DISEASE SURVEILLANCE

Clinical epidemiology of nosocomial infections - Deaths vary across treatment centres

Analysis of five independent, national studies of mortality from *Staphylococcus aureus* bloodstream infection (bacteraemia) has been carried out with the aim of establishing why the number of deaths varies widely in the prior research findings.

Data relating to 3,394 adult patients treated in 20 centres (15 in the United Kingdom, two in Spain and one in the USA) and consisting of details of demographic variables, community or healthcare location at the onset of infection, antibiotic susceptibility and source of infection was examined. Predictors of mortality by days seven, 14, 30, and 90 were assessed.

The researchers found a median patient age of 64 years, that 40.7% of bacteremias were nosocomial (acquired in hospital), 20.6% were with methicillin-resistant aureus (MRSA) and 28% were due to intravenous catheters, which was the commonest source of bacteraemia. However, these variables differed significantly between centres.

The study found 28.3% of patients died within 90 days, with old age and the source of bacteraemia independent predictors of death and the greatest risk factor an unidentified source. Mortality was also independently associated with centre, particularly within 14 days of the first positive blood culture.

Conclusions reached were that age, the source of infection, the susceptibility of the infection to the antibiotic methicilllin and the treatment centre were all independently associated with patient outcomes in *S. aureus* bacteraemia.

The researchers said the role of the treatment centre in success or failure in treating patients with bacteraemia may be explained by unrecorded differences in disease severity and comorbidities, but differences in patient management may contribute.

Further research will be required to understand why mortality varies between centres and to better define the optimum treatment of *S. aureus* bacteraemia.

[Abstract 3,303: Mortality in bacteraemic Staphylococcus aureus infection: a pooled analysis of five national prospective hospital-based cohort studies]

Family members share patient infections

A study has found a close relationship between colonisation of patients and their family members by extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae. ESBL is an enzyme that provides resistance to a range of commonly-used antibiotics.

The study also found cross-colonisation between patients and healthcare workers is rare.
Research was carried out in five rehabilitation centres – two in Israel and the remainder in Rome, Berck, France, and Barcelona. Rectal swabs were used to establish whether ESBL-PE was present in 286 family members of 194 patients identified as carriers.

The study of healthcare workers examined 73 physicians, 288 nurses, 179 nurse assistants, 205 physical therapists, 37 janitors and 219 other staff members.

Of the 286 family members, ESBL-PE was detected in 26 (9.1%). *Escherichia coli* was the most common (20 (76%)), followed by *Klebsiella pneumoniae* (5 (19%)). Older family members, those who spent more time with patients, daughters and female spouses and the family members of patients with chronic lung disease were most likely to carry the bacteria, and in 23 of the 26 positives analysis found species concordance between patients and family members.

Results from the study of healthcare workers were more positive, with ESBL-PE detected in 33 (3.3%) of participants. In 32 of the positives *E. coli* was found to be present, and the researchers found feeding patients was associated with carriage of the bacteria.

In Spain, more members of both study groups were carriers.

[Abstract 85: A multinational study of colonisation with extended-spectrum beta-lactamases (ESBL)-producing Enterobacteriaceae in healthcare personnel and family members of patients admitted to rehabilitation centres, BELGIUM, FRANCE, ISRAEL, ITALY, POLAND, SPAIN]

**Common source for outbreak**

A study reporting the first national outbreak of severe, invasive infections of the fungus *Geotrichum clavatum*, which impacted 33 patients with either acute cancers or neutropenia, a disorder leading to low white blood cell levels, in 14 French healthcare facilities between September 2011 and August 2012 has failed to establish a cause.

However, epidemiological data suggest a common source outbreak among the immunosuppressed patients and that antifungal selection pressure played an important role (94% of case-patients had received antifungal treatment with either caspofungin or posaconazole).

Preliminary genetic data suggest a single fungal clone was responsible for the outbreak, and apheresis platelet concentrates (APC) prepared with batches of the same processing set – set A – were received by 76% of case-patients and 91% of index-cases.

