

HIGHLIGHTS from ECCMID 2011 ABSTRACTS FOR MEDIA

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DISEASE BURDEN AND TRENDS

NDM-1 superbug gene is highly mobile and spreading fast

The notorious superbug NDM-1, first identified in New Delhi, India, is an enzyme that confers resistance to a broad range of antibiotics. Worryingly, the NDM-1 gene is highly mobile, according to a new study of the five NDM-1 enterobacteria isolates (variations) in Belgium which shows that NDM-1 exists alongside other resistance genes, in different species, and possibly on the chromosome of unrelated species isolates. In addition, multiple resistance genes were associated with NDM-1. NDM-1 is rapidly spreading worldwide mostly from the Indian subcontinent - two patients had no link with the Indian subcontinent but received hospital care in Balkan countries.

[Abstract 958: Characterization of the first NDM-1 producing Enterobacteriaceae in Belgium]

Dangerous form of MRSA spreading through Europe

A particular form of MRSA that scientists are worried about is characterized by PVL, short for Panton-Valentine leukocidin, which is a toxin produced by Staphylococcus bacteria. In the USA, one PVL-MRSA clone called USA300 has reached epidemic proportions in North America, effectively marginalising other MRSAs. Researchers have mapped the spread and dynamics of PVL-positive MRSA in England between 2007 and 2010. PVL-MRSA increased 1.5-fold, going from 477 in 2007 to more than 900 in 2010. At least 10 different lineages of PVL-MRSA were identified, three of which were dominant: European, South West Pacific and USA300 clones. In 2009, USA300 became the major PVL-MRSA clone in England, displacing the European clone which dominated in 2007 and 2008. USA300 strains were typically resistant to erythromycin with variable resistance to ciprofloxacin; the European clones were resistant to tetracycline and fusidic acid. The number of cases due to the multiply-resistant Bengal Bay clone (ST772-V) increased 6-fold from 10 in 2007 to 61 in 2009. Overall, most PVL-MRSA infections were community-acquired and sporadic in nature, although occasional clusters involving transmission of PVL-MRSA in community and healthcare settings were identified.

[Abstract 2993: Changing trends in the epidemiology of PVL-MRSA in England]

High rates of E coli and drug resistance in South American chicken

Imported meat is a worrying source of E coli infection, since exporting countries may be less rigorous with quality control than the countries they are importing to. A survey of frozen chicken meat imported into Sweden showed that 92% of meat from South America had E coli, compared with 19% for meat from elsewhere in Europe. E coli from both regions had some level of antibiotic resistance, but bacteria from South American meat were resistant to a wider range of antibiotics and had more genes for antibiotic resistance compared to the bacteria from European meat. E coli from Danish meat were the most susceptible to antibiotic treatment.

[Abstract 1279: High prevalence of ESBL-producing Escherichia coli in chicken meat imported into Sweden]

Specific variations in streptococcal pneumoniae bacteria linked to penicillin resistance

The bacteria streptococcus pneumoniae is a major cause of acute otitis media and invasive infections such as pneumonia, blood-stream infections and meningitis. Like all bacteria, there are different variations (or serotypes), and understanding the links between serotype and disease can help with the formulation of new anti-pneumococcal vaccines, and with monitoring bacterial resistance to penicillin. The most frequently isolated serotype was 14 in both acute otitis media and invasive infections. Serotypes 19A, 9V, 19F and 3 were isolated more frequently in acute otitis media than in invasive infections. 14, 19A, 6A, and 9V were most linked to penicillin resistance.

[Abstract 2081: Serotype distribution of Streptococcus pneumoniae isolated from Argentinian pediatric patients.]

COMMUNITY-ACQUIRED INFECTIONS**Lessons from vaccinating healthcare workers against H1N1 could help prepare for the next pandemic:**

Health experts who were trying to encourage the public to get vaccinated against H1N1 flu during the 2009 pandemic faced the awkward fact that some healthcare professionals did not want to be vaccinated themselves. The reasons behind this were varied, but according to this survey, two key factors in ensuring that staff got vaccinated were being included in interactive informative meetings at their institutions, and the credibility of national health policies. The survey of physicians and nurses interviewed a tertiary-care university hospital also showed that healthcare workers who had received the seasonal flu vaccine in the previous year and used the Internet as their main source of information were also more likely to take the H1N1 vaccine.

[Abstract 2655: Vaccination against pandemic influenza A/H1N1(2009) among health care workers: lessons for the next pandemic.]

