, an assessment of the "at-risk" population is conducted to set surveillance priorities. Second, key stakeholders are included in the selection of events or processes to be surveyed. A written surveillance plan containing initiatives in order of priority should be drafted with administrative support. The duration and frequency of surveillance, type of data for analysis and report distribution method and frequency should be delineated. The third step involves choice of methodology. In general, active (vs. passive), prospective (vs. retrospective), patient-based (vs. laboratory-based), incidence (vs. prevalence), priority-directed (vs. comprehensive), risk adjusted (vs. crude) are recommended for nosocomial infection surveillance. Fourth, in monitoring the event or process, all available information systems are utilized. Fifth, consistent and standardized definitions are used to enhance the precision of data. For reference, the CDC National Nosocomial Infections Surveillance (NNIS) has made detailed definitions for each type of nosocomial infections. (www.cdc.gov/ncidod/hip/surveill/nnis.htm) Sixth, data are turned into useful information by rate calculation and analysis of findings. Finally, reports are made available to stakeholders for timely feedback. Surveillance information will usually stimulate ideas for process improvement.

NNIS developed by CDC is one of the best developed and time tested systems for nosocomial surveillance and it forms prototype for many countries. It began in 1970 with 62 hospitals and has grown to over 300 today (3). Hallmarks of the NNIS system are its use of surveillance protocols that focus on high-risk

patients and antimicrobial use and resistance, standardized infection and data field definitions and risk-adjustment methods to render the data suitable for inter- and intra-hospital comparison. Aggregated device-associated infection rates, surgical site infection rates stratified by a risk index, antimicrobial use and resistance rates and trends in selected antimicrobial-resistant pathogens associated with nosocomial ICU infections are published annually in the American Journal of Infection Control.

After 3 decades of hard work, the NNIS published data showing substantial reductions in major nosocomial infection rates during the decade of the 1990s. For central line-associated bloodstream infections, these decreases were between 31% and 44% depending on the type of ICU. For these reasons, the NNIS system has been cited as a model for patient safety. (4)

Critical components for the success of the NNIS systems are 1) voluntary, confidential participation, 2) standardized definitions and protocols, 3) targeted monitoring of high-risk patients, 4) risk-adjustment of rates comparable across institutions 5) adequate numbers of trained infection control personnel, 6) dissemination of data to patient-care providers, and 7) links between monitored rates and prevention efforts.

Two areas for nosocomial surveillance will be highlighted to illustrate their roles in hospital infection control. Surgical site infections complicate 1 to 10 percent of operations. They are associated with substantial morbidity and mortality, doubled duration of hospitalisation and increased cost of healthcare. To prevent surgical site infections, the factors that increase the risk of infection need to be identified and where possible, minimized. Since a large proportion of surgical site infection can be detected after patient discharge from the hospital, infection control programs must decide whether or not to conduct postdischarge surveillance. Surveillance programs can lead to reductions in surgical site infection rate of 35 to 50 %. Appropriate feedback to surgeons is one of the most effective measures to reduce nosocomial infection rates and is strongly recommended.

Surveillance of hospital acquired bloodstream infections can help to determine baseline rates, identify cluster of unusual event and risk associated different classes of devices. Intervention strategies can then be appropriately focused and empirical antimicrobial therapy properly directed. The effective of quality improvement strategies to decrease bloodstream infection is best assessed if surveillance information is readily available.

Hong Kong is in a favoured position to develop a territory wide nosocomial surveillance system now that most hospitals are supported by electronic patient records and an optimal ratio of infection control personnel is achieved in major acute hospitals. A successful nosocomial surveillance system will surely improve patient outcomes in Hong Kong.

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Encephalitis related to influenza vaccination

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Introduction

Influenza has long been a big concern to the human being, not only because of its capacity to claim lives, but also of its versatility in genetic modification. This poses a constant threat to the world at large. Influenza vaccination has been proved to be effective in reducing the incidence and mortality from the circulating influenza virus. Unfortunately side effects of influenza vaccine have been reported from time to time with variable severity. We encountered a case of encephalopathy after influenza vaccination.

