King Kennard Holmes—Chair of the Department of Global Health of the University of Washington

Interviewed by Marc Vandenbruaene

For more information on the **17th International Society for Sexually Transmitted Disease Research conference** see http://www.isstdr.org

In 2006, King Kennard Holmes became the Chair of the Department of Global Health of the University of Washington, where he has held faculty, hospital, and administrative positions since 1969. He has been the Director of the university's Centre for AIDS and STD since 1989, and from 1995 has led the Section of Allergy and Infectious Diseases at the Harborview Medical Center, Seattle. Holmes earned a BA Cum Laude at Harvard in 1959 and an MD at the Cornell University Medical School in 1963. In 1967, he received his PhD in microbiology at the University of Hawaii. He was trained in Internal Medicine at Vanderbilt University and at the University of Washington (1963–69). The author or coauthor of 500 original papers in refereed journals, Holmes has contributed to more than 150 chapters in books, editorials, reviews, or symposia, and has edited more than 25 books, monographs, or journal supplements. He is known as the founding father and first editor of the textbook *Sexually Transmitted Diseases* (McGraw-Hill). Holmes has held more than 60 responsibilities or positions in national or international institutes, and has received numerous awards. He cofounded the International Society for Sexually Transmitted Disease Research (ISSTDR) and is President-Elect of the International Union Against Sexually Transmitted Infections (IUSTI). His 70th birthday was honoured during the 17th biennial ISSTDR conference held in his hometown of Seattle.

TLID: How did you become interested in medicine?

KH: Chemistry was my initial goal. My father was a chemical engineer. At Harvard we had some geniuses in chemistry, but I wasn't one of them. I really enjoyed biology and botany during my junior year, and that encouraged me to go on into medicine.

TLID: Have your interdisciplinary interests been useful in your further career?

KH: I do try to build interdisciplinary teams to work on difficult problems. I really love clinical medicine, but I also like public health, epidemiology, microbiology, and in recent years social sciences. I am hardly a laboratory scientist anymore, although I still have a laboratory run by people who provide innovative diagnostic technologies for international clinical and epidemiological research. Today when I go into my laboratory, the personnel gather protectively around the equipment and glassware so that I won't break anything.

TLID: What drew you into the sexually transmitted disease (STD) field in the 1960s?

KH: I was drafted into the US Navy during the Vietnam War in 1964. I asked the Navy officer responsible for my assignment if he could send me to Japan or Hawaii, and offered to serve for an extra year in that case. He sent me to Pearl Harbor. I had become interested in microbiology when I was an intern at Vanderbilt University, and I enrolled in the microbiology predoctoral programme at the University of Hawaii while I was at Pearl Harbor. After my first year, the Navy transferred me to a preventive medicine unit in Pearl Harbor, to become the epidemiologist for the Navy's Seventh Fleet. When I arrived at my desk, there was a stack of reports waiting for me about incurable gonorrhoea in the Seventh Fleet. The main epidemiological problem was penicillin-resistant gonorrhoea. That's the way I first became involved in STD research.

TLID: What was the extent of the gonorrhoea problem in the Navy at the time?

KH: My first study was on the aircraft carrier the *USS Enterprise*. When the ship went into port for 3 or 4 days, the men would go on liberty and some had sex with sex workers. After the ship left port, the typical epidemiological curves of gonorrhoea and non-gonococcal urethritis

(NGU) occurred, with about 200 men coming to sick bay with urethral discharge. We found that many of the cases diagnosed as gonorrhoea that weren't responding to penicillin were actually NGU, which responded well to tetracycline. The remaining cases that were not responding to penicillin were found to be gonorrhoea caused by penicillin-resistant strains of *Neisseria gonorrhoeae*. 30% of men with gonorrhoea failed on treatment with procaine penicillin.

I was horrified to see many of the patients who did respond to new treatment with procaine penicillin plus probenecid, starting to come back a week or two later with recurrent urethral discharge. Their cultures were negative for *N gonorrhoeae*. I suspected they had probably acquired two infections at the same time. The second one—post gonococcal urethritis—had a longer incubation period, and like NGU, responded to tetracycline.

TLID: How will we treat gonorrhoea 20 years from now in view of multiresistance?

KH: Looking back, as soon as sulfonamides were introduced, gonococcal resistance to sulfonamides emerged. Streptomycin resistance emerged immediately after streptomycin came into use. I entered the field when penicillin doses had already been steadily raised to cope with increasing gonococcal resistance, mediated by chromosomal mutations. In the Philippines, beta lactamase-producing gonococci appeared, and then ciprofloxacin resistance emerged, related to self-medication by female sex workers, who could readily buy antibiotics from a pharmacy.

