



8th Hospital Hygiene Congress

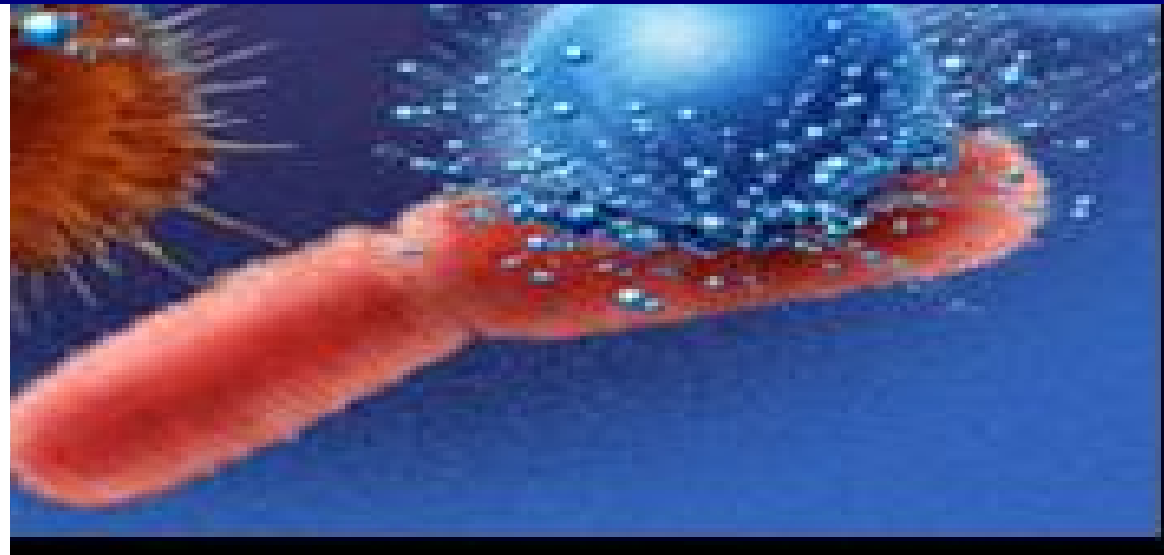
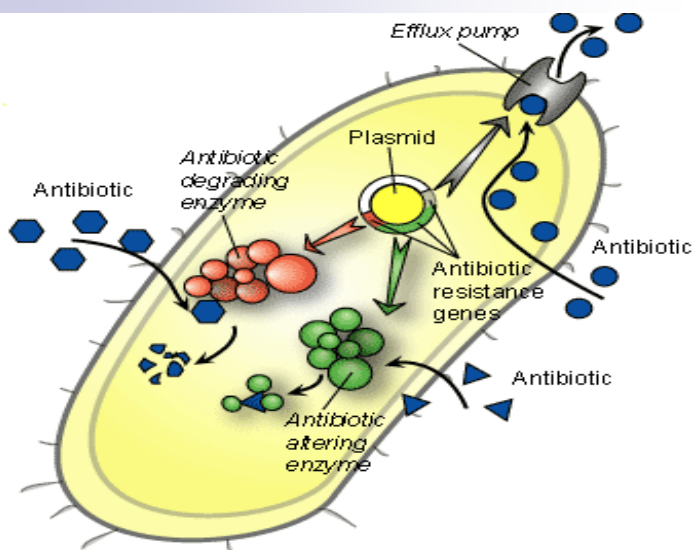
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CONGRESS CENTER VILLACH



Hygiene ist die präventive Medizin die Lehre, wie Krankheiten vermeidbar sind und darüber hinaus die Gesundheit selbst vermehrt werden kann, so dass Krankheiten überhaupt nicht entstehen.

Antibiotic resistance in antibiotic free environment

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Antibiotic resistance in the absence of antimicrobial use

- **An association between antibiotic use and the development of clinical resistance has been clearly documented in several cases**
 - Use of macrolides and resistance in *S. pyogenes*
 - Use of penicillins and resistance *S. pneumoniae*
 - Use of fluoroquinolones and resistance in *Enterobacteriaceae* and *P. aeruginosa*
 - Use of third-generation cephalosporins and resistance in *Enterobacteriaceae*
 - Use of carbapenems and resistance in *P. aeruginosa*
 - Use of linezolid and resistance in *E. faecium*