Portuguese public buses are rife with MRSA, suggesting that community control is needed

Portugal has the highest prevalence of hospital-associated MRSA (methicillin-resistant Staphylococcus aureus) in Europe at over 50%. It is usually transmitted via direct human-to-human skin contact, but S. aureus can survive for long periods on inanimate objects, such as handrails, which can also spread the infection. A study of 85 public city buses in Oporto, Portugal, showed that 22 buses had MRSA contamination. The strain found most often was the pandemic strain EMRSA-15, currently the major strain circulating in hospitals in Oporto, suggesting that the strain is escaping from hospitals to the community environment. Infection control measures are urgently warranted to limit the spread of EMRSA-15 to the general population and avoid a massive increase of MRSA in the Portuguese community, which so far remained low.

[Abstract 2045: High prevalence of EMRSA-15 in Portuguese public buses: a worrisome finding]

Gastroenteritis bugs in children becoming highly drug resistant

The bacteria that cause bacterial gastroenteritis are becoming increasingly resistant to antibiotics, according to a 7-year study in a children's hospital in Athens, Greece.

Worryingly, some of the most common bacteria have gone from not being resistant at all to being highly resistant in a short space of time - from early 2003 to late 2009.

Salmonella and Campylobacter jejuni were the most common stomach bugs, and both are increasingly developing resistance. For instance resistance of Salmonella to ampicillin went from 2.5% to 23.9%, and to clotrimoxazole, from 1.7% to 10.9%. The resistance of C. jejuni to ciprofloxacin went from 0% to 63% and to tetracycline from 0% to 45.7%. All Salmonella isolates were found susceptible to cefotaxime, and all C.jejuni strains were found susceptible to erythromycin.

[Abstract 1291: Epidemiologic study of bacterial gastroenteritis in Greek children (2003-2009)]

INFECTION SURVEILLANCE**Facebook and twitter can help monitor infectious disease outbreaks**

Social networks such as Facebook and Twitter can spread gossip like wildfire, but they can also disseminate vital news that can help with disease surveillance. Standard surveillance for infectious disease outbreaks means monitoring various indicators such as the symptoms that patients exhibit. A research team studied a recent community outbreak of Norovirus at a German university to determine if news articles and information posted to Facebook, Twitter and blogs were faster than reporting through established indicator-based surveillance. They found that these social media picked up and discussed the news quicker than the rest of the news media. Since social media are interactive, they facilitated information exchange about the event. Other surveillance and reporting is clearly still important, but investigating social media may help picking up potential outbreaks.

[Abstract 592: Social media and infectious disease surveillance: tweets indicate Norovirus outbreak at a university.]

Infectious disease database offers network for monitoring drug resistance

The Dutch Infectious Diseases Surveillance Information System on Antibiotic Resistance (ISIS-AR) and its interactive database, ISISweb, was developed to monitor trends in antimicrobial resistance. It links 27 medical microbiology laboratories to an open central database, where antimicrobial susceptibility test results and epidemiological data from 40 bacterial species are uploaded monthly. This can tell professionals and policymakers that, for instance, that between 2008 and 2010, the prevalence of MRSA (methicillin-resistant staphylococcus aureus) remained stable around 1%. On ISISweb, data can also be viewed and compared by institution type, hospital department and age groups. The system's success suggests it could be extended to track other bacteria or viruses.

[Abstract 2563: ISIS-AR and ISISweb: a new surveillance system for antimicrobial resistance surveillance.]

Tracking antibiotic resistance along the Silk Road

Even the most remote areas of the globe, from the Tibetan plateau to the Gobi desert, harbours drug-resistant bacteria, according to a study of wild animals living along the Silk Road. The Silk Road, an ancient trading route that connected Asia with Europe and Northern Africa, is home to several mammal species, many of which are near extinction.

Scientists analysed bacteria in faecal samples from five iconic mammal species (Mongolian wild ass, Przewalski horse, Grey marmot, Bactrian camel and Dhole) and found a high incidence of antibiotic resistance genes in the bacteria. The resistance was to key antibiotics used to treat human disease such as erythromycin, ciprofloxacin, gentamicin, and ampicillin. This surprising level of antibiotic resistance in animals living in such remote regions show just how extensive the spread of resistance is, and therefore, the importance of using antibiotics prudently.

