expressed gene was PLK1 by 12 times, and was also found to be over-expressed in Huh-7 cells. siRNA against PLK-1 validated by real-time PCR (RT-PCR) and Western Blotting showed a reduction of PLK1 expression up to 96% in huh-7 cells, and reduced cell proliferation by 68% and 92% in AT8 and BrdU cell proliferation assays respectively. There was 3-fold increase in apoptosis events, and TUNEL staining and caspase-3 assays suggested that this may be caspase-independent. The caspase inhibitor Z-VAD-FMK was unable to rescue apoptotic cells. Immunofluorescence studies co-localised endonuclease G to fragmented chromosomes, thus was postulated to be the main apoptotic effector. Knockdown of the FOXM1 transcription factor, thought to be a positive regulating factor did not affect PLK1 gene expression, suggesting other transcription factors may be important. Finally, huh-7 cells transplanted subcutaneously into nude mice using matrigel were treated with si-PLK1 and control si-RNA. Tumour regression of 33% occurred in the mice treated with si-PLK1 but not in controls. Conclusion: PLK1 overexpression in HCC was shown to be functionally important by gene silencing experiments, and may be a potential therapeutic target.

**Concurrent Session 16 – Global Monster – MRSA**

**CS16-01 A Work in Progress: MRSA and cMRSA in Latin America**

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MRSA is the leading cause of nosocomial infection in Latin America, and the number of reports of community-acquired (cMRSA) infections continue to rise. The full extent of the problem is unknown because surveillance information is only available from large hospitals, while much of the population is cared for in small centers that do not perform microbiological testing or use different methodology and definitions. Under these conditions, monitoring the epidemiology of MRSA remains a challenge and there is a need to improve detection and management. Nosocomial, multidrug-resistant MRSA is a growing problem in Latin America with estimated prevalence for the region currently near or above 50% for non blood stream infections and over 40% for bacteremia. Reports of CA-MRSA infections initially came from Brazil in 2003. Soon, a large outbreak of CA-MRSA infection that affected inmates in jails and people from the community in Uruguay was described; more than 1000 patients were affected and 12 died. In the region SSTIs account for the majority of cases, but severe forms of pneumonia were reported, including 4 deaths. In this outbreak, TMP-SMX remains active in vitro and is used for the treatment of skin infections. Interestingly, an apparent decrease in MRSA strains with vancomycin MIC greater or equal to 1 μg/ml suggests a shift in clonal dissemination, and further data are required to follow this trend, which may have important implications for treatment. Although surveillance systems in Latin America are improving, many limitations remain.

**CS16-02 Elucidating Geographical Spread of Methicillin-Resistant Staphylococcus aureus (MRSA): From Molecular Typing, Multilocus Sequence Typing to Microbial Genomics**

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Methicillin-resistant Staphylococcus aureus (MRSA) is a leading cause of hospital-acquired infections and an increasingly recognized pathogen from the community worldwide. MRSA infections are associated with high morbidity and mortality, and are a major financial burden to healthcare globally. A number of typing methods, including pulsed-field gel electrophoresis (PFGE), have been used by international surveillance networks to study the relationships and spread of MRSA isolates geographically. It was established that the large majority of MRSA isolates belong to a limited set of epidemic clones worldwide, namely the Brazilian, Iberian, New York/Japan, Pae- diatric clones. Methicillin resistance is conferred by the penicillin binding protein PBP2’, encoded by the mecA gene, present in a large fragment of mobile DNA designated “staphylococcal cassette chromosome”, SCCmec. More recently, sequence-based methods have been employed in the analyses of these isolates. Multilocus sequence typing (MLST) requires the sequence determination of internal fragments of 7 housekeeping genes for each strain. Each identical sequence is assigned an allele number, and the combination of alleles at each locus defines its sequence type (ST). The combination of MLST and SCCmec typing applied on international collections of MRSA revealed that these epidemic MRSA clones emerged on repeated acquisition (over 20 times) of SCCmec by successful methicillin-susceptible S. aureus (MSSA) clones belonging to five phylogenetically distinct lineages or clonal complexes (CCs): CC8, CC5, CC49, CC22 and CC30. MRSA is endemic in Hong Kong hospitals. Our previous study on MRSA causing bacteremia in Hong Kong hospitals belonged to four clonal complexes CC5, CC45, CC49 and CC239. The most prevalent MRSA clone in Hong Kong belonged to CC239, with PFGE types A-E, and H, SCCmec type III, and belonged to sequence type, ST239, with a multidrug resistance profile to tetracycline (T), erythromycin (E), clindamycin (D), gentamicin (G), tobramycin (To) and ciprofloxacin (Ci). Evidence also supports the prevalence of CC239 in Asian countries including China, Singapore, Taiwan, and Indonesia, whereas MRSA strains from Korea and Japan belonged to CC5 that had SCCmec type II. With advances in sequencing technology, the evolutionary history of the MRSA clone ST5 was further studied by mutation discovery at 108 loci (64kb) within a global collection. Sequence polymorphisms in 1.6% (46,483 bp) of the genome from each MRSA strain was screened. The SNPs defined a radial phylogenetic structure within ST5 consisting of at least 5 chains of mutational steps that define geographically associated clades. Mapping of the independent imports of the SCCmec demonstrated import occurred at least 23 occasions, and that the progeny of such recombinant strains are locally rather than globally. This further exemplifies that geographical spread of MRSA over long distances and across cultural borders is a rare event compared with the frequency with which SCCmec has been imported.