- **Reversal of antibiotic resistance following antibiotic-restriction policies has been documented in some cases**
 - Decrease of macrolide resistance in *S. pyogenes* after restriction in Finland
 - Decrease of penicillins resistance in *S. pneumoniae* after restriction in Hungary, Iceland, France



Antibiotic resistance in the absence of antimicrobial use

- High rates of acquired antibiotic resistance have been detected among commensal bacteria isolated from humans and wild animals not subjected to significant antibiotic exposure and living in remote areas of the planet
- This observations underscore the mechanisms involved in the emergence and spread of antibiotic resistance
- Better understanding of this mechanisms is crucial to improve strategies for antibioti-resistance control

Evidence for acquired under conditions of low or minimal antibiotic exposure

- The only available bacterial collection predating the antibiotic era is the Murray collection, including clinical isolates of Enterobacteriaceae from widely separated areas
 - collected during during 1917-1954
- In these isolates the presence of acquired resistance traits was found to be negligible
- This observation strongly emphasized the role of antibiotic use in promoting dissemination of acquired resistance among pathogenic bacteria

Hughes and Datta, Nature 302:725-726 (1983)

Studies on antibiotic resistance in commensal bacteria from humans living in remote settings

- The first studies was conducted in the 1960s in an isolated community of Kalahari bushmen in South Africa, which was free of drugs and had been in contact with other humans for a period of approximately 10 years
- In that community fecal carriage of enteric bacteria with acquired resistance traits was found to be low overall, and was limited to ampicillin resistance in *E. coli*

Summary of studies on acquired resistance in commensal enteric bacteria from remote human populations with low or minimal antibiotic exposure

Area	Date	Approximate population	Bacteria	Amp	Tet	Sxt	Chl	Nal	Reference
South Africa	1960	47	Enterics	11	0	NA	0	NA	Hughes <i>et al.</i>
Nepal	1997	330	Lactose-fermenting enterics	~70	~45	~55	~25	<5	Mare <i>et al.</i>
French Guyana	1999	388	Lactose-fermenting enterics	96	93	NA	52	8	Wakson <i>et al.</i>
Bolivian Chaco	1999	130	Escherichia coli	58	64	50	41	0	Grenet <i>et al.</i>
Peruvian Amazonas	2002	113	Escherichia coli	75	87	69	53	0	Bartoloni <i>et al.</i>
Sudan	2005	105	GNB/GPB	0	0	0	0	0	Sladeckova <i>et al.</i>

Nepal

- Nepalese village with very low access to allopathic medicines
- Investigation on the fecal carriage of antibiotic-resistant lactose-fermenting enterobacteria from healthy individuals
- Resistance: amoxicillin, tetracycline, trimethoprim-sulfamethoxazole, chloramphenicol, much lower quinolones



French Guyana



- Three traditional communities of Wayampis Amerindians, where exchanges with the exterior were limited and antibiotic consumption was moderate overall
- Resistance pattern similar to that found in Nepal
- Three individuals from this community were found to carry commensal *E. coli* resistant to expanded-spectrum cephalosporins due producing of the TEM-52 extended spectrum β -lactamase (ESBL)
- Resistant bacteria could be introduced into the community from antibiotic-exposed settings (e.g., through villagers that had been previously hospitalized)

Bolivian Chaco region

- To date, most remote human communities investigated for carriage of antibiotic-resistant bacteria are two Amerindian communities located in the Bolivian Chaco region and the Peruvian Alto Amazonas district
- High rates of fecal carriage of E.coli resistant to tetracycline, ampicillin, trimethoprim-sulfamethoxazole and chloramphenicol were detected in both communities
- No resistance was observed for quinolones
- Molecular characterization of resistant isolates from this area revealed a considerable variety of acquired resistance genes, entirely alike those encountered in resistant isolates from antibiotic-exposed settings in the same geographical areas



Sudan

- We tested 182 HIV negative patients from Mapuordit in South Sudan
- 105 isolates – most frequently were *Enterobacteriaceae*, *S. aureus*, *Moraxella catharralis*, *H. influenzae*, *S. pyogenes*
- All 105 isolates were 100% sensitive to all antibiotics



Cambodia


- We carried Cambodian children before of treatment with HAART
- High colonization with MR-GNB (e.g. ceftazidime-resistant) *Enterobacter spp.* and *Klebsiella pneumoniae* in children who were antibiotic and HAART-naive
- Colonization GPB - *S. pyogenes* ERY-R and MRSA



