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39.002

Antibiotic Practices and Resistance in Genocide Areas of Darfur and Southern Sudan

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Background: Due to 21 years of civil war in southern Sudan and 5 years conflict of Darfur, health care infrastructure in southern and western Sudan was destroyed. St. Elizabeth University Tropical programmes involve 2 hospitals in South Darfur (Nyamlell, Gordim) and 2 in Bahr Al-Gazal in southern Sudan (Mapuordit, Marialou), with patient flow of 35.000 a year. Antibiotic policy is based on WHO guidelines in those hospitals but no community health service is available yet and vaccination was sporadic or none.

Methods: On the market 4 antimicrobial drugs are available as OTC - Doxycyclin, Ampicillin, Cotrimoxazole and Cloroquine. We have tested 400 isolates from patients from this area as of antibiotic free environment.

Results: All isolates of *Str. pneumoniae* were Penicillin susceptible, all *S. aureus* Oxacillin susceptible and all S. pyogenes Erytromycine susceptible. All *H. influenzae* isolates were susceptible to Ampicillin and all *E. coli* to Ciprofloxacine, all but one to Cotrimoxazole. Tetracycline resistance vice versa in *S. aureus* and Streptococcus spp. isolates was up to 33%.

Conclusion: Antimicrobial resistance in respiratory pathogens is extremly low due to lack of antibiotics because of isolation during civil war. Tetracycline resistance is high because Doxycycline is extremely cheap and available.

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39.003

Antibiotic Practices and Resistance in a Rural Haitian Population Isolated by Previous Civil War Conflicts

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Background: Haiti was suffering from about 40 years of focal civil war conflicts when changing the dictatorship to a democratic government until 2004 and some rural areas have been cut from supply of health care services for several years. Antibiotics for infection were used only exceptionally except of TB which was merged in specialized state supplied TB centres.

Methods: We have cultured 500 consecutive outpatient department patients from Community Health Centre in Mole St. Nicolaus in north Haiti, in a rural area without road and only boat access. 139 respiratory isolates were transported by air to National Reference Laboratory of Antimicrobial Resistance in Nitra.

to Penicillin and 94% also to Doxyciclin. All but one of 32 Str. pyogenes were susceptible to Erytromycine.

Conclusion: The incidence of antimicrobial resistance in rural Haiti is exceptional because of limited access to pharmacy and shops or gasoline stations selling antibiotics as OTC.

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39.004

Antibiotic Practices and Policies in Slums of Nairobi and Among Economic Refugees in Turbana Area

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Background: About one third of 6 million slum population in Nairobi live without regular access to drinking water and toilets. Gastrointestinal infections (both bacterial and parasitic) and respiratory diseases due to overcrowding, pollution and malnutrition are very common. All antibiotics are OTC and available from pharmacies owned by Indian pharmacists with good education, who often supply doctor advice, because the number of doctors is very limited.

Methods: Antimicrobial resistance was surveyed regularly in 1999—2007 at Mary Immaculate Clinic in Nairobi. Swabs were transported to the reference laboratory for antimicrobial resistance in Slovak Republic at University Hospital Nitra and tested with disc diffusion method according to the NCLS standards.

Results: We discovered increasing resistance in Str. pneumoniae to Penicillin, S. aureus to Oxacillin and E. coli to Cotrimoxazole. Prevalence of HIV was 12—16% with decreasing trend and major opportunistic infection was TB, candidiasis and Salmonella/Amoeba diarrhoea.

Conclusion: Factors that contribute to unfavourable trends in antimicrobial resistance has to addressed by preventing the transmission of commonest infectious diseases and implementing proven effective rational drug use strategies (IMCI, DOTS). Unregulated drug availability, inadequate antimicrobial drug quality and surveillance must be addressed as well.

