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Managing the sexually transmitted disease pandemic: A time for reevaluation

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The serious implications of the sexually transmitted disease (STD) pandemic that currently challenges educators, medical practitioners and governments suggest that prevention strategies, which primarily focus on barrier protection and the management of infection, must be reevaluated and that initiatives focusing on primary prevention of behaviors predisposing individuals to STD risk must be adopted. Human immunodeficiency virus/acquired immunodeficiency syndrome, human papillomavirus, genital herpes, and *Chlamydia* are used to illustrate the pervasive presence of STDs and their serious consequences for individuals and national infrastructures. Long-term sequelae are discussed, including the emerging link between various sexually transmitted infections and cancer, and the psychosexual and psychosocial factors which impact infected individuals. Although risk reduction and treatment of existing infection is critical, the promotion of optimal lifelong health can be achieved most effectively through delayed sexual debut, partner reduction, and the avoidance of risky sexual behaviors.

The challenge of dealing with sexually transmitted diseases (STDs) and their sequelae is an increasing concern for medical professionals and public health officials as they struggle to deal with the swelling pandemic. Although the medical literature documents the insidious escalation of these infections in populations throughout the world, many health providers are confronted, on a daily basis, with the potentially devastating short- and longterm consequences of STDs in the lives of ordinary people. Health professionals, educators, and policy makers have promoted strategies that focus on risk-reducing barrier protection as well as disease management. The lack of impact on STD rates and the enormous personal and societal consequences of these infections make it imperative that primary prevention strategies, which focus on underlying problem behaviors, become a focus of prevention programs. In this article, 4 prevalent STDs will be discussed to illustrate the pervasive impact of this public health challenge; special concerns related to the sequelae of STDs and their vertical transmission will be highlighted; and, because the majority of these infections

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occur in teenagers or young adults, 2 approaches to dealing with STDs in this population will be explored.

The pervasive menace of STDs

Although STDs have profound impact on individual sufferers, it is important to assess the global and societal impact of these diseases to appreciate the urgent need to reevaluate current management strategies. In the following discussion, current research about human immuno-deficiency virus and acquired immunodeficiency syndrome (HIV/AIDS), human papillomavirus (HPV), herpes simplex virus (HSV), and *Chlamydia* will be reviewed and their significant impact on individuals and population groups will be highlighted.

HIV/AIDS

Although there are many STDs that dramatically affect the lives of individuals, none has attracted so much attention in both medical and lay publications over the last 10 years as HIV/AIDS, "the most complex problem facing humanity today."¹ This infection, the second leading cause of serious sickness and disability in the world,² is contracted most commonly by those aged 15 to 25 years³ and, with an estimated 14,000 people infected every single day, a recent medical article stated "despite the impressive advances in medicine since [the 14th century], HIV/AIDS is likely to surpass the Black Death as the worst pandemic ever."⁴ Recently published figures clearly reinforce previous warnings that civil order as well as economic and infrastructure sustainability in some developing countries is severely threatened by widespread HIV/AIDS infection.⁵

Although the tragedy of AIDS in Africa is well documented, the potential for widespread political and social impact by STDs is also evident in other regions of the world: increasing STDs rates in Eastern Europe and Asia raise serious concerns.⁵⁻¹² It is anticipated that the next wave of HIV/AIDS infection will be in the 3 largest countries of Eurasia-Russia, India, and China-and it has been hypothesized that burgeoning HIV/AIDS infection in this region of the world "threatens to derail the economic prospects of billions and alter the global military balance."¹³ It is critical to remember that although this STD has the potential to dramatically impact demographics and thus the political integrity of nations, there is another, equally important perspective: "AIDS does not threaten to destroy a great horde of faceless people-it is far worse. It is destroying lovely, interesting, vibrant, and extremely valuable individuals, one at a time, relentlessly."¹⁴

Although the urgency associated with AIDS appeared to have decreased in the mid 1990s as combination drug treatments both prolonged the lives of people with HIV and heightened hopes that this would

become a chronic rather than terminal illness, increasing worldwide rates of HIV/AIDS have recently brought this impending health disaster into sharp focus. Although clinical trials of HIV vaccines may offer hope for achieving some degree of protection from this virus in the future, testing is in the early stages and there is danger that a false sense of security will be engendered if individuals begin to believe that an effective vaccine is imminent. Despite considerable efforts and resources devoted to HIV/AIDS risk reduction, the Joint United Nations Program on HIV/AIDS (UNAIDS) recently announced that the pandemic is only in its early phases.¹