Reason for spread of MDR bacteria from SE Asia

- Not developing countries, any move, many high level hospitals
- Overproduction of generic antibiotic
- Exposition fake antibiotics with less antibiotic (low doses promote resistance)
- Huge concentrated population (Indonesia, India, China) on a square of SE Asia – 10% OF WS
- Diarrheic regions with *Enterobacteriaceae* spread





Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

- Identification of 44 isolates with NDM-1 in Chennai, 26 in Haryana, 37 in the UK, and 73 in other sites in India and Pakistan
- NDM-1 was mostly found among *Escherichia coli* (36) and *Klebsiella pneumoniae* (111), which were highly resistant to all antibiotics except to tigecycline and colistin
- Most isolates carried the NDM-1 gene on plasmids: those from UK and Chennai were readily transferable whereas those from Haryana were not conjugative. Many of the UK NDM-1 positive patients had traveled to India or Pakistan within the past year, or had links with these countries



- **Carbapenem resistance in *E. coli* from Australia due to metallo-beta-lactamase NDM-1**

- Emergence of MBL NDM-1 in Australia after its recent identification in India and UK, in an *E. coli* isolate accumulating emerging broad-spectrum resistance determinants, including the ESBL CTX-M-15 and two 16S RNA methylases

Poirel *et al.*, ICAAC, 2010

- **Dissemination of NDM-1-producing *Enterobacteriaceae* in India**

- A new metallo- β -lactamase, NDM-1 was identified in a *K. pneumoniae* (KPN) from a Swedish patient of Indian origin
- SENTRY program (2006-2007) – occurrence and characterization of NDM-1-producing strains from India
- 15 (1%; 6 *E. coli*, 6 KPN and 3 *E. cloacae*) isolates from New Delhi (2 sites), Mumbai and Pune carried bla_{NDM-1}
- All isolates were resistant to penicillins, cephalosporins and aminoglycosides, and susceptibility only to tigecycline and polymyxin B (two isolates were resistant)

Deshpande *et al.*, ICAAC, 2010

- **Recognition of NDM-1 AMONG *Enterobacteriaceae* in the United states**

- This is the first report of bla NDM in the United states and of metallo-beta – lactamase carriage among *Enterobacteriaceae* in the US
- These isolates are resistant to nearly all available therapeutic agents

Limbago *et al.*, ICAAC, 2010



- Antimicrobial resistance and Extended-spectrum β -lactamase (ESBL)-producing clinical isolates from urinary tract infections in Rwanda, East-Africa


- The findings of the present study reveal a significant increase of resistance to various groups of antimicrobial drugs and prevalence of ESBL producers is first described among UTI pathogens

Muvunyi, ICAAC, 2010

- Emergence of metallo- β -lactamase NDM-1 PRODUCING *Klebsiella pneumoniae* in Kenya

- Emergence of MBL NDM-1 in Africa, after the recent identification of NDM-1 producers in India and UK
- Worryingly the *K. pneumoniae* isolates studied here accumulated many threatening mechanisms of resistance to antibiotics

Poirel *et al.*, ICAAC, 2010

- 
- The characteristic of metallo- β -lactamase producing *E. coli* isolates in Canada from a patient with recent travel to India
 - This is the first report of *E. coli* ST101 with NDM-1 metallo-carbapenemase and Ctx-M15 ESBL from Canada

Peirano, ICAAC, 2010

- Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) in post-acute care facilities (PACF) IN Israel: A national intervention
 - There is a major burden of CRKP carriage in PACF

Ben-David *et al.*, ICAAC, 2010

- Multidrug-resistant *Enterobacteriaceae* including NDM-1 metallo- β -lactamase producers are predominant pathogens of HCAs in an Indian teaching hospital
 - Carbapenems were in little use but selection pressure exerted by other classes was sufficient to select carbapenemase due to co-selection suggesting role of single plasmid carrying multiple resistance genes