However, microbiological sampling of unused set A batches and blood products prepared with set A did not identify any fungus. A case-control study is now underway in order to better ascertain the contribution of set A to the outbreak.

[Abstract 2,675: A national outbreak of *Geotrichum clavatum* invasive infections in haematology wards, France, September 2011–August 2012, FRANCE]

**Global epidemic risk**

A global epidemic could occur if enteroviruses present in African primates jump to human populations and spread rapidly.
The discovery of several enteroviruses (EV-A76, B110 and D111) – members of a genus of positive-strand RNA viruses long considered to primarily impact humans – in faecal samples from Cameroonian chimpanzees has provided evidence of wider circulation of EVs in apes than previously thought.

Research has also found high levels of EV-A76 in chimps and baboons along with evidence the virus is only present in the Central African human population, supporting the proposition humans were recently infected following transmission from other ape species.

This has led researchers to conduct a wider study into the prevalence of EVs in other primate species by screening 200 faecal samples collected from forested areas of Cameroon with a minimal human presence.

Faeces screening identified 14 EV RNA-positive samples, with several strains found to represent new types within known species present in chimps, gorillas and bonobos.

That EVs known to infect humans are present in other primates is a potential source of virus genetic diversity that could drive turnover of variants and recombinant forms in human populations.

Four EV types were found to be shared between humans and primates – all restricted to African locations where both live in close proximity. The lack of prior exposure elsewhere means there is a risk of rapid epidemic spread from a Central African epicentre.

**[Abstract 3,175: Circulation of enteroviruses between humans and primates, UK/FRANCE]**

**Antibiotic-resistant bacteria rife in Pakistan**

A study in Karachi, Pakistan, has found the genes blaNDM which allow bacteria to produce the enzyme New Delhi metallo beta-lactamase-1 (NDM-1) – and the gene blaCTX-M-15 which confers resistance to a broad range of antibiotics – are widely carried by patients in Karachi hospitals, suggesting multi-drug resistant Enterobacteriaceae (MDRE) are widespread in the Pakistani community.

The study included 1,800 newly-admitted patients who were followed to discharge at two tertiary-care hospitals in Pakistan’s capital – Civil Hospital Karachi and Dow University Hospital – from Mar-Nov 2012.

Patients were sampled by rectal swab at admission and discharge, and the samples cultured in agar supplemented with the antibiotics vancomycin, vancomycin+ertapenem and vancomycin+cefotaxime.

The presence of the two enzyme-related genes in the total DNA of each bacterial culture was assessed using PCR (polymerase chain reaction) and those testing positive were further scrutinised to confirm their presence.

Among 273 faecal samples analysed so far – from Civil Hospital Karachi alone – blaNDM and blaCTX-M-15 were detected in 42% (118) and 89% (243) of samples respectively. Of 176 patients sampled on hospital admission, 41% had positive carriage in the blaNDM survey and 88% were positive for blaCTX-M-15.
Of 99 patients sampled on hospital discharge, 46% were positive for blaNDM and blaCTX-M-15 was detected in 88% of samples. The concomitant presence of both genes was detected in 40.6% (111) samples, of which 68 were taken at the time of admission and 43 on discharge.

[Abstract 1,865: Frequency of carriage of New Delhi metallo beta-lactamase-1 (NDM-1) and CTX-M-15 among patients from hospitals in Karachi: preliminary data assessing risk factors for carriage and infection, PAKISTAN]

Farm dust contaminated

A study of 80 samples from eight pig holdings in Germany has demonstrated the prevalence of antimicrobial resistant pathogens (ARP) such as methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum beta-lactamase (ESBL) producing enterobacteria in dust from farms.

Researchers detected 42 bacterial species, including Escherichia coli, S. aureus, various coagulase-negative staphylococci, pseudomonas spp, acinetobacter sp, corynebacteria, bacillus sp, enterococci and streptococci.

Resistance against fluoroquinolones, penicillin/ampicillin, tetracyclines and trimethoprim/sulfamethoxazole was detected in 13%, 61%, 61% and 36% of all bacterial isolates, respectively.