Over time, gonococci have also developed resistance to the tetracyclines. With rifampicin treatment, gonococci developed resistance almost instantly. Spectinomycin high-level resistance emerged fairly quickly where this drug was widely used. Now we have just taken fluoroquinolones off the list of drugs recommended for treating gonorrhoea and have also seen some macrolide resistance.

I fear that next we will see the spread of gonococcal resistance to third-generation cephalosporins. That would be a major threat. For sure, 20 years from now we will need different drugs. I am not sure whether we will be using single-dose regimens; however, I am confident that if new antimicrobial drug development is adequately supported, both in academia and in industry, we will not have to go back to irrigating the urethra with silver nitrate.

TLID: Do you think there is enough investment in antibacterial research?

KH: I don't see the end of the line of discoveries of new targets and products, particularly with new information on genomics and proteomics, high-throughput screening, etc. I agree the antibacterial pipeline is now very limited, but the potential is there if funding becomes adequate. Public-private partnerships will be essential.

I am also interested in what more we can do to prevent the emergence of antimicrobial resistance. I have chaired the antimicrobial resistance committee for the International Society for Infectious Diseases in the past. We need a lot more investment in surveillance for antimicrobial resistance in key pathogens. The surveillance systems we have for gonococcal resistance in the USA and globally can serve as models for what can be done for other microorganisms.

We need to promote prudent use of antimicrobial drugs, and develop and promulgate use of better diagnostics for developing countries, to help us avoid unneccesaary use of antibiotics.

TLID: Can you comment on stigma related to STDs at the time your career started in the 1960s?

KH: In the military during the Vietnam War, there was a lot of stigma related to STDs. There was the potential for administrative penalties for people who were found with STDs: officers never got STDs. Officers always came to see the doctors away from sick bay. Civilian STD clinics were typically not in the university hospitals, but they were often in the basement of public-health buildings and tended to attract only certain types of patients, not a mix of patients. In most of the clinics you predominantly found men. Women tended to avoid STD clinics.

TLID: Politicians have been unwilling to take AIDS on because they thought it would be bad for their reputation, for their business, or getting into power. How do leaders now deal with AIDS?

KH: I remember a meeting in Washington, DC, where former president Ronald Reagan finally used the word AIDS for the first time in public. He was introduced by Elizabeth Taylor, and endorsed health care for people affected by AIDS and everybody applauded. Then he said that he was making this endorsement even though it was immoral how people acquired AIDS. Most people in the audience then booed him. His view of people with HIV/AIDS as "immoral"—like the view of many leaders around the world at the time—was obviously stigmatising.

Today I think there is no question that stigma is still a major barrier, particularly to providing effective care and prevention for HIV in developing countries. For example, I'm involved in a project in Africa where about 30% of men and women who are randomly selected from the community for testing are HIV positive. Few of them had previously been tested, few knew they were infected. When a husband has died of AIDS and there is a funeral, the leaders often offer reasons why it couldn't have been AIDS, such as "It happened too quickly", etc.

For more information on **antibiotic-resistant gonorrhoea in the 1960s** see *JAMA* 1997; **202:** 461–66; DOI:10.1001/jama.202.6.461

Even today, few leaders around the world talk about AIDS or STD, although this is changing. For example, Uganda's President Museveni has been very open about HIV/AIDS. He is famous for his call for "zero-grazing" and describes HIV infection in terms that the public really understands. Nelson Mandela is another example, who after his presidency, has become active in advocating for HIV/AIDS care and prevention. Mechai Viravaidya of Thailand was incredibly important in leading the early fight against HIV/AIDS in that country. Albert Gore near the end of his term as US vice president influenced the G8 and the World Bank to talk about HIV/AIDS as a priority. The conservative US federal government now openly promotes and supports global efforts for HIV/AIDS care and prevention.

TLID: You are founding Chair of the Department of Global Health at the University of Washington. What is the mission of this department?

For **review of condom effectiveness** see *Bull World Health Organ* 2004; **82:** 454–61

KH: Our mission is to reduce the disparities between the health of the world's poorest 5 billion people and the much better health of the wealthiest 1 billion, through programmes that combine learning, discovery, and service. Our first priority is to meet the needs of students and professional trainees in international health both in the USA and in low income countries. The University of Washington has ten international research training programmes funded by the US National Institutes of Health Fogarty International Center. We have large student exchange programmes: more than 1700 international student exchanges per year at the University of Washington.

TLID: The University of Washington collaborates with the Coptic Orthodox Church in providing antiretroviral therapy in Nairobi, Kenya. How is it organised?