[Abstract 2955: Tracking antibiotic resistance along the Silk Road]

NEW TECHNOLOGIES

Nanosensor could stop drug resistance by offering personalised antibiotics courses

The emergence of “superbugs” such as methicillin-resistant *Staphylococcus aureus* (MRSA) is proof of the growing threat of antibiotic resistance, largely caused because antibiotics are overused or used inappropriately. Faced with a shortage of new antibiotics in the drug pipeline, existing antibiotics need to be used prudently to avoid fuelling resistance. One way of doing this is to ensure that precise doses of drugs are given to patients, but determining this dose depends to some extent on the way that an individual’s biochemistry processes the drug. Scientists have now developed a new nanosensor that can measure drug concentrations circulating in the bloodstream, and can also look at how well the drug latches on to the bacteria. This could mean that patients might one day be given a personalized course of antibiotics that is optimal for their body.

[Abstract number 415: Nanosensors for antibiotic discovery and therapeutic drug monitoring in real time]

Better tests for Lyme disease means quicker diagnosis

Doctors may now be able to spot Lyme disease in its very early stages. This is important because if left untreated, the tick-borne disease can affect the heart and central nervous system, and the joints. Until now, laboratory tests have not reliable enough to spot antibodies against the bacteria in blood samples in the early stages. Scientists investigated a new diagnostic test that extracts the DNA of the Lyme *Borrelia* bacteria from a blood sample, and amplifies it to a large enough quantity to be detected. They used the test on patients who had the tell-tale circular red rash associated with Lyme disease, and who had been run through the usual antibody tests. The DNA test spotted the bacteria in about two-thirds of patients. Crucially, the DNA test picked up two-thirds of Lyme disease cases that had initially seemed negative with the standard antibody test.

[Abstract 2929: Direct Detection of Early Lyme Borreliosis from Whole Blood]

Speedy diagnosis offers relief for ringworm sufferers

A speedy method of analyzing the fungus that causes the skin infection ringworm could mean patients get a diagnosis in days rather than weeks, and have treatment that stops it spreading. Ringworm, or dermatophytosis, is common in the general population, and one in five people are estimated to have the infection. The new technique, tested on thousands of samples, relies on identifying the DNA of different fungal species that cause ringworm.

[Abstract 3799: A clinical evaluation of two novel PCR based analyses for the diagnosis of dermatophytosis in skin and hair]

NEW TREATMENTS

Can Salmonella cure cancer?

Mutated Salmonella bacteria have shown promise as an experimental treatment for cancer. The mutant bacteria are strongly drawn to dying, tumorous regions of the body, destroying tissue that is inaccessible to conventional chemotherapeutic drugs. Researchers tested a new mutant on mice with cancer. When the mice were given enough of the bacteria to destroy the tumour, the animals died too. Lower doses reduced the tumour but didn't eliminate it totally, which suggests that more experiments are needed to fine-tune dosage.

[Abstract 1005: Can Salmonella cure cancer? Insights on a novel antitumoural mutant]

Two-step antibiotic treatment for E coli could eliminate fatal side-effects of regular treatment

Treating Escherichia coli O157:H7, which causes severe gastroenteritis, can be complicated. The very antibiotics used to treat the E coli can induce a potentially fatal condition called haemolytic uremic syndrome (HUS), which causes anaemia and severe kidney failure. The production of toxins called 'Shiga-like toxins' are thought to be key to the development of HUS. Researchers have now shown that a two-step treatment which first reduces these toxins with the antibiotic rifampicin, and then eradicates the E coli bacteria with gentamicin can be effective. 50% of E coli infected mice treated with both antibiotics survived, compared with 0% treated only with gentamicin and 25% treated with rifampicin only.

[Abstract 1586: Evaluation of combinational antimicrobial treatment using rifampicin and gentamicin for Escherichia coli O157:H7 in vitro and in vivo in BALB/c mice.]

A single high dose of treatment for leishmaniasis works as well as a multiple course

The usual treatment for visceral leishmaniasis is a multiple course of liposomal amphotericin B spread over several days (3 mg/kg bodyweight/day at days 1–5 and 10 in the Mediterranean; 2 mg/kg/day for 5 days in India). Two recent case studies, a 35-year-old Angolan man and a 20-year-old Afghan man, were treated with a single dose of 10 mg. Subsequent tests showed that they had no blood or liver toxicity, which suggests that a single high dose could be used instead of a long course. In addition, a single dose is cheaper than conventional therapy (2058 Euro vs 3740 Euro).