Dust samples contained the antibiotics and their derivatives: tetracyclines, enro-/ciprofloxacin, amoxicillin and sulfamethoxazole.

Researchers said their findings confirmed dust from pig farms partially contained high concentrations of antibiotics and a variety of bacterial pathogens, stressing the need to investigate in more detail interactions between bacteria that could lead to the exchange of transferable antibiotic resistance genes in the farm environment where there is constant antibiotic selective pressure.

[Abstract 1,170: Detection of antibiotics in dust from conventional pig holdings, GERMANY]

Two strains caused West Nile outbreak

Two unrelated strains of West Nile Virus were responsible for large outbreaks in Italy in 2008-09 and 2012, genetic analysis has found.

During 2008-2009, several human cases of WNV disease caused by an endemic lineage 1a strain – named Ita09 – were identified in areas surrounding the Po river. Since 2010, cases have been recorded in nearby northern areas, where in 2011 both lineage 1 and 2 were detected.

In 2011, two novel WNV genomes, named Piave and Livenza, were detected. Both belonged to lineage 1a and were related to WNV strains of the Western Mediterranean subtype, but differed both from each other and Ita09, demonstrating they were the result of new, independent introductions.

In 2012, a further relatively large outbreak caused by Livenza strain – with over 50 human infections – occurred in the same areas affected in 2011.
High MSRA risk for pig farmers

Carrying methicillin-susceptible *Staphylococcus aureus* (MSSA) protects pig farmers from acquiring livestock-associated MRSA (methicillin-resistant *S. aureus*), and continuous use of a mouth mask when working in stables prevents persistent carriage of the bacterium, a study of Dutch pig farmers has found.

Pigs (and veal calves) were identified as a source of LA-MRSA in 2005, and carriage rates among pig and veal farmers are much higher – at 20-40% – than is found in the general Dutch population (0.1%).

The study investigated 110 farmers from 50 Dutch pig farms. Nasal and pharyngeal (throat) samples and questionnaires were collected on six sampling moments during a one-year follow-up period in 2010-2011.

The mean MRSA prevalence per sampling moment was 63%, and 38% of pig farmers were found to be persistently carrying MRSA. MSSA nasal carriage proved to be a significant protective factor against acquisition of MRSA.

The analysis identified intense pig contact (for example, working in the stables for more than 40 hours per week), working with sows and being of medium age (40-49 years) as independent risk factors for persistent carriage of MRSA.

Continuous use of a mouth mask when working in the stables was a statistically significant protective factor that lowered the risk for persistent MRSA carriage, and the researchers recommend intervention studies are now carried out on their use in the pig farming sector.

DISEASE BURDEN AND TRENDS

Severe measles in UK adults

Following Merseyside in the North of England’s largest measles outbreak since the introduction of MMR vaccination, a study has been carried out reviewing both typical and atypical clinical features of adults with severe measles requiring hospital admission to an infectious disease unit in a Western setting.

Data showed that of 516 confirmed cases, 190 (37%) were adults aged 16 years or older, of whom 50 (26%) were admitted to hospital.

The main serotype responsible for the outbreak was B3, commonly seen in Africa but also implicated in recent Spanish and Norwegian measles outbreaks. Only five of 44 (11%) confirmed cases had been fully vaccinated with MMR. Along with the typical symptoms of fever, cough, coryza and conjunctivitis, other clinical symptoms included:

- Severe pneumonia
- Encephalitis
- Meningitis
- Bilateral hearing loss
- Myocarditis
- Neurological complications

The study highlights the importance of vaccination and the need for public health strategies to prevent measles outbreaks in adults.
features observed included severe oral mucosal and tongue ulceration in 28 of 36 (78%), upper respiratory tract involvement in 28 of 35 (80%) and early morbilliform rash involving the palmar and plantar surfaces in 25 of 38 (66%) patients.

Investigations of patients revealed significant lymphopenia (low levels of lymphocyte white blood cells) in 48 of 50 patients (96%), thrombocytopenia (low blood platelet levels) in 33/50 patients (66%) and transaminitis (high levels of an enzyme produced in the liver in the blood, a condition sometimes caused by acute viral fevers) in 34 of 50 patients (68%).