KH: With US federal funding, the University of Washington has provided training and technical assistance in 26 countries around the world to help establish HIV/AIDS and STD treatment and prevention programmes. The University of Washington faculty helped the Coptic Orthodox Church and Hospital in Nairobi to develop a new clinic—the Hope Clinic for HIV/AIDS treatment—and has helped to train their staff. The Hope Clinic's services are modelled on the services that are provided in the best clinics around the world. Some people think that is unpractical and unrealistic, but I think the clinic is a very feasible model; we can aim high.

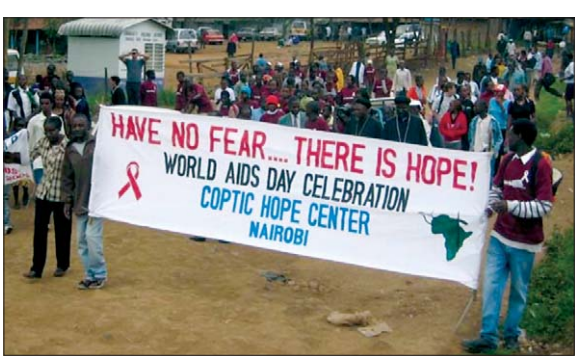

Figure: **Coptic Hospital in Nairobi**
The Coptic Hospital Hope Clinic in Nairobi, Kenya is a clinic where people can receive antiretroviral drugs, treatment, and counselling. King Holmes: "In Nairobi this clinic delivers a standard of care on the level offered in the USA. The clinic acts in a culturally sensitive way, without compromising the quality of care."

The Coptic Hope Clinic has developed two satellite clinics now, and they are providing antiretroviral therapy to 5500 people. 40% of the patients in the Hope Clinic are Muslims; the clinic makes therapy available to anybody, not just the Coptic Christians. People don't have to join the church to receive therapy and compassionate care. There is a very high retention of people under therapy.

TLID: In 2004 you wrote a review on the effectiveness of condoms. You concluded that although condoms are not 100% effective, partial protection can substantially reduce the spread of sexually transmitted infections (STIs) within a population. Do you think churches will ever be "comrades in arms" in condom promotion?

KH: What I typically see is that faith-based organisations are very committed to pastoral care for HIV/AIDS in a compassionate way. Many churches have been uncomfortable with a comprehensive approach to prevention and have tended to focus on promoting abstinence until marriage and fidelity within the marriage. But there are many exceptions in which religious leaders have supported—or at least not opposed—a more comprehensive prevention approach. For example, when we decided to work with the Coptic Church, I asked Bishop Paul—who had been trained as a physician—whether he would be comfortable with us working on prevention in his clinic, including discussion of condom use and he said: "yes".

TLID: You called male circumcision for HIV/AIDS prevention an "anatomic vaccine for life". What can we expect from male circumcision on a population level?

KH: The potential advantage of circumcision over other behavioural interventions or medical interventions that would require repeated use is that circumcision only has to be done once, and it reduces the risk of HIV acquisition by 50–60%.

The data from three trials are consistent with the epidemiological data. Ethiopia is a good example, where 60% of the population are Coptic Orthodox Christians and 40% are Muslims. Both groups circumcise infants. The prevalence of HIV appears to be substantially lower in

Ethiopia than in some surrounding countries. It will be very important to work with the sociobehavioural scientists and policymakers to promote male circumcision. There is the concern about risk compensation or disinhibition—that is, men might engage in riskier sex, thinking circumcision protects them against HIV infection. We don't have much evidence so far that this is happening. Furthermore, as with any biomedical prevention intervention, the potential for implementing links with sociobehavioural interventions is extremely important.

Should we implement circumcision programmes? Absolutely. I would recommend circumcising infants and catching up in young adults who were not circumcised earlier. Circumcision should definitely be linked to other types of preventive interventions. Circumcision is not 100% effective. Condom use, abstinence, and fidelity are still important.

TLID: What is your opinion on abstinence-only programmes for HIV/AIDS prevention?

KH: We have little or no evidence that abstinence-only policies work, either in producing self-reported behaviour change or in terms of preventing HIV or STDs. It is certainly important to promote abstinence to young people, to promote fidelity, and to promote condom use in a balanced ABC-approach, together with the other types of effective interventions that are available as well. I think that the requirement that "X%" of funding available for prevention must be spent on abstinence-only programmes is unwise. However, maybe abstinence-only programmes represent the tax we have to pay to keep getting HIV/AIDS treatment, care, and prevention funding approved by governments. If that is the case, it is an affordable tax. The US President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria are the most exciting programmes we have ever had to work with in HIV/STD treatment and prevention.