Sarma Male *et al.*, ICAAC, 2010

How to reduce the spread of resistance? Education



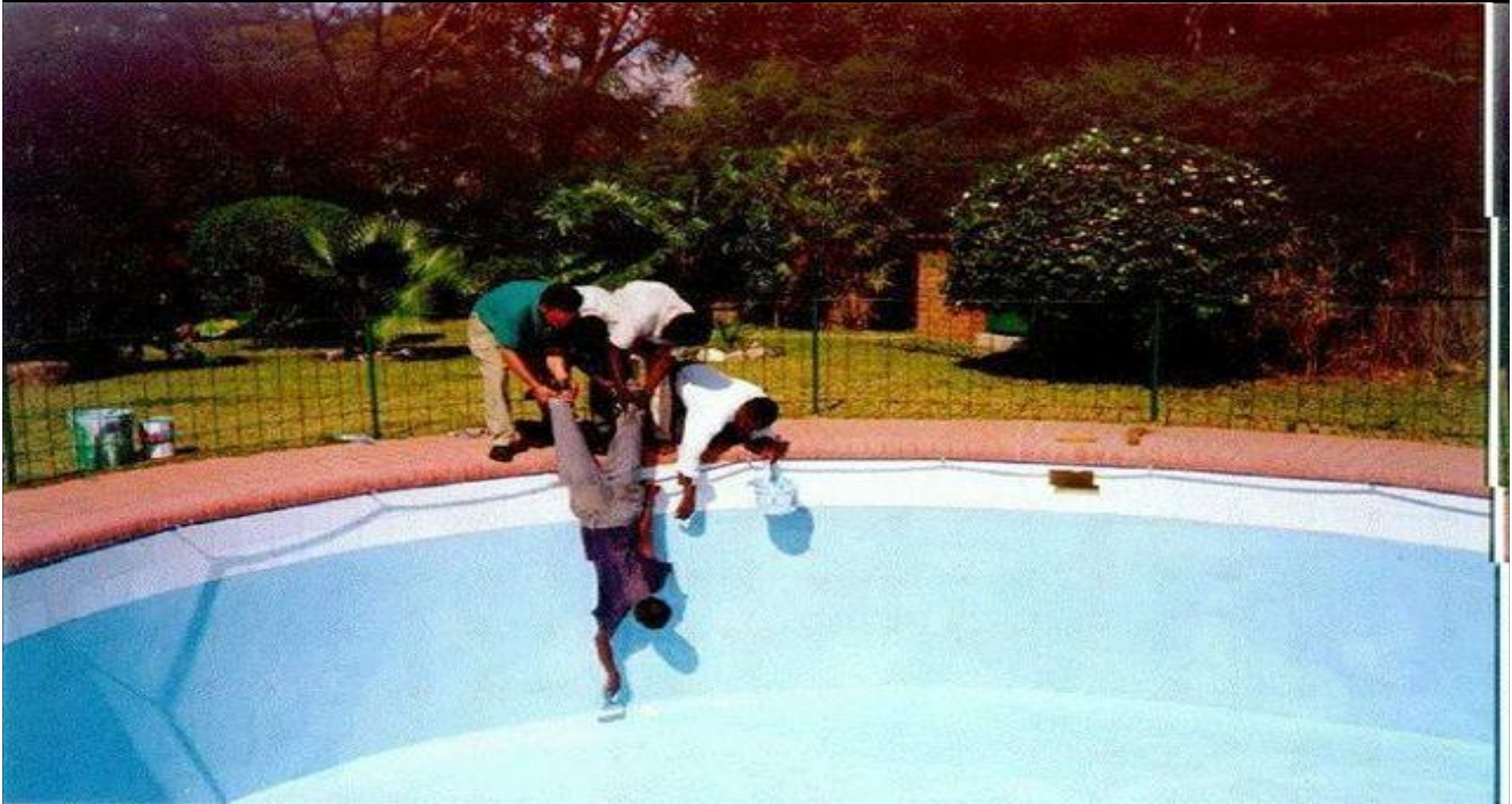
How to reduce the spread of resistance ?

Hospital antibiotic policy



How to reduce the spread of resistance ?

Internal cooperation and meetings



How to reduce the spread of resistance?
Improving health care infrastructure



Burundi Celebrity ATB-R free Environment

Conclusion



- In Sub-Sahara Africa and Latin America ATB-R in remote settings is minimal
- In South and SE Asia multiresistant strains are emergence and they spread all over the world from e.g. Taiwan, Hong Kong, India (e.g. PVDM-1, PRP, ERY-R *S. pyogenes*)
- Selective pressure generated by the use of antibiotics in clinical, veterinary, husbandry and agricultural practices is considered the major factor responsible for the emergence and spread of antibiotic-resistant bacteria since the beginning of the antibiotic era
- Acquired resistance traits can also be found in bacteria isolates from humans not subjected to significant antibiotic exposure and living in remote areas of the planet



Thanks for your attention!