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The Role of Neutrophils in Infection (invited)

51.001

The Role of Neutrophils in Infection

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Polymorphonuclear leukocytes (PMN) represent the dominant cellular contributor to innate host response to infection, dramatically evidenced by the increased frequency and severity of infections in individuals with compromised numbers of normal PMN. In circulation, the

unstimulated PMN remains in a resting state, with critical components of its antimicrobial machinery segregated into different subcellular compartments. Upon exposure to soluble host factors, microbial products, or microbes, the PMN phenotype rapidly transforms; first ingesting the microbe and thereby sequestering it in the phagosome, and then recruiting and activating a variety of responses targeted to kill and degrade the trapped microbe. This presentation aims to discuss some of the mechanisms underlying specific features of the PMN response within the context of innate immune response to and resolution of infection. Concomitant with PMN activation, membrane-bound granule compartments fuse with the nascent phagosome, thereby delivering enzymes as well as antimicrobial peptides directly to the microbe. Concurrently, the NADPH oxidase is assembled and activated at the phagosome membrane, generating reactive oxygen species that directly and indirectly contribute to microbial killing and degradation. Collectively, these orchestrated responses of the PMN create an intraphagosomal environment inhospitable to the phagocytosed microbe. The mechanisms underlying the generation and antimicrobial action of several bioactive species will be highlighted, as will the specific synergies between soluble circulating proteins and PMN responses that collaborate to eradicate invading microbes. PMN contribute to host defense in ways other than those directly associated with phagocytosis, as they release IL-8 and other chemokines to recruit additional immune cells to the fray and to modulate the antimicrobial activities of resident cells at the site of infection. Lastly, PMN direct biochemical and cellular events that contribute to the subsequent resolution of the inflammatory response, an essential step in returning to a homeostatic, resting state.

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Community-Acquired MRSA: What in the World is Going on? (invited)

52.001

The Origin and Evolution of MRSA

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Since the identification of the first methicillin resistant *S. aureus* (MRSA) isolate in 1961, there is extensive literature on its successful spread in the nosocomial setting, its incremental rise in antibiotic resistance and more recently, its emergence as a community associated pathogen spreading in otherwise healthy populations. Extensive genotyping of *S. aureus*, including genome sequencing of six MRSA strains, and determining the organization of the staphylococcal chromosomal cassettes that harbor the methicillin resistance gene, mecA, have identified six major pandemic clones that have spread along epidemic waves, consistent with the historic outbreaks caused by penicillin resistant in the 1950s. The current epidemic strain, commonly referred to as USA300, has aggressively spread across the United States causing an inordinate number of skin and soft tissue infections in diverse healthy populations ranging from children to senior citizens. Comparative genomic sequencing of 10 chosen USA300 isolates representative of different types of infections and from different regions of the US revealed the molecular scars of an epidemic strain that is rapidly changing. This lecture will discuss *S. aureus* epidemic waves and the current emergence of community associated MRSA.

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52.002

Evasion of Innate Host Defense by *Staphylococcus aureus*

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Human polymorphonuclear leukocytes (PMNs or neutrophils) are essential to the innate immune response against invading microorganisms. Although most bacteria are killed readily by PMNs, pathogens such as *Staphylococcus aureus* have evolved multiple mechanisms to circumvent destruction by neutrophils and thereby cause human infections. Notably, prominent community-associated methicillin-resistant *S. aureus* (CA-MRSA) strains have enhanced ability to evade killing by human PMNs and rapidly destroy these critical innate immune cells. CA-MRSA immune evasion is multifactorial and includes resistance to antimicrobial peptides, detoxification of neutrophil reactive oxygen species, production of cytolytic molecules, and reprogramming of normal neutrophil apoptosis or turnover. Collectively, the current data indicate enhanced CA-MRSA virulence is linked to evasion of killing by neutrophils, which likely underlies (at least in part) the ability of prominent CA-MRSA strains to cause disease in individuals without known risk factors for infection.

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52.003

Microbial Pathogenesis of Community-Acquired MRSA Infections

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Staphylococcus aureus is a commensal of the anterior nares. It permanently colonizes the moist squamous epithelium of about 20% of the population and intermittently colonizes another 60%. Several different bacterial surface proteins promote adhesion to desquamated nasal epithelial cells. Clumping factor B and iron-regulated surface determinant IsdA have been shown to stimulate efficient colonization of the nares of rodents, and in the case of ClfB, humans. ClfB binds to host cytokeratin 10 which is exposed on the surface of desquamated epithelial cells. When *S.aureus* breeches the skin it can cause both localized and invasive infections. The bacterium can express a plethora of surface-located and secreted molecules that promote infection. Surface proteins promote adhesion of bacteria to host cells and tissues. Surface polysaccharides and proteins help the bacterium to evade innate immune responses by inhibiting phagocytosis by neutrophils. The organism secretes proteins that can intefere with neutrophil migration and with complement