Measles pneumonitis (inflammation of the lungs) affected 37 of 50 (76%) patients, of whom 23 of 37 (62%) required assessment by the critical care team and 8 of 37 (22%) required higher level respiratory support. All recovered fully.

The researchers reiterated the important of high MMR vaccine uptake in both the community and healthcare facilities in order to mitigate against the risk of similar outbreaks.

[Abstract 2,304: Adult measles on Merseyside, UK in 2012, UK]

**High prevalence of amoeba infections in immigrants**

A study carried out between 2008 and 2011 at the Tropical Medicine Unit of Hospital Universitario Central of Asturias, in the north of Spain, investigated the prevalence of amoeba infections caused by the parasitic protozoans *Entamoeba dispar* and *E. histolytica* in immigrant populations in the country.

While the two organisms are morphologically indistinguishable, identifying which is responsible for infections is essential for both appropriate patient treatment and epidemiological purposes. For this reason, the study of 406 patients attending the unit used a PCR assay with specific primers for each species.

One hundred and sixty-four patients (40%) presented *Entamoeba* spp [*E. histolytica* (30.5%), *E. dispar* (11.6%), *Lodamoeba butschlii* (2.4%) and the rest *E. spp* (55.5%)]. No coinfections were diagnosed.

*Entamoeba* spp were most frequent in female (57 versus 34) and *E. histolytica* in male (33 versus 17). There was no significant difference in average age or the average time patients had spent in Spain in any group.

The most frequent countries of origin in *E. spp* group were Equatorial Guinea (30%), Senegal (15%) and Ecuador (11%). *E. histolytica* were frequent in patients from Senegal (22%), Ecuador (18%), Spain (14%), Equatorial Guinea (11%) and Ivory Coast (5%).

*E. dispar* was more frequent in Latin-American patients (seven versus three), with the most frequent countries of origin Spain (27%) and Cuba (16%), then Ecuador, Colombia and Venezuela (11%). Patients carrying *L. butschlii* were all from Latin-American countries.

The study found *E. histolytica* infection to be a prevalent parasitosis in the immigrant population in Spain, particularly in patients from Sub-Saharan Africa and most frequently from Senegal.
E. dispar and L. butschii are more prevalent in Latin-American patients. Non-pathogenic Entamoeba spp were more frequent in those originating in Sub-Saharan Africa, particularly Equatorial Guinea.

The researchers also said polimerase chain reaction assays offer a useful technique in discriminating pathogenic Entamoeba species from non-pathogenic.

[Abstract 441: Geographic distribution of Entamoeba spp. in an immigrant population in Spain, SPAIN]

Coxiella burnetii antibodies do not pose pregnancy complications

The presence of antibodies for Coxiella burnetii does not lead to problems during pregnancy, a study carried out in Denmark has found.

C. burnetii causes Q fever when transmitted to humans through inhalation of aerosols from animal birth products, which is suspected to be a potential cause of both fetal morbidity and mortality although the mechanism through which this could occur is poorly understood.

Researchers sampled 397 pregnant women with occupational or domestic exposure to cattle or sheep and a random sample of 459 women with no animal exposure and measured outcomes of spontaneous abortion, preterm birth, birth weight and the occurrence of fetuses that were small for their gestational age.

Among the 856 women, 179 (20.6%) tested positive for antibodies, 157 (87.8%) of whom had occupational or domestic contact with livestock. Two abortions were experienced by women testing positive against six negative; and three preterm births were to positives versus 38 negatives.

Women testing positive for antibodies tended to have heavier babies, and no increased risk of fetuses being small for their gestational age was found.

[Abstract 545: No excess risk of adverse pregnancy outcomes among women with serological markers of previous infection with Coxiella burnetii: evidence from the Danish National Birth Cohort, DENMARK]

Consider Brucella

Medical staff need to consider Brucella infection in patients presenting with inflammation of the testes, researchers say.