The case

A 39-year-old airline manager had unremarkable past health. He received a subcutaneous injection of inactivated influenza vaccination in September 2003 prescribed by his family physician. Approximately 1 week later he had influenza-like symptoms with mild headache and he took paracetamol by himself. No other medication was taken. Four days passed, but his symptoms did not subside. He was brought to the hospital when his family noticed that he was confused and breathless. He had no recent travel to farm or rural areas. No recent contact with animals, birds or poultry was documented. Physical examination of this patient did not reveal any neurological signs except disorientation in time, place and person. No rash, insect bite marks, petechiae or injection marks could be found. No nuchal rigidity could be elicited. His chest examination was unremarkable. He developed repeated convulsion shortly after admission and required intensive care. Elective intubation was performed for the protection of the airway and he was put on phenytoin for refractory convulsion.

His admission serum white blood cell count was 13.4 x 10^9/L with neutrophil and lymphocyte counts of 11.1 and 1.9 x 10^9/L respectively. Eosinophil count was normal. His platelet count was 266 x 10^9/L. Renal function test results were normal with mildly elevated alanine transferase level of 47 U/L (normal range: 1-40 U/L). Clotting profiles were unremarkable. Lactate dehydrogenase and troponin I level were normal. Creatinine kinase was elevated to 362 U/L and this was possibly related to convulsion. No sign of rhabdomyolysis was detected. The serum pH and bicarbonate levels were all normal with adequate oxygenation. Nasopharyngeal aspirate (NPA) for direct antigen tests of influenza A and B, respiratory syncytial virus, adenovirus and parainfluenza virus were all negative. NPA for severe acute respiratory syndrome (SARS) coronavirus PCR was also negative.

His chest X-ray showed bilateral lower zone alveolar infiltration. Computer tomographic scan and subsequent magnetic resonance imaging of the brain did not reveal any intracranial lesions. Electroencephalogram (EEG) showed significant slow delta background activity, with highest amplitude at the frontal region and the tendency to spread posteriorly. There were occasional sharp waves over the frontal region. Lumbar puncture was performed with an open pressure of 25 cm of water. The cerebrospinal fluid (CSF) was slightly blood stained with elevated protein content of 76 mg / 100 ml and a glucose level of 4.3 mmol / L (spot serum glucose level was 6.7 mmol / L). Total white blood cells and red blood cells count in the CSF were 5 and 104 / mL respectively. Gram stain, India ink stain

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to first and second regimen failure. For the primary endpoint — time to second regimen failure — a strong trend favoured efavirenz over nelfinavir in patients receiving zidovudine plus lamivudine (hazard ratio, 0.71; 95% confidence interval, 0.48-1.06). In addition, time to first regimen failure was impressively longer in patients treated with zidovudine, lamivudine, and efavirenz (HR, 0.39; 95% CI, 0.24-0.64) than in those receiving any other regimen. The authors concluded that based on efficacy, simplicity, and toxicity profile, zidovudine and lamivudine plus efavirenz is the best option among the initial regimens examined in this study. Yet it should be noted that options for HIV therapy have greatly increased since this study began, and more potent PIs are available now. Thus, the question of whether to start antiretroviral therapy with an NNRTI or a PI remains open.

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Ginsburg AS, Hooper N, Parrish N et al. Fluoroquinolone resistance in patients with newly diagnosed tuberculosis. Clin Infect Dis. 2003 Dec 1;37(11):1448-52.

Synopsis: Fluoroquinolones have demonstrated in vitro activity against Mycobacterium tuberculosis, including strains resistant to other agents. They are currently recommended for treating patients who are infected with multi-drug-resistant strains or are intolerant of first-line agents. However, the role of fluoroquinolones as first-line therapy for TB remains unclear. Two recent studies add information on this important issue. In the first study, Gosling and colleagues randomly assigned 43 Tanzanian patients with newly diagnosed smear-positive, mild to moderately severe pulmonary TB to monotherapy with isoniazid, rifampin, or moxifloxacin for the first 5 days of treatment. Serial sputum samples were obtained from patients for the first 5 days. It was found that isoniazid reduced viable bacilli by 50% significantly faster than did rifampin or moxifloxacin (0.46 days vs. 0.71 and 0.88, respectively; P=0.03). In addition, early bactericidal activity, defined as decrease in viable bacilli from day 0 to day 2 of therapy, was 0.77 for isoniazid, significantly greater than for rifampin (0.28; P=0.006) but not for moxifloxacin (0.53). In the second study Ginsburg and colleagues tested the fluoroquinolone susceptibility of M. tuberculosis isolates from 55 patients with recently diagnosed TB at a single Baltimore hospital. Isolates from 2 of the 19 patients with previous exposure to fluoroquinolones, as opposed to 0 of 36 patients with no fluoroquinolone exposure, showed resistance to the antibiotic. The resistant isolates were both obtained from HIV-positive patients with CD4 counts <50 cells/mm^3. These studies provided further insights into the relative activities and merits of antituberculous drugs. Moxifloxacin was found to fall between isoniazid and rifampin in activity. However, fluoroquinolone resistance was noted in 11% of patients with active TB who had previously received fluoroquinolones. Taken together, these studies suggest that although fluoroquinolones might have a role in TB treatment, their utility may be limited by their widespread use for other illnesses, especially in places where such antibiotics are commonly used for treating infections in the community setting.