[Abstract 3566: Two cases of Visceral Leishmaniasis treated with a single-dose of Liposomal Amphotericin B]

Primate studies show potential treatment for ebola and Marburg viruses

Zaire Ebola virus and Marburg virus are both highly virulent and cause severe haemorrhaging, vomiting, bloody diarrhoea, and later, multiple organ failure and death. There are currently no antivirals or preventative medicines for these deadly diseases. A new class of drugs called phosphorodiamidate morpholino oligomers (or PMOplus) were tested on nonhuman primates infected with the viruses.

60% of ebola-infected animals treated with a PMOplus called AVI-6002 survived to the end of the 28-day study period, whereas all the animals not treated died within 8 days. All

Marburg-infected animals treated with a high dose of AVI-6003 survived to the end of the study, and 60% of those treated with a lower dose of AVI-6003 survived. Early DNA analysis suggests that neither virus developed resistance to the drugs.

[Abstract 3670: PMOplus™ Antisense Oligomers Protect Nonhuman Primates Against Ebolavirus and Marburgvirus]

Antimicrobial peptide could treat MDR cystic fibrosis

In cystic fibrosis (CF), lung infections are often caused by multidrug-resistant (MDR) bacteria. Not only that, the excess mucus present in the lungs of people with cystic fibrosis create bacterial microenvironments called biofilms which also hinder antibiotic therapy. Researchers have found that a group of peptides called 'bovine myeloid antimicrobial peptides' cleared bacteria species such as *Staphylococcus aureus* that commonly infect CF lungs. So far, these experiments have been done under lab conditions that simulated a CF lung environment (in a 5% CO₂ atmosphere and using a synthetic medium that mimics the nutritional composition of CF sputum). The next step will be to test the peptides in animals.

[Abstract 1447: In vitro bactericidal and anti-biofilm activity of bovine myeloid antimicrobial peptides against multidrug-resistant bacteria from patients with cystic fibrosis.]

TUBERCULOSIS

Simpler test could reveal hidden TB

The TB bacterium stays hidden in the lungs of one in three of us. This latent TB is estimated to develop into full-blown diseases about 10% of the time, so diagnosing it is important. Existing tests to detect latent TB measure an immune protein called interferon gamma (IFN-gamma), which is triggered in response to the TB bacterium. But measuring this requires a highly-sensitive test and a laboratory close to the patient, or cooling or freezing capacity during transportation of the samples. These requirements can hamper diagnosis especially in developing countries. Researchers have come up with a way around this. They measured another immune protein called IP-10 that is released alongside IFN-gamma and therefore as reliable an indicator of latent TB. Since the volume of IP-10 released is about a 100 times that of IFN-gamma, detecting it is easier and it can be detected on blood samples dried on filter paper. More than 90% of IP-10 dried on filter paper was recovered after more than 9 weeks storage at room temperature, or 4 weeks at more than 37C. This means that diagnosis can be done by sending the filter paper through the post.

[Abstract 2645: IGRAs on paper - Specific diagnosis of latent TB sent via mail]

TB and HIV are strongly linked in Thailand

Although it is a major public health threat in many cities, especially in developing countries, the clinical situation of TB in large cities of Thailand has not been well established. This study looked back at hospital records of TB patients in Bangkok and Nonthaburi during 2008. 38% of patients also had HIV (TB and HIV co-infection is common worldwide) and 6% also had diabetes. Drug resistance to antibiotics was common – 11% to isoniazid, 6% rifampicin, and 5% had multi-drug resistance. People

with HIV only had an 81% chance of being alive after 2 years. Better management and collaborative treatment is needed to improve TB services.

[Abstract 1470: Clinical Characteristics and Treatment Outcomes of Tuberculosis in Hospitals of Two Large Cities in Thailand]

World's largest TB gene study shows high levels of drug-resistance and HIV co-infection

A study of more than 5000 people in Russia has led to the creation of a “biobank” of human DNA samples from people with TB, TB strains, and associated clinical and demographic information. The aim will be to scan the entire human and TB genomes to identify major genetic factors in people that make them susceptible to TB, and also to investigate the way the TB bacterium interacts with its human host.

This genetic analysis is ongoing, but the scientists involved already understand some of the disease dynamics. For instance, a quarter of patients had a history of imprisonment, 16% used drugs recreationally, and 17% abused alcohol. Almost half of participants (46%) were unemployed. 17% were HIV-positive compared to 4% in a 2005 study. 50% of cases were MDR (multidrug resistant) and 9% XDR (extensive drug resistant). In 2002, there had been no cases of XDR TB at all.