HPV

HPV is the most widespread sexually transmitted infection in many parts of the world. It is thought to be the most common STD in the United States and the US Centers for Disease Control and Prevention (CDC) estimates that "50% to 75% of sexually active men and women acquire HPV at some point in their lives."¹⁵ Although Health Canada summarizes overall epidemiologic research about HPV and women by stating: "the prevalence of all types of HPV (cancer and non-cancer-causing) in different groups of Canadian women ranges from 20%-33%,"¹⁶ a 2003 report in the Canadian Medical Association Journal revealed that about 1 in 4 participants aged 15 to 19 years in an HPV prevalence survey in Ontario were infected with carcinogenic HPV.¹⁷ It has been reported that more than 35% of teens and young adults in various Western countries have acquired HPV, many having contracted this infection from their first sexual partner.¹⁸⁻²⁰

Sexual debut at an early age and a lifestyle involving serial monogamy-a series of consecutive sexual relationships-places individuals at particular risk for contracting HPV. Transmission is facilitated by the following: there are high rates of communicability with at least a 50% chance of transmission in a single sexual encounter with an infected individual²¹⁻²³; HPV is transmissible even in its early stages when it is frequently without symptoms; and few infected individuals are informed that although symptoms such as genital warts may respond to treatment, the underlying virus is generally untreatable and often remains transmissible. A study at 1 American university illustrates the pervasive nature of this STD among average Americans and highlights practical concerns: 60% of the sexually active female population were infected at some time during the 3-year period of the study.²⁴ A sexual relationship with a female on this campus thus presents an overwhelming risk of being in direct contact with this potentially oncogenic virus. It is important to note that depending on the host immune system function, a large proportion of HPV infections will resolve in the early stages,^{17,25} suggesting that the incidence of primary infection may

be even higher than is indicated by the prevalence of ongoing infection and subsequent neoplasia. With the widespread prevalence of this infection, some researchers have concluded that HPV in the teenage population "should now be considered an inevitable consequence of sexual activity."¹⁸

High-risk HPVs are potent human carcinogens²⁶ and, according to information from the National Cancer Institute, they are associated with a variety of genital cancers in men and women.²⁷ The escalating incidence of cervical cancer, the second most common cause of cancer-related deaths among women worldwide,^{25,28} is directly linked to increasing rates of persistent infection with carcinogenic HPV; whereas 5 HPV subtypes are responsible for most cancers, about 30 different subtypes have been associated with cervical carcinoma.²⁹ Highrisk HPVs have also been implicated with other serious cancers, including cancer of the penis and anal area in men, and head and neck tumors, including some forms of oral, respiratory, and esophageal cancers.^{16,30-39} Given the many potential sequelae of this infection, the development of an effective multivalent vaccine containing the majority of high-risk HPV subtypes would contribute significantly to the reduction of associated morbidity and mortality worldwide.⁴⁰ Although there are currently more than twenty different vaccines against specific HPV types being studied, vaccine development is still in the early stages.^{26,41,42} The increasing prevalence of HPV, its high level of transmissibility, and the association of high-risk HPVs with various premalignant and malignant lesions makes this STD a serious public health concern, not only from the perspective of personal suffering, but also from an economic perspective.

HSV

HSV is a widespread sexually transmitted pathogen and remains one of the most common STDs worldwide.43,44 Although the incidence of this infection varies from country to country, an article in the Journal of the American Medical Association reports that in the United States more than 20% of the adult population is infected.⁴³ This represents an increase of at least 30% in the last 25 years.⁴⁵ The incidence of HSV is escalating in other countries as well: in Sweden, a nation frequently cited as being progressive in the area of sexuality education,⁴⁶ the prevalence of this STD among pregnant women has risen from 19% to 33% over the last 2 decades⁴³; and HSV-2 is widespread in some parts of eastern and southern Africa "with seroprevalence rising to 70% to 80% by age 30 years."⁴⁷ Although the symptoms experienced by afflicted individuals can be personally devastating-many have recurrent pain, ulceration, and a sense of personal stigma-this virus has other concerning implications. HSV increases the risk of acquiring other STDs, including HIV,⁴⁸ and it appears to be a cofactor that augments the risk of developing cervical cancer.⁴⁹ In addition to the serious and documented risk posed by mother-child transmission of this virus, recent evidence confirms that many individuals with asymptomatic or unrecognized infection are unknowingly transmitting the virus to sexual partners and offspring.^{43,50} Vaccine prospects are still at a very preliminary stage and initial findings suggest that some vaccines in early testing are not effective for men or for those women who are seropositive for HSV-1 and seronegative for HSV-2.⁵¹