(4) Guan Y, Peiris JS, Zheng B et al. Molecular epidemiology of the novel coronavirus that causes severe acute respiratory syndrome. Lancet. 2004 Jan 10;363(9403):99-104.

Synopsis: The epidemic of severe acute respiratory syndrome (SARS) has resulted in much morbidity and mortality across the territory and worldwide in early 2003. SARS coronavirus (SARS-CoV) samples from early 2003 are now providing new insights about patterns of spread of this disease. Investigators recently analysed 138 viral isolates from Hong Kong (collected from February through March 2003) and 3 from Guangdong (collected in February 2003). They examined total RNA and sequences obtained by direct reverse transcriptase-PCR amplification, focusing on the S1 gene fragment. Phylogenetic comparisons of these sequences, and of 27 others downloaded from public databases, showed 2 distinct clusters. Cluster A comprised 7 isolates from Beijing and Guangdong patients, plus 3 from Hong Kong patients who had recently travelled to Guangdong. All other viruses from Hong Kong were genetically similar to the virus from a Hong Kong index patient who had arrived from Guangdong in late February, and they fell into cluster B. Cluster B also included viruses from Vietnam, Singapore, Taiwan, and Canada. Two isolates from the Amoy Gardens outbreak showed no significant genetic variations when compared with other SARS-CoV, leading to speculation that the explosive spread within this apartment block resulted from route of transmission rather than differences in the virus. Virus isolates from mainland China showed greater genetic diversity, suggesting that SARS-CoV has been circulating longer there. These results suggested that several independent introductions of SARS-CoV from mainland China into Hong Kong had occurred during February. Apparently, a single introduction was associated with spread in Hong Kong and several other countries.

and auramine O stain of the CSF were negative for organisms. Bacterial, fungal, viral and mycobacterial cultures of CSF were negative. Molecular studies by polymerase chain reaction for herpes simplex virus and *Mycobacterium tuberculosis* were also negative. CSF and serum for Venereal Disease Research Laboratory titre were non-reactive.

He was treated with intravenous acyclovir and phenytoin on the day of admission. Cloxacillin was later added for the management of hospital-acquired methicillin-sensitive Staphylococcus aureus pneumonia. His convulsion was brought under control and he was successfully weaned off the ventilator in one week's time. Cloxacillin and acyclovir were continued for a total of 2 weeks. His condition improved noticeably and he was discharged after 2 weeks' hospitalization. Chest X-ray cleared up in 2 weeks. Repeat of EEG 3 months after discharge still showed some residual slow wave activities over right temporal region, but was considered less prominent compared to his previous EEG. Phenytoin was continued.

There was no significant elevation of serological titers in his convalescent sera for Japanese encephalitis virus, influenza B virus, mycoplasma, herpes simplex virus, enterovirus or varicella zoster virus. Dengue IgM antibody was negative. Influenza A serological titre by complement fixation method increased from 20 to 40. Cultures of throat swab, stool, sputum, urine and CSF gave no evidence of bacterial or viral infection. Enzyme immunoassay for human immunodeficiency virus was negative.

Discussion

Southern China has long been regarded as the epicenter for the emergence of potentially pandemic influenza virus. Evidence has shown that the viruses that caused pandemics of H2N2 influenza in 1957, H3N2 influenza in 1968, H1N1 influenza in 1977 and the recent outbreaks of H5N1 and H9N2 in 1997 and 1999 respectively all originated from this region. As a result of the proximity of human being and wild animals or poultry, especially in Southeast Asia, viruses which are common in animals can jump to human, causing a great catastrophe. The H5N1 influenza virus is a good example to demonstrate this scenario. Countries in Southeast Asia are currently still fighting hard to combat this virus and hitherto 22 lives were lost. The Fujian type of H3N2 that spread throughout North America and Europe also caused significant mortality. The most effective armamentarium in preventing influenza is vaccination. Unfortunately, side effects from vaccine appear from time to time.

