

rine containing disinfectant and to take specific precautions for the use of devices (disposable or dedicated to individual patient). Patient isolation must continue at least until diarrhoea has ceased. Each hospital should have an appropriate surveillance system to recognize an increase of the incidence of CDI in an early stage. All infection control measures should be written in a local protocol so that additional measures can be carried out as soon as a problem with CDI arises. When outbreaks occur, additional recommendations include a reinforcement of general and hand washing measures, intensifying of testing patients with diarrhoea for *C. difficile*, reinforcement of environmental cleaning, information and education of health-care workers, cleaning department and visitors, cohorting of infected patients, and eventually closure of the unit followed by intensive environmental cleaning. Restricted antibiotic prescribing is also highly recommended to reduce polypharmacy and duration of administration. Second and third generations cephalosporins and more recently fluoroquinolones have been identified as potential risk factors. Although some hospitals report successes for enhanced environmental cleaning with potentially effective agents such as hydrogen peroxide vapour, the evidence is too scarce to consider this as an evidence-based approach.

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61.003

Molecular Biology of Protein Glycosylation in the Symbiotic Anaerobe *Bacteroides Fragilis*

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B. fragilis is one of the most abundant gram negative anaerobes living symbiotically in the human intestine, where it digests carbohydrates for the host and has been implicated in immune system development. It is also an opportunistic pathogen and a reservoir of antibiotic resistance genes. *B. fragilis* produces multiple capsular polysaccharides and fucosylated glycoproteins. Mutant strains deficient in production of either of these cannot compete with wild-type in colonization of germ-free mice, indicating that both types of molecule are vital for symbiosis. Here we characterize the molecular biology of the protein glycosylation system. A cell lysate was enriched for glycosylated proteins by lectin affinity chromatography and proteins identified by mass spectrometry. These candidates were expressed from a plasmid in *B. fragilis* with a C-terminal His tag, purified and glycosylation confirmed by periodate reactivity and release of oligosaccharides. The glycoproteins include a secreted lipoprotein and several soluble periplasmic proteins, the first time that the latter has been observed in a bacterial species. Deletion of a genetic region containing a gene resembling an O-antigen flippase and multiple

lating and suggesting that it occurs in the periplasm. The smallest and most abundant glycoprotein was investigated in detail. Similar glycans were released by beta-elimination and hydrazinolysis, consistent with O-linkage to Ser or Thr. Point mutations in peptides that were rarely or never observed by mass spectrometry, and therefore likely to be glycosylated, identified one Ser and three Thr residues as probable glycosylation sites. Deletion of the signal peptide prevented glycosylation of the protein, consistent with it occurring in the periplasm. We continue to investigate the biochemistry and genetics of the glycosylation system, the biological functions of the glycoproteins and the role of glycosylation.

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61.004

Anaerobes As Biofilms

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Although anaerobes are predominant in humans, largely outnumbering aerobic bacteria, experimental data concerning their biofilm forming ability are still relatively few and essentially focused on the anaerobic flora of the mouth (including dental plaque, buccal mucosa and tongue biofilm) and the vaginal mucosa.

As the oral environment is concerned, its complexity has induced the development of a number of artificial mouth models able to simulate the different conditions of microbial growth within the microcosms of the oral cavity. With regards to the vaginal mucosa, recent studies have elucidated that the biofilm phenotype confers to *Gardnerella vaginalis* a survival advantage in the presence of hydrogen peroxide and lactic acid producing resident lactobacilli; on the other hand, the ability of probiotic strains of *Lactobacillus* to interfere with *Gardnerella vaginalis* and disrupt its biofilm, has been recently reported as a promising tool to reduce the need for antibiotics in the treatment of bacterial vaginosis.

As the intestinal tract is concerned, investigations by microscopic and FISH techniques have shown that mucosal bacteria, including bacteroides and bifidobacteria, occur in microcolonies and are distributed throughout the mucus layer.

Our group is currently investigating the role of anaerobes in the occlusion of biliary stents. SEM observations revealed that biliary sludge occluding the lumen of the 18 so far examined polyethylene stents was constituted by a multi-species (aerobes and anaerobes) microbial biofilm immersed in an amorphous material containing also dietary fibers and crystals of bile salts. The ability of the isolated anaerobic strains, belonging to the species *Bacteroides*, *Clostridium*, *Fusobacterium*, *Peptostreptococcus*, *Prevotella* and *Veillonella*, to form biofilm has been assessed in vitro. On the

light of the higher antibiotic-resistance reported in biofilm-growing bacteria, our findings on the role of anaerobes in the occluding process should be considered in selecting and dosing antibiotics for the prophylaxis of biliary stent blockage.

