for invasive fungal infection can ensure use of preemptive therapy in selected cases. Better diagnostic modalities including radiology like high resolution computed tomograms of the chest, earlier invasive procedures including bronchoscopy and biopsy coupled with serological studies like beta d-glucan, and galactomannan have shortened the time to diagnosis of fungal infections. Simultaneously, advances in fungal identification, both culture and molecular techniques have helped the clinician use the most appropriate antifungal agent. We also have an expanding armamentarium of drugs, both new drugs in existing classes and a new class of antifungal agents, to best suit the individual patient. There is still scope for significant improvement in areas, which include evaluation of new markers which could hasten time to diagnosis, and new agents which can tackle some of the more difficult or resistant fungi.

http://dx.doi.org/10.1016/j.ijid.2016.02.152

Type: Invited Presentation

Final Abstract Number: 30.002
Session: Infections in the Era of Cancer Treatments, Transplants and New Biologics
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 1

Neutropenic sepsis
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Abstract: Chemotherapy-induced neutropenia is the leading cause for bacterial and fungal infections in patients with haematological malignancies. The drop of neutrophils count below 1000 cells/cmm increase the risk of febrile episodes (TC>38 °C) and infectious complications but most of the bacteremic episodes are documented when neutrophils count is below 100/cmm (severe neutropenia). The duration of neutropenia also play a pivotal role in determining the risk of infection: prolonged neutropenia is defined by a duration of 3 weeks. Among 100 febrile episodes occurring during neutropenia 40% are FUO, 20% are clinically documented, 20% are microbiologically documented and 20% are bacteremia. Gram-positive cocci (CNS, St. aureus, streptococci, enterococci) represent around 50% of the blood isolates and gram-negative bacilli (Ps. aeruginosa, enterobacteriaceae) are documented in the same rate. Recently, an increasing rate of MDR gram-negative bacilli (i.e. K.pneumoniae KPC-producing and other carbapenem-resistant gram-negative bugs) are responsible for local epidemic clusters. Empiric antibiotic therapy is recommended in patient with febrile neutropenia: blood cultures (at least 2 sets) should be taken immediately and therapy started in 1 hour (febrile neutropenia is a medical emergency). Monotherapy with a beta-lactam antibiotic with anti-pseudomonal activity (meropenem, piperacillin/tazobactam) is usually started, adding an anti gram-positive agent (vancomycin, daptomycin) in case of a documented gram-positive bacteremia or in patient with local sign of CVC infection (“escalation” strategy). A de-escalation strategy is preferred in patient presenting with severe sepsis or septic shock and in the setting of a cluster of MDR gram-negative bacilli. Combination therapy is started (beta lactam, aminoglycoside, antistaphylococcal agent) then de-escalated on the basis of microbiological documentation and/or clinical response. In case of KPC-producing K. pneumoniae epidemic a combination of colistin, tigecycline and gentamicin should be considered; some clinicians suggest the use of high-dose meropenem (although many of the isolates shows a MIC >128 mg/l). It is noteworthy that the use of rectal swab to identify colonized patients may be important for the infection control procedures (patient isolation) and to predict the subsequent sepsis. In neutropenic patients with fever not responding to 3 or 4 days of antibiotic therapy the start of an empiric antifungal therapy (echinocandin, amphotericin B) should be considered. Serological markers (betaglucan, mannan/anti-mannan etc.) may be useful to select patients at higher risk of yeast infection; galactomannan is otherwise useful to suspect Aspergillus infection.

http://dx.doi.org/10.1016/j.ijid.2016.02.152
Type: Invited Presentation

Final Abstract Number: 30.003
Session: Infections in the Era of Cancer Treatments, Transplants and New Biologics
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 1

Infectious complications of biologic therapeutics
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Abstract: An expanding array of new biologics are entering clinical practice to supplement existing therapies in the management of neoplastic diseases, organ transplantation, rheumatic diseases and numerous other inflammatory disease states. These biologics include monoclonal antibodies, soluble cytokine receptor constructs, growth factors and recombinant proteins. Their use have revolutionized treatment for some severe forms of rheumatoid arthritis, multiple sclerosis (MS) and inflammatory bowel disease where biologics have now become the standard of care. Such agents are not without risk as a number of common infections and at times rather unusual infections are being recognized with increasing frequency following the institution of biologics. Opportunistic infections are particularly a concern in patients receiving combination therapy with multiple biologics in addition to standard immunosuppressive agents such as corticosteroids, anti-metabolites and calcineurin inhibitors.