Postvaccinal encephalomyelitis is a recognized complication of several vaccines including smallpox, hepatitis B, Japanese encephalitis and rabies. However only few case reports were published on the side effect for influenza vaccines and most cases were children (1-4). Even World Health Organization (WHO) has not considered encephalitis a possible sequelae for influenza vaccine in their latest report on vaccine safety. Although we could not be absolutely certain that our patient suffered from merely side effect of influenza vaccination, since there are multitudes of viruses including influenza virus that could also cause encephalitis in this gentleman, the rapid onset of disease and the temporal relation seem to suggest that the first explanation is more likely. Actually the usual time interval between influenza vaccine inoculation and onset of neurological symptoms is not defined. It varies from a few hours to 2 weeks in different reports (1-4), while it was 1 week in our patient. An underlying immunopathogenetic mechanism was proposed (2-4). Hypersensitivity to egg protein is regarded as an important trigger of abnormal immunologic reactions (1) although our patient is not egg protein-allergic and his eosinophil count was normal. However, one can never prove or disprove the existence of this side effect since its incidence is so low. Other possible inactivated influenza vaccine related neurological problems include Guillian-Barré syndrome, delirium, optic neuritis, brachial neuritis and cranial palsies (5). Recently, the newly introduced inactivated intranasal influenza vaccine has also been found to be associated with increased risk of Bell' s palsy (6). Together with the reservation on the effectiveness of the existing flu vaccine combination on the circulating Fujian strain of influenza A H3N2, vaccine safety and informed consent advocates challenged the government on the vaccine recommendation (7).

In the other extreme, however, flu vaccine has become a fashion in many nations and many people are its ignorant believers. In a developed city like Hong Kong, one can easily consult a private practitioner for an injection at an affordable cost. Particularly, after being hit hard by SARS, people in Hong Kong, as well as in other parts of the world, have become more health-alert. Moreover, because of the similarity in symptomatology between influenza and SARS, WHO has suggested to offer flu vaccination to those at-risk population so as to avoid confusion and wrong cohorting. The same also applies to H5N1 since the existing inactivated trivalent vaccine does not confer protection to this avian flu. Therefore many people will treat flu vaccine as an indispensable tonic. The latest meeting of the Advisory Committee of Immunization Practices of the Centers for Disease Control and Prevention also suggested to move from "encouragement" to "recommendation" of flu vaccination for children 6-23 months of age, besides the usual recommendation for the at-risk population, suggesting that more and more people will become vaccinated (8). Beyond doubts, flu vaccination is efficacious in preventing influenza-like illnesses and reducing hospitalization and mortality caused by the circulating virus, especially in the elderly. However, it has to be reiterated that influenza vaccine is not a risk-free energizer. The current case illustrates that people should be given the correct information and be warned about the potential side effects despite their rarity before the vaccine inoculation. Informed consent should be signed by the vaccinees. The government should educate, recommend and inform the public not only on the beneficial effect of vaccination, but also on its adverse reactions.

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Tuberculosis meningitis

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Introduction

It is not uncommon to diagnose patient with tuberculosis meningitis, especially in Hong Kong. However, from time to time the diagnosis is often missed or only confirmed when complication emerged. Here, we present a case of tuberculosis meningitis, followed by a literature review.