Chlamydia

One of the major causes of tubal infertility, ectopic pregnancy, pelvic inflammatory disease, and chronic pelvic pain is the pathogen, Chlamydia trachomatis. This is the most common bacterial STD in North America and Europe^{52,53} and a prevalent STD in many areas of the developing world.⁵⁴ This infection is also a cause of urethritis, cervicitis, epididymitis, proctitis, and reactive arthritis and has recently been found to be a risk factor for the development of cervical cancer.⁵⁵ Despite that Chlamydia can be treated and eradicated, infection is frequently asymptomatic in the early stages; as a result, irreparable damage to adnexal structures frequently occurs before diagnosis and many people unknowingly transmit this organism to sexual partners.⁵⁶ It is estimated that 13% of American women are affected by this infection and about 300 million cases are reported on an annual basis worldwide.⁵⁷⁻⁵⁹ The highest rates of Chlamydia are found in those between 15 and 24 years⁵⁸ and, although infertility may not be of primary concern during the teen and young adult years, the need for expensive, emotionally draining, and sometimes controversial assisted reproductive interventions later in life is a noteworthy, long-term concern. For those who do become pregnant, untreated Chlamydia during pregnancy may result in complications such as spontaneous abortion, premature rupture of membranes, premature delivery, low birth weight, and neonatal infections, including conjunctivitis and pneumonia.⁵² Although the personal and medical challenges of this bacterial infection cannot be minimized, it is important to note that the economic burden of managing Chlamydia is also significant: in the United States the cost of managing this infection and its recognized complications was approximately 2 billion dollars in 1994.⁶⁰

Special concerns related to STDs

In addition to the many challenges directly related to individual STDs, there are emerging concerns that relate to the impact of sexually acquired infections over the life span of the affected individual and the potential sequelae of these infections for offspring.

Long-term sequelae of STDs

Although some STDs cause symptoms in the short-term, many sexually transmitted infections become manifest over a longer period and present as a variety of medical problems.^{61,62} Maladies such as vaginal discharge, dyspareunia, cervical intraepithelial neoplasia, pelvic inflammatory disease, tubal infertility, ectopic pregnancy, and genital sores, may be common reasons for seeking medical care; however, many people do not realize that these concerns are frequently the direct result of previously acquired STDs. The correlation of various sexually transmitted infections, including HPV, hepatitis B, and Chlamydia, with certain cancers that develop some time after initial STD infection,^{55,63,64} has become a particular concern. This emerging link between STDs and a variety of cancers clearly suggests that risky sexual behavior, including early sexual debut, must be considered a significant risk factor, not only for more familiar symptoms such as infertility, but also for the development of cancer over the life span.^{16,32-37,55,65-67}

Although research most commonly focuses on the physical consequences of STDs, the psychosexual and psychosocial sequelae of contracting an STD, although difficult to quantitatively measure, should not be underestimated. While infected individuals may experience increased feelings of anger, depression, isolation, rejection, and guilt,⁶⁸⁻⁷⁴ research also indicates that STDs may have a long-term negative effect on sexual enjoyment and that infected patients may experience the following: "partial or complete cessation of sexual activity," "a total or partial loss of interest in sex," a "more inhibited and less spontaneous" sex life, or "anxiety related to sexual desirability."68 A recent conference paper exploring the psychosexual impact of HPV reported that this diagnosis "can be expected to have repercussions in different spheres of the infected person's life, such as physical and sexual health, and social and interpersonal relations."⁷⁵ With therapeutic encounters between busy physicians and patients frequently limited to the treatment of physical symptoms, it is critical that the longterm psychosexual and psychosocial sequelae of STDs be considered in discussions related to medical management of STDs.

