that clinical care will not be harmed by control measures such as: de-escalation of therapy, dose optimization, and parental or oral conversion of antimicrobials with excellent bioavailability can decrease the length of hospital stay and healthcare costs.

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61.004

New Antibiotics: Which Role in a Antimicrobial Stewardship Program?

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Infections caused by multidrug-resistant bacteria continue to challenge physicians in the daily practice. We face growing resistance among Gram-positive and Gram-negative pathogens that cause infections in the hospital and in the community. Rice recently reported these as the "ESKAPE" pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, and Enterobacter species) to emphasize that they currently cause the majority of worldwide hospital infections and effectively "escape" the effects of antibacterial drugs.

In this context, controlling antibiotic use and bacterial resistance through an antibiotic stewardship program (ASP) is of major importance to all professionals involved in infectious diseases.

A critical need to develop new antimicrobial compounds and to use the recently approved agents appropriately are components of all ASP. Unfortunately, most of the agents which are in the late stage of development have activity only against Gram-positives and none is active for treatment of infections caused by the Gram-negative ESKAPE pathogens.

We have analyzed the body of the literature with the aim to define, within a ASP, the opportunity of use and the potential advantages of new antibiotics in order to reduce the emergence and selection of resistant pathogens.

Related with the role of the new antibiotics in a ASP, it is possible to consider the following points: i-the use of tigecycline instead of carbapenems in clinical settings with high rates of carbapenem-resistant pathogens (ie. in nosocomial peritonitis), ii-the use of doripenem in extended-infusion (ie. in severe infections due to Pseudomonas aeruginosa); iii-the use of daptomycin at high doses (ie. in infections due to methicillin-resistant Staphylococcus aureus) and iv-the use of ceftobiprole as empiric monotherapy (ie. in some suspected mixed infections).

The use of the new antibiotics in the daily practice based on the individual patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug is an important part of an ASP.

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Current challenges in HIV care (Invited Presentation)

62.001

State of the Art on ARV Therapy: How Many Standards of Care?

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Albeit nobody would support the idea of "first and second class medicine", in real life we confront AIDS with at least two standards of care. When to start ART therapy remains a matter of debate. No disagreement exists for symptomatic patients, as well as for asymptomatic individuals with CD4 counts of 350/μm³ or below. In resource-poor settings, WHO recommended until late 2009 that adolescents and adults should start ART when they have advanced HIV disease, mildly symptomatic and asymptomatic disease, WHO Stage II or I HIV disease with CD4 counts <200/μm³. These recommendations were updated in November 2009 and look now closer to those released by other international bodies. Some Western countries guidelines panels, like the DHHS recommends now treatment initiation in asymptomatic patients when the CD4 count falls below 350/μm³, and have shown a divided opinion regarding the if treatment should be considered in patients with CD4 cell counts <500/μm³, particularly if the patient has high viral load, age above 50 and/or comorbidities like HBV or HCV coinfections, among others. Increasing amount of data suggest that by starting earlier, the so called "non-AIDS" diseases driving to mortality in the HAART era might be dramatically reduced. On top of the benefits at the individual level, ART has been shown as a prevention tool by reducing the median viral load at the community level. Currently available co-formulations are the best options for ARV backbone in naive patients. Issues such as childbearing potential and baseline resistance need to be taken into consideration when selecting a regimen. Controversies remain on whether to use a PI or an NNRTI as the third drug in initial therapy, particularly important in the presence of advanced disease. The bottom line is that one size does not fit for all in this challenging field.

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62.002

Drug Resistance and Other Laboratory Monitoring Assays in HIV infection

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Although CD4 cell counts and plasma viral load assays are the principal laboratory tests used to monitor the progress of HIV-1 infections, several other assays are assuming increasing importance to adequately assess the benefits of antiretroviral therapy (ART) in infected individuals. The accessibility of such assays will vary greatly, depending on the resources available to treat HIV infections.

Where testing capability exists, HIV drug resistance testing is useful when patients enter care prior to initiating therapy and again when considering change of regimens.
during virologic failure. Genotypic assays are generally preferred because of cost and rapidity, except in situations where multiple ART regimens have been used, when phenotypic assays may be of value.