The case

A 72 years old gentleman was admitted to a local hospital in August 2003. His initial complaint was intermittent chest discomfort and fever for two days. He had an arduous trip to the Scandinavia one month ago and stayed there for two weeks. He had a past medical history of hypertension, diet controlled diabetes mellitus and had a right hemicolectomy for carcinoma of the ascending colon 5 years ago. Electrocardiograph and cardiac enzyme were both unremarkable. Complete blood picture, renal and liver function tests were normal. Septic workup was carried out and he was empirically started on oral ciprofloxacin. The patient continued to have a low-grade fever and dev7eloped mental confusion four days later. Initial septic workup including blood culture and mid-stream urine were negative. Weil-Felix and Widal tests were also negative. Urgent computerized tomography (CT) of the brain revealed periventricular ischaemia. Antibiotics later changed to maxipime and vancomycin. Nevertheless, his fever persisted and his mental state worsened. Finally, a lumbar puncture was performed ten days after the onset of confusion. Lumbar puncture result revealed a total cell count of 256 with lymphocyte predominant. Protein was more than 6 and glucose was 7.7 (serum glucose 13.4). Cryptococcal antigen was negative. Glascow Coma Score fell from 14 to 3 after the lumbar puncture. Urgent CT brain revealed hydrocephalus and ventricular shunting was carried out. Chest x-ray showed evidence of active pulmonary tuberculosis in the right upper lobe. Review of the old medical notes revealed that the patient had a sputum culture positive for *Mycobacteria tuberculosis* two years ago. The treatment detail was uncertain. He was promptly started on antituberculosis therapy, including isoniazid 300mg daily, rifampacin 600mg daily, pyrazinamide 1250mg daily and ethambutol 800mg daily, together with pyridoxine 10mg daily. Subsequent sputum smear was positive for acid fast bacilli and culture positive for *Mycobacteria tuberculosis*. The CSF was culture negative for *Mycobacterium tuberculosis*. The patient unfortunately suffered from long-term sequel with ataxia and impaired cognitive function as a result.

Discussion

The pathogenesis of tuberculosis meningitis is believed to be either secondary to rupture of a subependymal tubercle into the subarachnoid space or haematogenous spread. The foci may remain quiescent before rupturing and may follow depression of host immunity. It may also develop several weeks after the onset of miliary tuberculosis.

Meningeal involvement is most pronounced at the base of brain. Vasculitis may involve perforating vessels to basal ganglia and pons. It may lead to aneurysm, thrombosis or haemorrhagic infarction. Involvement of middle cerebral artery may cause hemiparesis. In chronic cases, fibrous tissue may encase the cranial nerves.

The patient may present with malaise, intermittent headache, low grade fever, protracted headache with meningismus, vomiting, focal neurological signs or confusion. Fever may be absent. Other laboratory features include mild anaemia, and hyponatraemia. Peripheral white cell count is usually within the normal range. Abnormal chest radiograph may help to clinch the diagnosis. CSF examination usually shows cell count in the range of 0 to 1500/mm^3 with lymphocytic predominance. Protein level is usually moderately elevated. Glucose level is characteristically low. Stains of sediment revealed acid fast bacilli in around 40% of the cases on examination. Nucleic acid amplification examination for *Mycobacterium tuberculosis* may be very helpful in confirming the diagnosis. CT or magnetic resonance imaging (MRI) of the brain may be normal or reveal round lesions of tuberculoma. It may show basilar arachnoiditis, cerebral infarction or hydrocephalus. Formation of hydrocephalus in tuberculosis meningitis is believed to be due to blockade of the CSF pathway or impaired CSF absorption.

Treatment of tuberculosis meningitis includes a four drugs regimen of isoniazid 300mg daily with pyridoxine 10mg daily and rifampicin 450mg (weight < 50kg) to 600mg (weight > 50kg) daily for twelve months, pyrazinamide 1.5g (weight < 50kg) to 2g (weight > 50kg) for three months and ethambutol 15mg/kg for 5 months. Ethionamide may substitute for ethambutol. Adjunctive corticosteroid for the first month has been shown to decrease complications. Ventricular shunting should be carried out on patients with symptomatic hydrocephalus.

A local study by Chan KH et al analyzed the clinical relevance of hydrocephalus as a presenting feature of tuberculosis meningitis (1). Thirty-one patients with tuberculosis meningitis were reviewed between January 1997 and September 2001. 29% had hydrocephalus at presentation. Eight of them underwent urgent neurosurgical intervention. Hydrocephalus at presentation was associated with a longer duration of presenting symptoms (p=0.01), ataxia (p=0.001), later stages of tuberculosis meningitis (p=0.045), longer delay before commencement of anti-tuberculosis chemotherapy (p=0.001), stroke (p=0.012) and poor outcome at 1 year (p=0.001)

A recent study investigated the diagnosis of adult tuberculosis meningitis by use of clinical and laboratory features (2). It compared the clinical and laboratory features of 251 adults at an infectious disease hospital in Vietnam. 143 of them have tuberculosis meningitis and 108 have bacterial meningitis. Features independently predictive of tuberculosis meningitis were modeled by multivariate logistic regression to create a diagnostic rule and by a classification tree method. Five features were predictive of a diagnosis of tuberculosis meningitis, including age (<36), length of history (>6 days), white cell count (< 15000/mm^3), and CSF neutrophil proportion (<75%). An index score ≤4 suggested tuberculosis meningitis. A score of >4 suggested bacterial meningitis instead. When this scoring system was applied prospectively, it has a 86% sensitivity and 79% specificity respectively. This can be used in settings with limited clinical resources especially in the developing countries.

