**Synopses of Research Articles**

**Injections and HIV in Rural Zimbabwe**
DOI: 10.1371/journal.pmed.0020054

Of the 40 million people worldwide with HIV, 30 million live in the developing world. By far the worst hit region is sub-Saharan Africa, where nearly four million children have lost one or both parents to HIV/AIDS since 2000. Is heterosexual transmission the driving force behind the HIV epidemic in sub-Saharan Africa? In a controversial debate, some researchers have suggested that other factors such as unsafe medical injection practices may also be to blame, and that by overlooking, and even suppressing, analysis of this possible route of transmission, the current focus on preventing sexual transmission may be misguided. In this month’s *PLoS Medicine*, Ben Lopman and colleagues argue that although it is right to criticize the lack of evidence on unsafe medical injection, field data are hard to collect. They note that in the only published study addressing this issue, Kiwanuka and colleagues found no link between unsafe injections and HIV spread in rural Uganda. In an effort to “inform the debate” further, Lopman and colleagues looked at the association between HIV and unsafe injection practices in rural Zimbabwe.

The team analyzed data from adults in Manicaland, a rural part of Zimbabwe, who were taking part in the Manicaland HIV/STD Prevention Study. In 1999 and 2000, eligible patients were tested for HIV and surveyed (86.7% were HIV negative at the start of the study), and were followed up three years later.

In 2002 and 2003, 505 of the men and 1,342 of the women, representing a 69.7% follow-up, were again interviewed and tested for HIV infection. Of these, 40% reported having had an injection or needle prick during the study period. A total of 67 patients developed HIV during the study; of these 13 (19%) said they had not had sex during the study period and 40 (60%) said they had not had an injection. The statistical analysis found no significant association between injections and HIV infection in men or women.

Patients who had HIV when the study began did not have higher rates of injections. Instead, injections were highly associated with childbirth and pregnancy. But since HIV-positive women have reduced fertility, a reduction in the use of maternal services may partially explain why injections were not more common in these HIV-positive patients. In this study, the strongest predictor of HIV infection was symptoms of sexually transmitted disease.

Despite problems of recall bias and under-reporting of sexual activity—a particularly difficult problem in studies in Africa—sexual behavior seems to be a major source of infection, and local policy-makers would therefore do best to concentrate on the prevention of sexually transmitted infections.

Lopman BA, Garnett GP, Mason PR, Gregson S (2005) Individual level injection history: A lack of association with HIV incidence in rural Zimbabwe. DOI: 10.1371/journal.pmed.0020037

**Mass Spectrometry–Based SARS Genotyping**
DOI: 10.1371/journal.pmed.0020052

To quickly control infectious disease outbreaks, extensive information is required to identify the source and transmission routes, and to evaluate the effect of containment policies. Traditionally, scientists have used travel- and contact-tracing methods, but the recent SARS epidemic showed that sequence-based techniques for pathogen detection can also be important tools to help understand outbreaks. Jianjun Liu and colleagues adapted mass spectrometry (MS)–based genotyping, already used as a high-throughput way of detecting single nucleotide polymorphisms in human DNA, to the analysis of the SARS virus from clinical samples.

The major breakthroughs against SARS were the discovery of the SARS coronavirus (SARS-CoV) as the etiological agent and the sequencing of the SARS genome. Liu’s colleagues at the Genome Institute of Singapore had previously shown that common genetic variants in the SARS-CoV genome could be used as molecular fingerprints to help trace the route of infection. However, as “sequence analysis of large numbers of clinical samples is challenging, cumbersome, and expensive,” they felt that “what is needed is a rapid, sensitive, high throughput, and cost-effective screening method.” Towards this goal, Liu and colleagues now demonstrate that an MS-based technique can quickly yield accurate information on clinical isolates (in this case from the 2003 SARS outbreak in Singapore).