[Abstract 1339: Genetic analysis of the host-pathogen interaction in tuberculosis (“TB-EURO-GEN”) study – progress and current tuberculosis epidemiology]

Anti-psychotic drug could treat highly drug-resistant TB

A tranquilizer used to treat psychiatric patients seems to be effective against MDR (multidrug resistant) and extensive drug-resistant (XDR) TB. To get an overview of the evidence, researchers analyzed several studies on the use of the drug, called thioridazine, on drug resistant TB. The studies were a mix of laboratory tests on bacteria, in a MDR-TB mouse model, and records from the treatment of XDR-TB patients. At high concentrations of 15 to 20 mg/L the drug stopped the bacteria from replicating in the lab, but these concentrations are much too high to use on people. But even concentrations as low as 0.1 mg/L (below that used in psychiatric disorders) can kill MDR and XDR strains.

Thioridazine also cured mice infected with both antibiotic-susceptible and multidrug-resistant strains of TB. Crucially, however, the drug works in people – 10 out of 12 patients with XDR-TB were cured within a few months after treatment with thioridazine in combination with three anti-tuberculous drugs. Thioridazine is cheap, has been in use for more than four decades, and the doses anticipated for therapy of tuberculosis are far smaller than those used for chronic therapy of psychiatric disorders (5 to 75 mg/day vs 600 to 1000 mg/day), which minimises the risk of cardiac toxicity, which is a potential side-effect.

[Abstract 2044: In vitro, ex vivo and in vivo studies indicate that the neuroleptic thioridazine cures multidrug resistant tuberculosis.]

DISEASE MECHANISMS

Human papillomavirus behaves differently in men and women

Human papillomavirus (HPV) is a risk factor for cervical and anal cancer. Sometimes the virus clears up spontaneously (ie, without treatment), and a new study looked at which HPV strains were more likely to clear up than others over the course of a year. The researchers analysed cervical samples from healthy women and anal samples from men who had poor immune systems. They found that different strains of HPV were present in men and women, and with one exception of a strain called HPV-31, the virus tended to linger for much longer in the men than in the women. Since HPV-31 spontaneously cleared much more often from anal samples from immunodeficient patients than in female cervical samples, it could suggest that this strain has a different mechanism of persistence in the body or triggers a different response from the immune system. The genotype that seems to persist in a higher proportion of cases is HPV-11, a low-risk type, instead of HPV-31, a high-risk type. Further evaluations are needed to assess whether these differences are primarily due to the different type of mucosal tissue (in the anus compared with the cervix) or to the different degree of immune response.

[Abstract 1287: Different rates of spontaneous clearance of HPV infections in anal and cervical lesions.]

MDR TB

MDR TB (multidrug-resistant tuberculosis), in which the tuberculosis bacterium resists antibiotics like isoniazid and rifampicin, is becoming a major barrier to treating the disease. The tuberculosis bacterium has miniature efflux pumps that shunt out antibiotics, and one theory for how it develops resistance is that the pump genes are mutated so that the pumps go into overdrive and therefore the bacterium can ward off the antibiotic. Researchers were able to confirm through DNA analysis that the pump genes in bacteria resistant to isoniazid were more heavily activated than normal. They also found that pump inhibitors were able to reverse resistance, so that the antibiotics worked again. Although rifampicin resistance didn't cause any phenotypic or genotypic changes in the bacteria, bacteria that were resistant to isoniazid also then became resistant to rifampicin after enough exposure, leading to MDR strains.

[Abstract 2149: Phenotypic adaptation to isoniazid in Mycobacterium tuberculosis: a pathway to multidrug resistant tuberculosis]

Getting closer to understanding the genetic basis of drug resistance in Staphylococcus strains

Understanding the genes that help bacteria to resist antibiotics goes some way to developing ways to counter that drug resistance. Researchers studied the genes of Staphylococcal strains that can resist the antibiotic vancomycin to tease out bacterial gene mutations that seemed to trigger resistance. They found several mutations that were linked to antibiotic resistance, but their most interesting discovery was finding that in some resistant strains, a bacterial gene called *stp1* was entirely deleted. When this gene was reinserted in the bacteria, it was susceptible to vancomycin.

[Abstract 2389: A novel mechanism of reduced susceptibility to vancomycin in Staphylococcus aureus]