Vertical transmission

There is increasing evidence in the medical literature that vertical transmission of various pathogens via intrauterine or perinatal spread is occurring on a wider scale than was previously recognized.⁵⁷ Most physicians understand that the upsurge in adult cases of syphilis in certain high-risk populations has led to a corresponding increase of congenital syphilis,^{76,77} that mother-child transmission of HIV is increasing child morbidity and mortality in many developing nations,^{5,78-80} and that the potential of HSV to cause death or serious neurologic consequences in newborn infants necessitates careful obstetric management of HSV-infected women.^{50,81} The potential implications of vertically transmitted STDs are, however, continuing to emerge in the medical literature.

There is now substantial evidence for the vertical trans-mission of high-risk HPVs.^{28,82-84} In 1999, for example, Reviews in Medical Virology reported that although the consequences of infection are uncertain, "high-risk HPVs are present in at least 20% of healthy children."²⁸ Despite evidence that surgical delivery by cesarean section may decrease vertical transmission, the possibility of transplacental transmission before delivery has become a concern.⁸⁴⁻⁸⁶ Although documented reports of sequelae resulting from vertically transmitted HPV are uncommon in the literature, HPV has recently been implicated in retinoblastoma, a common childhood cancer.^{39,63,87} Another research study, which explored maternal infections and subsequent psychosis among adult offspring, found a troubling correlation between maternal herpes infection (HSV-2) and certain types of psychotic disorders, including schizophrenia, in offspring.⁸⁸ Although the consequences of STDs in the lives of individuals can be serious and debilitating on a physical and social level, increasing concern about vertical transmission brings new intensity to the question of how to address the prevention and medical management of STDs.

Reevaluating STD management

Despite the many attempts over the last number of years to impact the enormous prevalence of STDs, rising infection rates suggest that objectives are not being met and that reassessment of prevention strategies should be a priority. Given the serious long-term health problems that STDs present to individuals over their life span, it is critical that current strategies are reevaluated and that underlying lifestyles and behaviors be addressed in an attempt to manage STDs through the primary prevention of problem behaviors. The World Health Organization estimates that two thirds of the sexually transmitted infections worldwide occur in teenagers and young adults; it is therefore essential that this population is specifically targeted as physicians and educators seek to address the STD epidemic.⁸⁹

Risk reduction strategy

With the increasing recognition that risky sexual activity places adolescents at significant risk for a variety of sexually transmitted infections and their sequelae, physicians, educators, and governing bodies have sought to impact escalating rates of disease by promoting various strategies aimed at reducing risk. These strategies have, for the most part, focused on preventing the spread of disease through the use of barrier protection in the form of the condom. Two major reasons account for the limited success of this approach and the persistently high STD rates despite extensive "safe sex" and "safer sex" campaigns throughout much of the world.

First, condom barrier protection provides little protection from the "SS" ("skin-to-skin" and "skin-to-sore") transmission of STDs such as HPV, HSV, syphilis, lymphogranuloma venerum (LGV), or chancroid.^{57,90,91} Although condoms prevent contact between the skin of the penis and the mucosa inside the vagina and appear to offer some protection in women when viral lesions are confined to this area,⁹² intercourse generally involves skin-to-skin contact in external genital areas; therefore, the protection offered by the condom against SS pathogens often found throughout the external genital tract is limited. It should also be noted that risk-reduction strategies aimed at encouraging nonintercourse sexual activity through "outercourse" and oral sex leave participants at risk for these types of infections.⁹³ HPV and HSV, for example, can be transmitted by oral as well as genital sex.94,95 Because HPV and HSV, 2 infections that transmit through SS contact, are the 2 most common STD pathogens in many countries, the condom clearly provides inadequate protection against the spectrum of STDs.

