

Need for chemoprophylaxis for travelers to the Americas: Yes

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International travelers may sometimes acquire infectious diseases such as malaria during their journeys. This session will be a debate about the usefulness of malaria chemoprophylaxis for travel to the Americas. Malaria can be a fatal disease even when it is diagnosed early and treated correctly. It is preferable for persons at risk of infection with malaria to prevent the infection.

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19.003

Need for Continuous Prophylaxis for Travelers to the Americas: No

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The risk a traveler becomes infected by malaria will depend on the overall rate of malaria transmission in the area to be visited and the extension of the traveler's contact with infected mosquitoes.

Topics like: 1. Wearing long-sleeve shirts and long trousers; 2. Applying insect repellent; 3. Spraying aerosolized insecticides in living and sleeping places; 4. Sleeping in a screened or airconditioned rooms; 5. Sleeping on netted bed; and 6. Use mosquito coils containing pyrethroids are consensual measures in all malaria transmission areas, and the use of chemoprophylaxis are not consensual in low endemic areas (Wyer, NEJM 1993)

My aim is convincing you that the routinely use of malaria chemoprophylaxis is not needed in America.

The use of anti-malarial chemoprophylaxis should be carefully directed at high risk travelers when the benefit of using anti-malarial drug regimens outweighs the risk of adverse events. The risk for adverse events during the anti-malarial drugs for prophylaxis is in the range of 30-40%.

Everyone knows that malaria is a disease of low incidence in America and most of these cases are in topic areas where tourists only occasionally reach.

A retrospective study conducted on Italian travelers found that malaria incidence was 1.5/1000 for trips to Africa, 0.11/1000 for trips to Asia, and 0.04/1000 for trips to Central and South Americas. Another study among Swedish travelers found a number four times lesser among travelers to America (Croft AM. BMJ 2007).

The use of chemoprophylaxis against malaria in this scenario, where contra-indications overlap the benefits, show us the inadequacy of routinely use of drugs to prevent malaria in Americas. In a restrict number of cases when the travelers must stay in remote malaria transmitting areas in America, for long period o time, we recommend standby treatment.

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Choice of drugs for the Prophylaxis of malaria in the Americas

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Preparing a traveler for a trip to the Americas often includes a discussion about the prevention of malaria with personal protection measures to minimize mosquito bites and the recommendation to use a drug for chemoprophylaxis when appropriate. The characteristics of malaria in the Americas that differ from many other areas of the world include the relatively low transmission rates, the predominance of vivax malaria in most locations, and the relatively wide availability of quality medical care for tourists. Use of all current approved malaria chemoprophylaxis drugs will be discussed with special emphasis on primaquine, the only currently available drug that can prevent vivax malaria.

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Current issues in multi drug resistant gram-negatives (Invited Presentation)

20.001

Escherichia coli

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Escherichia coli is a remarkably versatile organism able to easily acquire antimicrobial resistance as well as virulence determinants. *E. coli* is the leading pathogen causing urinary tract infections and one of the most common organisms implicated in bloodstream infections. Its ubiquity in the community and hospital setting, together with antibiotic overuse, have delineated a scenario in which multidrug resistant isolates are not infrequent and appear as a foremost challenge for clinicians to achieve therapeutic success.

Beta-lactam resistance owing to the presence of extended-spectrum-beta-lactamases (ESBLs) is globally spread among *E. coli*, particularly due to CTX-M-type enzymes, and coexistence of more than one beta-lactamase in the same isolate has also been observed. Moreover, co-resistance to non-beta-lactam antimicrobials is a common feature among ESBL-producers as resistance genes to unrelated antimicrobial compounds such as aminoglycosides, tetracyclines, sulfonamides, trimethoprim, and chloramphenicol are simultaneously harboured by conjugative plasmids carrying transposons and/or integrons where these genes are located. The prevalence of certain phylogroups exhibiting these multiresistant phenotypes has recently been associated with a genetic island that comprises genes encoding antibiotic resistance and virulence in particular *E. coli* clones such as the ST131 clone. Concomitant resistance to fluoroquinolones due to mutated topoisomerases in many of these isolates is an alarming reality.

Incidence of *E. coli* isolates carrying plasmid-AmpC cephalosporinases is raising in many countries and, although

carbapenems are still broadly active against *E. coli*, the incidence of carbapenemases merits strict supervision mainly in geographic areas where this resistance appears to be endemic in other species such as *Klebsiella pneumoniae*.