**CS16-03 Molecular Characteristic of Community-Acquired, Methicillin-Resistant Staphylococcus aureus**

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MRSA became the most common nosocomial pathogen in many hospitals since the 1980s, especially in many Asian countries. Epidemiologic reports showed that ~30% of S. aureus isolates from the hospitals in Korea, Japan, Taiwan, Hong Kong, Singapore, and Sri Lanka were MRSA. MRSA infection is now increasingly reported in the community. According to the ANSORP study from 2004 to 2006 in 9 Asian countries, the prevalence of MRSA among community-associated S. aureus isolates was 20.8% in Asian region and it was the highest in Taiwan (40.5%), followed by Sri Lanka (38.8%), the Philippines (30.1%), and Vietnam (28.2%). Skin and soft tissue infection was the most common infection by community-associated MRSA (CA-MRSA) followed by respiratory tract infection and primary bacteremia. CA-MRSA isolates from Asian region showed diverse microbiologic and genetic features
with regard to in vitro resistance, SCCmec type, frequency of pvl gene and MLST type. There have rare report about molecular characteristic of CA-MRSA infections in children from China, this prospective study was undertaken in order to characterize the molecular characteristic of CA-MRSA in children in China. We collected 99 CA-MRSA isolates from 8 hospitals in 7 cities in China between 2008 and 2009. All isolates were analysed by a combination of different genotyping methods, including MLST, SCCmec type, and spa typing. pvl gene was also detected.

In all of the CA-MRSA isolates, twelve STs were obtained, and ST59 (58.6%) was the most prevalent type throughout China. SCCmec type IV (67.7%) was the most popular type, and subtypes IVa, IVc, IVg were found in 77.6%, 11.9%, 2.9% of those isolates respectively. Eleven spa types were identified, and four new spa types were firstly registered on the net in our findings. ST59-SCCmec IVa with t437, was the most prevalent clone. In addition, 57.6% of those isolates were PVL positive. CA-MRSA isolates were found to be resistant to non-β-lactam antimicrobial, and multidrug resistance was observed in 85.9% of them.

In conclusion, the recent increase in CA-MRSA infections in children of China is largely associated with the spread of the ST59-SCCmec IVa with t437 clone and the multiresistant rate is high.

Concurrent Session 17 – End Stage Liver Diseases and Complications

CS17-01 Management of Hepatitis Related Liver Cirrhosis (TBC)
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Fibrosis is a frequent, life-threatening complication of most chronic liver diseases. Up to now liver biopsy is still the gold standard for assessment of hepatic fibrosis and cirrhosis. However, it is invasive with possible complications, costly and afflicted with a high degree of sampling error. There is a strong demand for reliable, liver specific, non-invasive biomarkers of fibrosis and cirrhosis to replace or to complement the invasive method of needle biopsy. Class I biomarkers are defined as serum components which reflect ECM turnover (fibrogenesis and fibrolysis) and fibrogenic cell changes, mainly of hepatic stellate cells, which are the dominant profibrogenic cell type in liver. The development of hepatic fibrosis or cirrhosis is due to increased synthesis, deposition, and possibly reduced degradation of hepatic extracellular matrix components, especially collagens, such as interstitial type I and III, basement membrane type IV, microfibrillar type VI, and pericellular type V, non-collagenous proteins, such as laminin, fibronectin, undulin, etc. Class II biomarkers comprise in general rather simple standard laboratory tests, which are grouped into panels. Class II biomarkers are based on algorithmic evaluation of commonly observed functional alterations of the liver that do not necessarily reflect ECM metabolism and/or fibrogenic cell changes. About 20 numerical scores or indices are reported for parameters, which are mostly routine laboratory tests and frequently multiparametric (panels). They fulfil most criteria for detection and staging of fibrosis and to a lesser extent grading of fibrogenic activity. The Fibrotest is the most investigated combination of serum markers for fibrosis. However, the diagnostic use of many of these scores is still limited and standardization of the assays is only partially realized. Transient elastography (Fibroscan), which measures the stiffness of the liver by means of ultrasound as a measure of fibrosis and cirrhosis, is simple to perform and the inter- and intra-observer variability is small. The accuracy is high in discriminating between cirrhosis and fibrosis, but lower for discriminating between the different stages of fibrosis in both chronic hepatitis B and C. All the makers of liver fibrosis can be combined for a better diagnosis.

CS17-02 Non-Invasive Assessment of Liver Fibrosis and Cirrhosis
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The development of infection with antibiotic-resistant organisms that have been listed in several studies are: underlying severe hepatic dysfunction, nosocomial infection, longer hospital stay and ICU stay, presence of indwelling vascular catheter, prior administration of an antibiotic and higher severity of illness. Although the impact of a delay in effective initial treatment was controversial, several studies suggest that ineffective initial therapy may be a cause of the higher mortality.

Conclusions: SBP due to antibiotic-resistant organism had higher mortality than SBP by susceptible strain and ineffective initial therapy may be a cause of the higher rates of treatment failure and mortality. Therefore, it would seem reasonable to treat patients with SBP due to antibiotic-resistant organism with effective antibiotics straight away. However, the injudicious use of broad antimicrobial regimen is likely to result in further emergence of resistance. To promote the prudent use of antimicrobial agents, we need further efforts to identify the risk factors for antibiotic-resistant infection.

Concurrent Session 18 – Pneumonia – Yesterday, Today and Tomorrow

CS18-01 Pneumococcal Diseases in the 21st Century
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The introduction of the 7-valent (types 4, 6B, 9V, 14, 18C, 19F and 23F) pneumococcal conjugate vaccine has brought a significant reduction in invasive pneumococcal disease in the United States and Europe. In the ≤ 2 years old, the incidence of pneumococcal bacteraemia has decreased from 188 to 59/100,000