Brucellosis is a bacterial infection caused by ingestion of meat or dairy products from infected animals, and is most common in areas where cheese or milk that has not been treated with heat is consumed.

Patients may present as asymptomatic or suffer a range of complaints such as night sweats, undulating temperature and muscle or joint pain, through to toxic shock and death due to endocarditis or neurobrucellosis.

However, the paper emphasises the possible link between Brucella infection and acute inflammation of the scrotum in areas where the bacteria is endemic. Three cases are described,
two of which led to surgical removal of a testicle (orchidectomy), despite treatment for the
infection having been administered.

[Abstract 18 Brucellosis with epididymo-orchitis, TURKEY]

MECHANISMS

Blood test could improve malaria care

Low blood platelet levels (thrombocytopenia) are a significant predictor for severe forms of
malaria, according to a study carried out in Serbia.

Examining whether patients have increased levels of pro-inflammatory cytokines may also prove
to be a diagnostic procedure valuable in determining the most effective therapeutic approach to
malaria sufferers, researchers said.

The conclusions were reached during a study that aimed to establish the most common
manifestations of severe forms of imported malaria and determine the most important
predictors for infection in countries where malaria is not endemic.

Of 22 patients studied, 20 had severe malaria caused by *Plasmodium falciparum*. Thirteen
(59.10%) had one criterion for severe malaria, while nine (40.90%) had two or more criteria.
Jaundice was the most frequent manifestation, followed by hyperparasitemia, anemia, renal
failure, cerebral malaria and pulmonary edema/ARDS.

Three of the patients (13.6%) died as a result of the malarial infection.

[Abstract 299: Severe forms of imported malaria in Serbia, SERBIA]

TREATMENT

In vitro antibacterial susceptibility and drug interaction studies; Combination has
potent impact on resistant bacteria

Following the establishment of a synergy between the two antibiotics colistin and vancomycin,
research has been carried out that has found a potent impact on both colistin-susceptible and
colistin-resistant strain of *Acinetobacter baumannii*.

Six strains of the bacteria – two colistin-susceptible and four colistin-resistant - were studied.
While a potent synergy between the two antibiotics were observed, their combined action was
insufficient to bring the minimum inhibitory concentration (MIC) below the susceptibility
breakpoint index – in layman’s terms, the levels at which the combined antibiotics were
effective would do more harm than good by damaging other systems within the human body.

researchers said, however, their study should encourage investigation of combinations of
colistin- and vancomycin-derived drugs capable of reducing the MIC to less than the
susceptibility breakpoint.

[Abstract 2,761: Effect of the combination colistin/vancomycin in colistin-resistant
*Acinetobacter baumannii* strains, SPAIN]
Possible new treatment for multidrug-resistant bacteria

Researchers have found a potential new treatment for multidrug-resistant *Acinetobacter baumannii* (MDRAB), a very difficult-to-treat hospital pathogen.

The antibiotic colistin (COL) has been used as a treatment of last resort for the bacteria, but resistant strains have emerged, often forcing clinicians to resort to antimicrobial combinations. The researchers investigated what they described as an unconventional mix of COL with the relatively new antibiotic daptomycin (DAPTO).

Ten MDRAB blood isolates were tested. Seven were epidemiologically unrelated, and three were closely related to others. COL minimum inhibitory concentrations (MICs) ranged from 0.125 to 0.5 micrograms per millilitre (µg/ml). DAPTO MIC was >256µg/ml versus all isolates, but when plates were supplemented with sub-inhibitory concentrations of COL, MICs were reduced versus all isolates (4-64µg/ml) exhibiting a two- to six-fold reduction, which researchers said was suggestive of a significant in vitro synergy.

From a total of 30 isolate-concentration combinations in time-kill studies, a synergistic interaction was detected in 19 (63.3%). COL-DAPTO exhibited synergy against seven isolates at five hours and against eight at 24 hours of incubation. No antagonism was detected.

Despite low MICs, COL alone was bactericidal against only two isolates at 24 hours, whereas the combination was rapidly bactericidal against nine isolates at five and 24 hours.