Other resistance traits have been described in *E. coli* clinical isolates as plasmid-mediated quinolone resistance due to *qnr* and *aac(6')-Ib-cr* genes, and the efflux pump QepA. Moreover, production of plasmid 16S rRNA methylases has recently drawn attention as a novel aminoglycoside resistance mechanism in pathogenic gram-negative bacteria including *E. coli*. It confers high-level resistance to all aminoglycosides that are currently available.

Multiresistance in *E. coli* affects almost all antimicrobial families, it is easily transmitted through successful and virulent clones and can be spread from and among not only humans but animals and food. The role of continuous antimicrobial pressure in this phenomenon is unquestionable and requires control measures to curtail the spread and maintenance of these multiresistant isolates with high likelihood of causing serious and almost untreatable infections.

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20.002

Multidrug resistance in *Klebsiella pneumoniae*

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Hospital-acquired and clinically-important Gram-negative pathogens remain mostly *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Among those Gram negatives, *Klebsiella pneumoniae* remains an important source of hospital spread of multidrug resistance. Wide-spectrum β -lactamases are increasingly reported in *Enterobacteriaceae* being either clavulanic-acid inhibited extended-spectrum β -lactamases (ESBLs) or carbapenem-hydrolyzing β -lactamases (CHBLs). Although first reported in *Klebsiella pneumoniae* mostly from 1980's to 2000's, ESBLs are developing rapidly among community-acquired *Escherichia coli*. These novel ESBLs of the CTX-M-type are reported worldwide with important structural and genetic diversity. Those ESBL genes may be transmitted from *E. coli* to *K. pneumoniae* providing a novel source of hospital-acquired multidrug-resistant *K. pneumoniae* since there are associated to other plasmid-mediated resistance determinants. The CHBLs identified in *Enterobacteriaceae* are mostly metallo- β -lactamases (Ambler class B enzymes) of the VIM/IMP-types in hospital-acquired *K. pneumoniae*. The Ambler class A carbapenemases of the KPC-type are also identified mostly in *K. pneumoniae*, first from the USA and then worldwide. The latest reported CHBL in *K. pneumoniae* is OXA-48 mostly from Mediterranean countries. All this carbapenemase producers are difficult to detect in a clinical laboratory and may be the source of multidrug resistance leading to therapeutic deadend. *K. pneumoniae* will remain the most important enterobacterial species as a source of multidrug resistance in hospital-acquired Gram negative isolates.

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20.003

Pseudomonas aeruginosa

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20.004

Evolution of antimicrobial resistance in *Acinetobacter baumannii*: Factors affecting multiresistance

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Acinetobacter baumannii are an important cause of nosocomial infections mainly in patients in the intensive care units. In this presentation I will analyse the evolution of antimicrobial resistance, the molecular bases associated with the increase in antimicrobial resistance, the factors affecting multiresistance and the current treatment of *Acinetobacter* infections.

Antimicrobial resistance has steadily increased in the last decade. Nowadays *A. baumannii* clinical isolates resistant to all antimicrobial agents even to colistin (panresistant) have been isolated in the nosocomial setting. Three major factors favour the acquisition of multiresistance: 1. Intrinsic resistance, mainly related to the interplay between decreased permeability (small number of porins) and constitutive expression of efflux pump(s) (AdeIJK, CraA); 2. Persistence in the environment, in this sense, biofilm-producing *A. baumannii* clinical isolates survive in inanimate surfaces longer than those non-producing biofilm. 3. Acquisition of genetic elements. It has recently been shown that resistance islands with a variable composition of resistance determinants interspersed with transposons, integrons and other genetic elements play an important role in the acquisition of multiresistance. However, this is not an universal contributor to multiresistance since target mutations, overexpression of efflux pumps, and IS elements located upstream from some resistance genes have also been found to be implicated in multiresistance. Although some clinical isolates are still susceptible to carbapenems and colistin, and therefore these antimicrobial agents can continue to be used, few options are available to treat infections caused by this microorganism. Tygecycline has been used to treat infections caused by *A. baumannii*. However, emergence of resistance to this antimicrobial agent has been reported during treatment when this monotherapy.

This microorganism, albeit with slight differences depending on the country, presents resistance to multiple antimicrobial agents, occasionally including resistance to colistin, hence, it can be considered the paradigm of nosocomial multiresistant bacteria.

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