When abacavir is being considered as part of an ART regimen, genetic screening for HLAB*5701 is helpful to reduce the risk of severe abacavir hypersensitivity reactions. These reactions, reported in 5-8% of white and 2-3% of black patients occur primarily in individuals with the MHC class I allele HLA-B*5701. Individuals who screen positive for HLA-B*5701 should not receive abacavir.

When a CCR5 antagonist (e.g., maraviroc) is being considered as part of an ART regimen, a coreceptor tropism assay is useful, since an agent of this class will only suppress viruses that utilize this receptor (R5 viruses). CCR5 antagonists should not be used in individuals who carry primarily X4 or dual/mixed tropic viruses. Currently, the principal assay available to measure HIV-1 tropism is phenotypic, though genotypic tests are under study.

Although therapeutic drug monitoring is recommended by some, its use remains controversial, and no clear-cut recommendations can be made regarding its utility.

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62.003

Opportunistic Infections and IRIS in the Era of HAART

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Despite the important advance that cART represents for the prognosis of the HIV-1 infection, OIs continue to be an important cause of morbidity and mortality in developed countries. This is due to late presentation (up to one-third of new HIV-1 infections), lack of adherence to cART and prophylaxis or virological failure of cART. In addition, OIs are very common in developing countries, being tuberculosis (TB) the most common one. The ACTG A5164 results recommended to start cART during the first 2 weeks after starting antimicrobial treatment for the OI (patients with TB were not included in this RCT). Some of these patients, despite having an excellent viral and immune response to cART, will present a paradoxical worsening of the OI known as the immune reconstitution inflammatory syndrome (IRIS). The microorganisms most commonly associated with IRIS are mycobacteria, fungi, and herpes group viruses. The IRIS has also been reported in tumors, such as Kaposi sarcoma, and causes autoimmune diseases. The percentage of patients who develop IRIS is variable. In cohort studies of patients starting cART, IRIS affects between 15% and 25%. In OIs series like TB the frequency is higher, and can reach 50%. Clinical effects of IRIS range from a mild, self-limiting illness to severe morbidity and mortality. The lack of evidence-based treatment guidelines poses challenges in the management of these patients. Patients are generally recommended to continue with cART and specific treatment against OIs. Adjuvant nonsteroid anti-inflammatory drugs (NSAIDs) and corticosteroids are commonly used. Corticosteroids have demonstrated their usefulness in a recent clinical trial in TB patients. Surgery is necessary to debride abscesses. In life-threatening cases, the possibility of interrupting cART should be considered until the patient’s situation has improved. Clinical experience with immunosuppressors or TNF-alpha inhibitors is very limited.

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62.004

Why are patients dying in the HAART Era?
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Biomarkers in infectious diseases (Invited Presentation)

63.001

Clinical Use of Biomarkers in the Diagnosis and Management of CAP

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Community-acquired pneumonia (CAP) is a serious health problem worldwide with an annual incidence of 0.3-0.5% in the adult population. Besides, CAP remains the leading cause of death from infectious diseases. This justifies the interest in studying all clinical aspects affecting CAP. A new approach is to evaluate biological markers of infection and inflammation, as an expression of the host’s inflammatory response against the microorganism, in order to achieve diagnosis, aetiology, prognosis and treatment information. The most widely studied biomarkers have been C reactive protein (CRP), procalcitonin (PCT) and cytokines. Other biomarkers are now obtaining promising results. Most authors conclude that biomarkers can help in the diagnosis of CAP. Fewer data analyse the capacity of biomarkers in identifying the potential causative agent and the best results have been settled down in children. Linked with the above mentioned, biomarkers, mainly PCT, have been used successfully guiding antibiotic prescription in patients with suspected CAP. Treatment guided by serum PCT was a safe way to avoid antibiotics, although economic savings were overshadowed by PCT analysis costs. Approximately 10-15% of patients hospitalised for CAP develop treatment failure and almost 6% may manifest rapidly progressive pneumonia, it has been demonstrated that serum levels of biomarkers can identify patients at risk of treatment failure and therefore could guide treatment handling. Clinical data scoring systems have been recognized as a useful tool to assess stability and prognosis of patients with CAP. Analysis of systemic biomarkers in addition to clinical scores has shown to improve either the prediction of absence of severe complications and the 30-day mortality prediction by PSI or CURB65/CRB65 scales. Current data from literature seem to support the use of biomarkers in the daily medical practice concerning CAP.

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