Another study investigated the diagnostic accuracy of nucleic acid amplification for tuberculosis meningitis by systemic review and meta-analysis (3). The authors searched six electronic databases. 14 studies by commercial nucleic acid amplification tests demonstrated a sensitivity of 0.56 (95% CI 0.46, 0.66), specificity 0.98 (0.97, 0.99), and odds ratio 96.4 (42.8, 217.3). The study established the potential role in confirming tuberculosis meningitis. However the low sensitivity precludes the use to rule out tuberculosis meningitis.

All in all, tuberculosis meningitis is becoming more common. One should always suspect this diagnosis when the patient presented with clinical features of meningitis. Past medical history, chest radiograph and the diagnostic scoring system may help in clinching the diagnosis before complications arise so that prompt treatment can be given.

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ID journal scan March 2004

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(1) Naimi TS, LeDell KH, Como-Sabetti K et al. Comparison of community- and healthcare-associated methicillin-resistant Staphylococcus aureus infection. JAMA. 2003 Dec 10; 290(22): 2976-84.

Synopsis: Community acquired methicillin-resistant Staphylococcus aureus (MRSA) infection is becoming increasingly common in the US. A group of researchers from the Minnesota Department of Health recently conducted a prospective cohort study comparing community acquired MRSA (CR-MRSA) and hospital or healthcare associated MRSA (HA-MRSA). During the year 2000, the researchers prospectively collected clinical data and patient information on 1100 MRSA isolates identified at 12 microbiology laboratories in Minnesota (approximately 25% of all S. aureus infections determined at these facilities). A total of 131 isolates were identified as CR-MRSA, whereas 937 were classified as HA-MRSA. As compared to HA-MRSA patients, CA-MRSA patients were younger, were more likely to be nonwhites, and had a lower median household income. CA-MRSA infections, as compared to HA-MRSA infections, were more likely to be skin and soft-tissue infections as opposed to respiratory or urinary tract infection; CA-MRSA isolates were also more likely to be susceptible to antibiotics such as ciprofloxacin, clindamycin, erythromycin, and gentamicin. Molecular typing showed that 76% of CA-MRSA isolates belonged to 2 clonal groups, and 80% of HA-MRSA isolates to a third group. Panton Valentine leukocidin (PVL) genes were found in 77% of tested CA-MRSA isolates, but in only 4% of HA-MRSA isolates; this might account for the increased propensity for skin and soft tissues infections caused by CA-MRSA. CA-MRSA isolates were more likely to carry the SCCmec IV allele of the mecA gene; and HA-MRSA, SCCmec II. The authors concluded that these CA-MRSA strains appeared to have arisen from the insertion of a mecA gene into a community methicillin-susceptible S. aureus strain. In treating severe community associated Staphylococcal infections not responding to empirical therapy, the possibility of MRSA infection should be considered.

(2) Robbins GK, De Gruttola V, Shafer RW et al. Comparison of sequential three-drug regimens as initial therapy for HIV-1 infection. N Engl J Med. 2003 Dec 11; 349(24): 2293-303.

Synopsis: The optimal sequencing of antiretroviral regimens for HIV infection is currently unknown and remains a challenging aspect in care of HIV infected patients. In a large, randomised study conducted in the U.S., researchers at Harvard Medical School assessed the overall benefit of starting therapy with a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI), as well as the performance of 2 different nucleoside reverse transcriptase inhibitor (NRTI) backbones. In this multi-centre trial, treatment-naive individuals were randomly assigned one of four 3-drug initial regimens, including stavudine (NRTI) and didanosine (NRTI) plus either efavirenz (NNRTI) or nelfinavir (PI); zidovudine (NRTI) and lamivudine (NRTI) plus either efavirenz or nelfinavir. Patients who experienced either virologic failure or treatment-limiting toxicity were switched to the converse regimen (i.e., the regimen containing none of the same drugs). A total of 620 patients with a median CD4 count of 280 cells /mm^3, and a median viral load of 4.9 log copies/ml, were enrolled in the study. Endpoints of the study included time