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Antiretrovirals for Prevention of HIV (invited)

62.001

Can Expanded Treatment Slow the AIDS Epidemic? The Public Health Perspective

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The introduction of antiretroviral therapy has changed the course of HIV disease by improving survival rates. But ART has equal potential for prevention, since it reduces the HIV RNA level and the probability of HIV transmission from an infected person to their sexual partners. Currently NIH is undertaking a large randomized clinical trial (HPNT052) in serodiscordant couples to study the effect of antiretroviral therapy in preventing HIV transmission to their partner. Although there have been no randomized controlled clinical trials on the subject, antiretroviral drugs are currently used in clinical practice for post-exposure prophylaxis after inadvertent occupational exposure or after sexual exposure to the virus. The success story in using antiretrovirals for HIV prevention has been shown from trials involving Mother to child HIV transmission interventions. Hence Can Expanded Treatment through the Public Health approach slow the AIDS Epidemic?

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62.002

Can Expanded Treatment Slow the AIDS Epidemic? The Behavioral Scientist's View

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This presentation explores existing and potential behavioral and social science contributions to consideration of the impacts of expanded antiretroviral (ARV) scale-up on the global HIV epidemic. Behavioral science literature commonly evaluates sexual behavior ("risk compensation") and medication adherence. While such analyses are critical to evaluation of overall impact and will be reviewed here, the presenter seeks to highlight approaches and empirical research that set (and sometimes problematize) such typically individually-based approaches in their social, cultural, political, economic, and human-rights/ethical contexts. It, furthermore, brings behavioral and social science contributions to bear on the critical question of: "how do we define and measure success?" The presentation addresses the ways in which interdisciplinary behavioral and social science work can illuminate key questions about feasibility and sustainability as well as "unintended consequences" of these biomedical interventions on non-biomedical HIV pre-

vention interventions and social and health systems. From a practical standpoint, such analyses can 1) assist identification of appropriate methods and criteria to evaluate impacts; 2) assist targeting and revision of patient and community educational materials and involvement strategies; and 3) aid development of uptake, retention and medication and general program adherence schemes that more explicitly address economic, cultural, and social barriers. A systematic analysis of lay media (primarily print sources) about recent ARV scale-up will be used as a case study to demonstrate how social/behavioral science perspectives may shed light on popular conceptions of such programs and technologies, how scientific information is interpreted by media and the general public, and how consequential misconceptions may arise. In the overall presentation, special emphasis is placed on examination of approaches and perspectives that are likely to inform questions and solutions relevant to both ARV treatment and biomedical prevention technologies under testing, particularly implementation of ARV pre-exposure prophylaxis.

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62.003

Antivirals in Uninfected People: PrEP and PEP

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Background: With the exception of male circumcision and some behavioural interventions, randomised controlled trials (RCTs) of HIV prevention interventions have reported disappointing results. In this presentation, data on post-exposure prophylaxis (PEP, the provision of anti-retrovirals (ARVs) after exposure to prevent HIV infection) and pre-exposure prophylaxis (Pre-EP, ARVs provided before exposure to prevent infection) will be reviewed.

Methods: A guided literature review on the efficacy, cost-effectiveness, implementation policy and likely public health impact of PEP and pre-EP was conducted.

Results: No RCTs examining the efficacy of PEP were identified. Nevertheless, a variety of animal and observational evidence suggests that PEP prescribed within 72 hours of HIV exposure is likely to substantially reduce the risk of HIV transmission. PEP use at the population level is generally not cost-effective, unless its use is highly targeted towards the highest risk exposures. Despite these limitations, policies recommending PEP after sexual and other HIV exposures exist in many settings. Although it is possible that post-EP may prevent cases of transmission, a substantial public health impact on the HIV epidemic is unlikely. RCTs evaluating the efficacy of Pre-EP are currently underway in a number of settings. Animal data strongly suggest that Pre-EP will need to consist of combinations of more than one ARV. The cost effectiveness of Pre-EP will depend strongly on the risk setting. No locations were identified which currently recommend Pre-EP, and there has been little study of the potential public health impact of this preventive intervention.

Conclusion: PEP is being increasingly utilized as a form of HIV prevention, despite the lack of any efficacy data from