Because of their frequency and severity, the infections of greatest importance following a biologic are tuberculosis, opportunistic and endemic mycoses (histoplasmosis and coccidioidomycosis), and high risk viral infections (HIV, hepatitis B and C, adenoviruses and the JC virus that causes progressive multifocal leukoencephalopathy (PML). While these infections should receive the most attention, an array of pathogens ranging from viruses (herpes viruses, paramyxoviruses), bacteria (e.g. Listeriosis, mycobacterial infections, skin and soft tissue pathogens, respiratory infections), numerous opportunistic fungi, and parasitic organisms including toxoplasmosis, pneumocystosis, and strongyloidiasis should also be considered. The greater the intensity, duration and combinations of biologics all increase the risk of secondary infection. Many biologics have prolonged immunosuppressive effects, thereby limiting cost and improving convenience, but this long pharmacodynamic effect leads to infection risk for prolonged periods up to years after stopping the treatment. A number of these infections can be detected in latent forms allowing for prophylaxis or avoidance of some biologics such as screening for PML by serology before using natalizumab (alpha-4 integrin
monoclonal antibody), or screening for latent TB before using TNF inhibitors.

http://dx.doi.org/10.1016/j.ijid.2016.02.153

Type: Invited Presentation

Final Abstract Number: 30.004
Session: Infections in the Era of Cancer Treatments, Transplants and New Biologics
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 1

Cytomegalovirus

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Abstract: Cytomegalovirus (CMV) remains an important pathogen in transplant patients. Sensitive and rapid turnaround quantitative PCR based monitoring coupled with the availability of effective antiviral therapy has reduced the overall burden of CMV disease after transplantation. However, in hematopoietic stem cell transplant (HSCT) patients, the increasing use of new donor and stem cell sources present new challenges in the prevention and treatment of CMV. Gastrointestinal disease is now the most common end-organ manifestation of CMV infection after HSCT, whereas pneumonia remains associated with high mortality. In addition, indirect effects of CMV infection continue to have both positive and negative effects on outcomes after HSCT. Antivirals with novel mechanisms of action and improved toxicity profiles compared to those currently available are in late phase clinical trials. Also CMV vaccines are in development. Despite these advances, CMV is likely to remain a significant pathogen in transplant recipients.

http://dx.doi.org/10.1016/j.ijid.2016.02.154

Type: Invited Presentation

Final Abstract Number: 31.001
Session: New and Recently Approved Antibiotics: Challenges and Opportunities
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 2

New antibiotics: What do we need?

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Abstract: Lack of effective antimicrobial therapy for multidrug-resistant organisms (MDROs) has been a growing concern particularly due to spread of extended-spectrum beta lactamase (ESBL) and carbapenem resistant Enterobacteriaceae (CRE). Better therapeutics for MDROs are needed. Common MDROs include methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus (VRE), ESBL and CRE. Gram-positive organisms such as MRSA and VRE are stable or declining in frequency while gram-negative ESBLs and CREs are increasing. Recent antibiotics generally focus on MRSA and gram-positive MDROs with few new agents effective against gram-negative organisms. Outside of common healthcare-associated MDROs, Gonococcus has become highly antibiotic-resistant in many parts of the world. Furthermore, most therapy for MDROs is intravenous and associated with a high rate of adverse effects and burden of disease related to long courses of treatment.

New antibiotics are needed with novel mechanisms of action against MDRO organisms, fewer side effects, less impact on the microbiome and easier, non intravenous delivery. Studies of new drugs need to focus on rational use with minimal duration, easiest form of delivery and clear recognition of effects on the microbiome. Use of new antibiotics must be appropriate and avoid overuse. Choosing Wisely and the growth of Antimicrobial Stewardship may help appropriate use.

Finally, a new model of infectious disease management is developing based around the microbiome. Manipulation of the microbiome may become a mainstay for treatment of many diseases. Currently, fecal transplants for C. difficile are the only approach to microbiome manipulation proven to work. Other uses may include decolonization of MDROs from the gastrointestinal tract. Future microbiome manipulations may include targeted microbiome changes via capsules to the GI tract and possible inoculations to the skin or mucosal surfaces. Development of ways to manipulate the microbiome could improve treatment of infectious disease without producing antibiotic resistance.

Development of antimicrobials active against ESBLs, and CREs that are safe and easy to use is needed. Longer range antimicrobial therapies will likely involve microbiome manipulation.

http://dx.doi.org/10.1016/j.ijid.2016.02.155

Type: Invited Presentation

Final Abstract Number: 31.002
Session: New and Recently Approved Antibiotics: Challenges and Opportunities
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 2

The antibiotic pipeline: What can we expect?

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Abstract: Antibiotic resistance is widespread. Despite the recognized and growing need for new antibiotics, today most large pharmaceutical companies have dropped active antibacterial drug discovery programmes. While antibiotics are regarded as non-profitable compared to other fields, small companies—mostly backed by promising academic discoveries—are stepping in to drive research and early clinical development in the antibiotics field. In the 1980s and 90s the antibiotic pipelines were satisfying the need for improved antibiotics against the prevalent resistant strains at that time. Currently, extensively- or pan-resistant Gram-negative bacteria require novel antibiotics without co- and cross-resistance to known drug classes. A few research&development programs based on classical antibacterial compounds against Gram-negative bacteria that bind to new targets or have a new mode of action are in the early research phase and their potential is difficult to assess. Due to such thin discovery pipelines, attitudes have changed and antibacterial approaches outside the mainstream are increasingly pursued and publicly funded. These alternative methodologies range from peptides and peptidomimetics to antibodies, prophylactic and therapeutic vaccines, adjunctive