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Snippets

RESEARCH SNIPPETS FROM THE WORLD OF MEDICINE

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Intense public support for clinical research can be a mixed blessing — and the hunt for a vaccine against AIDS offers an important lesson for many biomedical initiatives on what can go wrong. Last year's failed clinical trial for Merck's HIV vaccine led many to claim that AIDS vaccine research was facing a crisis (*Nature 452:503, April 2008*). The decision to move Merck's candidate vaccine into clinical trials was partly based on the need to show progress, in order to justify the millions of dollars in funding received from philanthropists and taxpayers. The vaccine not only failed to lower patients' viral loads, it even boosted the risk of infection in some groups. This dealt a double blow to the field of HIV research, leading to a setback in the search for therapies while eroding public support.

In Africa, as elsewhere, fever is often treated presumptively as malaria, resulting in misdiagnosis and overuse of antimalarial drugs. In this scenario, rapid diagnostic tests (RDTs) for malaria may play an important role in improved fever management. A study carried out in Uganda (*J Infect Dis. 15;197(4):510-8,2008)* compared RDTs based on histidine-rich protein 2 (HRP2) and RDTs based on *Plasmodium* lactate dehydrogenase (pLDH) with expert microscopy and PCR-corrected microscopy for 7000 patients at sites of varying malaria transmission. HRP2-based RDTs were found to have high positive predictive and negative predictive values and were identified as good diagnostic choices for areas with medium-to-high malaria transmission rates in Africa.

Each of us carries a community of microorganisms in our intestinal tract that is necessary for optimal health but varies in composition from person to person. In order to identify gut microbes that maximally influence human physiology, a study was carried out on seven members of a four-generation Chinese family (*Proc. Natl. Acad. Sci. U.S.A. 105, 2117, 2008)*. A phylogenetic picture of the resident microbes was assembled by sequencing rRNA genes. Parallel analysis of urine samples from the same family allowed the authors to correlate variations in resident microbes with variations in excreted metabolites. They found that *Faecalibacterium prausnitzii* was associated with the presence of dimethylamine, a tentative indicator of metabolic syndrome and diabetes. It may therefore eventually be possible to have bacterial indicators of disease states and of human well-being.

A "safe" version of Ebola virus has been developed by researchers at the University of Wisconsin to help increase opportunities to study the deadly virus (*Proc. Natl Acad. Sci. USA 105, 1129-1133, 2008)*. The gene coding for VP-30 in the wild virus was replaced with a marker gene, thus disabling its capacity to multiply in normal human cells. If approved by regulatory authorities, this non-infectious virus could be studied in a broader variety of laboratories and enable speedier development of vaccines and antiviral compounds. Currently, work on Ebola viruses is conducted only in a small number of laboratories rated at biosafety level-4 (BSL-4).

For more than 500 years, Christopher Columbus has been alternately blamed and exonerated for bringing syphilis to Europe. Now, a genetic analysis of *Treponema* strains indicates that syphilis is a close cousin to yaws, which is endemic in South America, suggesting that the malady has its roots in the Americas (*PLoS Negl. Trop. Dis. **2**, e148, 2008*). Twenty-two *Treponema* samples isolated from human infections, including two collected from a Guyanese village with an active outbreak of yaws (*T. pertenue),* were studied. Four of 17 base pairs were identical between *T. pallidum and T. pertenue*. The overlap with any other kind of *Treponema* was limited to one or none of the sites.

We usually live in harmony with tens of millions of bacteria in our gut. It is a commonly held perception that an imbalance in the normal commensal microbiota contributes to the development of inflammatory bowel diseases. A study (*Nature* 453, 620–625, 2008) provides some basis for this perception. Using specific pathogen-free mice, it was found that a factor produced by *Bacteroides fragilis*, a common commensal bacterium in mammals, could actually prevent colitis caused by *Helicobacter hepaticus*.

Use of prophylactic antibiotics for infective endocarditis before tooth extraction is becoming increasingly controversial. Using 16*S* ribosomal RNA sequencing and quantitative polymerase chain reaction assays, a study (*Circulation 117, 3118, 2008*) profiled the bacteria in sequential blood samples drawn from patients who had undergone tooth extraction with or without antibiotic treatment and from untreated patients who simply brushed their teeth. It was found that brushing alone caused a substantial increase in bacteria in blood samples. The risk of bacteremia following brushing was comparable to that

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following a tooth extraction. This underscored the need for controlled clinical trials to evaluate current practices.

It is a common assumption that most recurrent urinary tract infections (UTIs) caused by uropathogenic *Escherichia coli* (UPEC) are caused by the persistence of UPEC strains in the faecal flora, which re-infect the bladder. Recent work on mice, however, suggests an additional explanation for UPEC persistence and recurrent UTIs (*PLoS Med. 4, e329, 2007*). In this model, UPEC strains invade the epithelial cells that line the bladder and form intracellular bacterial communities (IBCs). Some infected epithelial cells are expelled into the urine, whereas others release bacteria, many of which adopt a filamentous morphology. These filamentous bacteria can resist the host immune response, and ultimately the pathogen establishes an intracellular reservoir that is protected from both antibiotics and host immune surveillance. This finding will have important implications for treatment of recurrent UTIs.

Finally, there is some good news for travellers. Enterotoxigenic *Escherichia coli* (ETEC) are a major cause of travellers` diarrhoea. In a phase II trial, a candidate vaccine containing heat-labile enterotoxin, derived from ETEC, delivered by a skin patch, was tested among travellers to Mexico and Guatemala (*Lancet 371(9629):2019-25, 2008*). Participants were vaccinated before travel, with two patches given 2 to 3 weeks apart. They were found to be protected against moderate-to-severe diarrhoea.

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