The scientists demonstrate the sensitivity of the assay in detecting SARS-CoV variations and test it further in cultured viral
is equitable antiretroviral allocation strategies in resource-constrained countries. DOI: 10.1371/journal.pmed.0020050
One of the most common and most serious complications of both type 1 and type 2 diabetes is diabetic nephropathy. It occurs in around 30% of patients with type 1 diabetes and 10% to 40% of patients with type 2 diabetes. Diabetic nephropathy is the leading cause of renal failure in the developed world. The main effect of diabetic nephropathy is proteinuria, initially in very small amounts but which increases, leading to nephrotic syndrome and end-stage renal disease in most cases.

Various risk factors in individuals with diabetes are known to increase the chance of developing diabetic nephropathy, including South Asian or African background, male sex, long history of diabetes, poor blood sugar control, high blood pressure, and smoking. One early change associated with diabetic nephropathy is degeneration of the renal tubular epithelium, but the exact cause of this at the cellular level is unclear. Erwin Böttinger and colleagues have dissected out one key point in the progression to diabetic nephropathy. They looked at cell lines of renal tubular cells from humans and mice and kidney biopsies for the disease. Diagnosis is usually based on chest radiographs, which are not very specific for pneumococcal disease.

In their quest for a more specific diagnostic test, Shabir Madhi and colleagues—who are conducting clinical trials on pneumococcal vaccines in children—examined whether serum concentrations of procalcitonin and C-reactive protein could improve the specificity of chest radiographs to diagnose pneumococcal pneumonia and thus be useful in the future evaluation of pneumococcal vaccines. Elevated levels of both proteins are associated with bacterial disease. They might therefore help to differentiate bacterial from nonbacterial causes of pneumonia, and thus allow to "enrich" the analyzed disease cases for those of pneumococcal origin, against which the vaccine is potentially active.

This study represents a first step, in which the researchers tested whether adding information about procalcitonin and C-reactive protein levels to data from a completed vaccine trial would affect the outcome regarding vaccine efficacy. When re-analyzing previous trial data under these conditions, the vaccine appeared more efficacious compared with placebo when either elevated procalcitonin or elevated C-reactive protein levels were taken into account. The efficacy estimate was greatest when cases of pneumonia that had elevated levels of both procalcitonin and C-reactive protein were compared against placebo.

These data suggest that elevated levels of C-reactive protein and procalcitonin, in conjunction with chest radiography, could improve the specificity of a diagnosis of pneumococcal pneumonia over that of chest radiography alone. This combined diagnostic test could be useful for further evaluation of pneumococcal vaccines. The hope is that among patients identified as having pneumonia by the combined test, a higher proportion would have pneumonia of pneumococcal origin. As a consequence, there would be less “background noise” caused by other forms of pneumonia, and this should make it easier to assess the efficacy of vaccine candidates. However, as the researchers point out, this analysis was not a primary objective of the present trial. This analysis can therefore serve only as a hypothesis-generating study, and as such the hypothesis must be tested in other study settings.

The study was sponsored by Wyeth, manufacturers of the pneumococcal vaccine used.

Madhi SA, Heera JR, Kuwanda L, Klugman KP (2005) Use of procalcitonin and C-reactive protein to evaluate vaccine efficacy against pneumonia. DOI: 10.1371/journal.pmed.0020038

Why Blood Glucose Control Matters for the Kidney

DOI: 10.1371/journal.pmed.0020056

One of the most common and most serious complications of both type 1 and type 2 diabetes is diabetic nephropathy. It occurs in around 30% of patients with type 1 diabetes and 10% to 40% of patients with type 2 diabetes. Diabetic nephropathy is the leading cause of renal failure in the developed world. The main effect of diabetic nephropathy is proteinuria, initially in very small amounts but which increases, leading to nephrotic syndrome and end-stage renal disease in most cases.

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Towards Better Evaluation of Pneumococcal Vaccines

DOI: 10.1371/journal.pmed.0020053

Pneumonia remains the leading cause of death worldwide in children. Several vaccines against pneumococcal pneumonia are at various stages of development, but the testing of their efficacy is hampered by the lack of noninvasive tests that are sensitive and specific for the disease. Diagnosis is usually based on chest radiographs, which are not very specific for pneumococcal disease.

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