TLID: STD incidences are rising among men who have sex with men in the USA and in Europe. Do you see ways to reinforce prevention in these men?

KH: We see two phenomena now in men who have sex with men. One is disinhibition related to availability of highly active antiretroviral therapy; the other is HIV sero-sorting. Sero-sorting is a strategy used by some men who now disclose their HIV sero-status to potential sex partners and have unprotected sex only in seroconcordant situations—that is, with those whose HIV serostatus is the same as their own. These men avoid sex or use condoms in serodiscordant situations or when the serostatus is unknown. This approach may reduce, but not eliminate, the risk of HIV transmission, but it obviously increases the risk of transmitting other STIs. I believe that sero-sorting is a major reason for the new epidemics of syphilis, gonorrhoea, and chlamydial infection—including lymphomagranuloma venereum—in men who have sex with men.

There are two messages we have to communicate about sero-sorting. First, it needs to be more widely known that sero-sorting is a very risky approach for preventing transmission of HIV, even if everyone knew and honestly disclosed his serostatus. The second message is about super-efficient HIV transmission during acute HIV infection. If either of two partners who were HIV-seronegative when last tested has subsequently acquired new HIV infection, that partner could be a super-efficient HIV-transmitter during the period of acute but still undiagnosed HIV infection.

Another important approach to HIV prevention is postexposure antiretroviral prophylaxis, which also affords the opportunity for risk reduction counselling. There is also interest in studies of pre-exposure prophylaxis. The potential effectiveness of this approach has to be balanced against the likely effect on disinhibition and on promoting HIV drug resistance, and other potentially negative outcomes.

Addressing the comorbidities that are crucially important in putting men who have sex with men at risk for HIV acquisition is also a neglected area so far. The EXPLORE study in the USA did not find a significant reduction in long-term protection of men who have sex with men against HIV acquisition with sociobehavioural interventions. What the study did show, however, was that the risk of acquiring HIV was associated with comorbidities such as alcohol use, illicit drug use, or depression. Dealing with addiction and depression is another important approach to preventing infection in men who have sex with men.

TLID: Has AIDS modified your thinking and practice about STDs?

KH: Very much. I have learned about the importance of involving communities—the affected communities—in the clinical and public-health work that we do.

Community involvement is essential in the planning, design, implementation, and evaluation of programmes. Ultimately, such partnerships have been amazingly important for research and prevention programmes as they are developed.

We have a Community Advisory Board for the Center for AIDS and STD in Seattle. We have changed the name to Community Action Board to encourage active involvement in our various programmes. The board includes people who represent men who have sex with men in Seattle, youth, African-born populations, and other people of colour.

TLID: Looking back on your career, what do you see as your main contributions?

KH: Let me quote Bob Brunham, one of my first post-doctoral fellows, who today is the head of the communicable diseases programme in British Columbia (BC, Canada). He told me, "King, do you know why you have been successful? It's because you had such good pre and post-doctoral fellows." He was absolutely right. If I can be subjective about my main contribution, it has been recruiting, training, and mentoring many of today's leaders in STD and HIV research, patient care, and disease prevention around the world. That is certainly what I have enjoyed the most.

TLID: What are your major disappointments?

KH: My major disappointment is our failure to take prevention research and prevention programmes seriously. We have too many polemics and debates stemming from different values and norms of the different "silos" working in the prevention field. The silos divide us. Our disciplines have become silos for the people who work in them. In the antiretroviral therapy field today, no clinician would give one antiretroviral drug. We give HAART, highly active antiretroviral therapy. Three drugs and they all have to be active drugs. In the prevention field we still have people who are arguing about abstinence-only, condom-only, circumcision-only, STD-suppression-only, etc. For HIV/AIDS prevention we need the concept of HARP: highly active retrovirus prevention, in which we combine potentially synergistic prevention activities.

I had also been disappointed in the past because we had major deficiencies at the level of funding for global health. However, this has obviously changed for the better. PEPFAR, the Global Fund, the World Bank, and other support organisations for HIV/AIDS, tuberculosis, malaria, and for combating poverty over the past 4–5 years have finally begun to make much more work possible. However, we urgently need more rigorous and systematic measurement and evaluation of the effect of these investments, as well as more investment. There is now approximately 13 billion invested annually in global health, but the currently estimated need is approximately four to five times that much.

TLID: How do you disengage at the end of the day?

KH: I am going to continue celebrating my 70th birthday on a barge trip down canals in France with some friends. They promised 60 wines during the trip. So I like good wines. What I also have to say is that I like to stay engaged. In terms of disengaging, I like to do it periodically with lots of laughter during the day.

See **Online** for webappendix

King Holmes answers more questions in a webappendix.

Acknowledgments

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