The researchers said the observed potent in vitro synergistic interactions between COL and DAPTO provide evidence the unorthodox combination may be a useful therapeutic option for treatment of MDRAB, and is probably due to the ability of COL to permeabilise the bacterium’s outer membrane, allowing DAPTO to enter the bacterial cell.

[Abstract 2,455: Unconventional antimicrobial combinations: a possible option for the treatment of multidrug resistant (MDR) *Acinetobacter baumannii* infections? GREECE]

T Biofilm: Green tea offers possible antibacterial agent

Researchers have proved the efficacy of EGCG, a component of green tea, in preventing the formation of biofilms of the difficult-to-treat bacterium *Stenotrophomonas maltophilia* in patients with cystic fibrosis.

*S. maltophilia* was cultured with two clinical CF isolates (Sm1 and Sm2) to obtain young (24-hour-old) and mature (seven days) biofilms, which were then exposed to bactericidal and subinhibitory concentrations of EGCG, as well as the two in-use antibiotics colistin and tobramycin for comparison purposes.

The metabolic activity of the biofilms was measured and EGCG was found to exhibit disruptive traits in approximately 40% of both young and mature biofilms, compared to 57% and 43% for COL, and 46% and 45% for TOB, respectively.
Curiously, the researchers found COL, EGCG and TOB were able to significantly reduce the metabolic activity of young and mature biofilm cells produced by tested samples, except for Sm2 biofilms.

Relative effects on the viability of both young and mature biofilms were strain-specific and not dose dependent.

With both young and mature biofilms of *S. maltophilia* biofilms found to be markedly disrupted by EGCG, as well as COL and TOB, the researchers concluded there is a good case for the future use of EGCG in the prevention of biofilm formation and the treatment of *S. maltophilia* mature biofilms in CF patients.

[Abstract 1,367: Effects of epigallocatechin-3-gallate (EGCG) in young and mature biofilms produced by cystic fibrosis *Stenotrophomonas maltophilia* isolates, GERMANY]

**Telavancin could replace vancomycin**

With bacteria emerging that exhibit resistance to vancomycin (VAN), the current standard of care in the use of antibiotic lock solutions for prevention and management of catheter-related bloodstream infections, the hunt is on for effective alternatives.

Researchers have found telavancin (TLV), a semi-synthetic derivative of VAN, achieved a greater log reduction in growth of *Staphylococcus epidermidis* (SE) and methicillin-susceptible *S. aureus* (MSSA) biofilms in an established in vitro central venous catheter (CVC) antibiotic lock model.

The results demonstrate further evaluation is warranted, the team said.

A comparison was made of the activity of VAN and TLV against biofilm-forming strains of bacteria including SE, MSSA, vancomycin-resistant *Enterococcus faecalis* (VRE), vancomycin-susceptible *E. faecalis* (VSE) and methicillin-resistant *Staphylococcus aureus* (MRSA). Lock solutions of VAN at 5mg/ml, VAN 5mg/ml plus heparin 2500units/ml (VAN+hep), TLV 5mg/ml, and TLV 5mg/ml plus heparin 2500units/ml (TLV+hep) were investigated.

Pharmaceutical grade TLV was used, which contained cyclodextrin (solubilising) and mannitol, along with preservative-containing heparin. The lock solution was introduced after 24 hours of bacterial growth in a CVC incubated at human blood temperature of 37°C.

Each CVC was then drained, flushed, and cut into segments after an additional 72 hours of incubation, and the level of colony-forming units per millilitre (CFU/ml) measured.

VAN, TLV and TLV+hep demonstrated >2log reduction in CFU/ml against SE strains in an ALS with an established biofilm. For one MSSA strain, only TLV demonstrated a >2log reduction. For the other MSSA strain, a >2log reduction was observed with VAN, TLV, and TLV+hep.

[Abstract 2,625: Activity of telavancin and vancomycin antibiotic lock solutions against biofilm-producing *Staphylococci and Enterococci* in an in vitro central venous catheter model, US]