Second, although condoms offer some protection against discharge-related infections such as HIV, *Chlamydia*, and gonorrhea,⁵⁷ protection may be compromised by compliance issues, incorrect use, or mechanical failure.^{90,96-98} Extensive research demonstrates that average people, particularly youth, do not use condoms consistently in the long-term, regardless of knowledge or education.^{92,96,99-109} Even among stable, adult, HIV-discordant couples who received extensive ongoing counseling regarding HIV risk and safer-sexual practices, only 43.3% used condoms consistently.⁹⁹ Widespread evidence confirms "irregular use of condoms provides no protection against transmission of HIV and STD."¹¹⁰

Reports of decreased rates of new sexually acquired infections as a result of advertising campaigns and increased condom usage by commercial sex workers (CSW) and their clientele¹¹¹⁻¹¹⁴ are reinforcing the focus on condoms as the primary preventative strategy for STDs. Careful analysis of the data, however, suggests that partner reduction played an important role in STD decline. After the "100% Condom Program" in Thailand, for example, which sought to encourage CSWs to use condoms 100% of the time, there was a precipitous decline not only in discharge-related STDs, but also in SS diseases such as syphilis, chancroid, and LGV.^{111,112} These SS infections are commonly not within the scope of protection of regular condoms and frequently transmit despite condom use. In addition, the data reveal that mass advertising campaigns and widespread HIV education in various nations, including Thailand, Cambodia, Ethiopia, and the Dominican Republic, was associated with a sharp decline in reported casual sex and relations between female sex workers and male clientele.^{113,115-117} Furthermore, according to research published in 1999 in the *Journal of Acquired Immune Deficiency Syndromes*, those who commenced the sex trade after the implementation of the mandatory condom program had higher rates of HIV than CSWs who initiated work prior to the program.¹¹⁷ These combined findings suggest that abstinence from coitus with sex workers and partner reduction contributed significantly to decreased STD rates after advertising campaigns in these nations.^{113,115,117,118}

In addition, the sexual behavior of CSWs cannot be legitimately extrapolated to other populations. Increased condom use in select groups of sex workers and their clientele in response to HIV education campaigns is not necessarily predictive of the behavior of ordinary adolescents. The practical reality is that individuals, especially young people, are less able to make consistent, safer health choices when they are sexually aroused. Like people throughout the world, recent evidence confirms that most ordinary Thai citizens, particularly adolescents, are not consistently using condoms, despite extensive educational programs.¹¹⁹⁻¹²¹

Although there is little doubt that proper, consistent, use of barrier protection will reduce the risk of discharge-related STDs, the lack of protection of the condom against the spectrum of STDs and the unsuccessful attempts to achieve sustained compliance in the general population restricts the impact of most current risk-reduction strategies. To meet the challenge presented by escalating rates of serious STDs, risk reduction must address the primary behavior that predisposes individuals to sexually acquired infections.

Addressing underlying risky behaviors

Condoms provide only limited protection against SS STDs and there is currently no cure for viral STDs, such as HPV, genital herpes, and HIV/AIDS. These facts, coupled with the serious life-long implications of many STDs, compel the medical profession to face 2 contrasting options when considering the optimal health and well-being of young people. Practitioners must either accept the high and worsening rates of STDs as inevitable and unavoidable; alternatively, they must consider an approach that focuses on addressing the underlying behaviors that predispose young people to acquiring STDs. Increasing evidence appears to support the adoption of a health-oriented approach that addresses sexual attitudes and behaviors by both educating about STDs and consistently recommending delayed sexual debut and partner reduction.90,122-126

The earlier a person experiences sexual debut, the more lifetime sexual partners they are likely to have and consequently, the higher their risk of contracting an STD.¹²⁷⁻¹³⁰ Because the sexual lifestyle of young people frequently involves the early onset of sexual activity and subsequent serial monogamy, it must be recognized that the sexual lifestyle of numerous teenagers is, from a health perspective, inherently risky. Although the danger of acquiring a sexually transmitted infection increases with each additional sexual partner, it has also been documented that many individuals contact an STD as a result of their first sexual experience.¹⁸ Recognizing that, from a STD perspective, sexual encounters include not only present partners, but also past partners and all of their partner's partners,¹³¹ primary prevention through behavioral intervention is of key importance to long-term health.

It is fundamentally important to recognize that not unlike other adolescent high-risk behaviors, teen sexual activity is often an "expression of nonsexual need"¹³² and is frequently a concomitant behavior associated with other basic problems or difficulties.^{124,131-148} Although some practitioners may believe that modifying the sexual behavior of young people is unrealistic, it should be pointed out that "every successful form of prevention requires change in behavior."¹⁴⁹ Research confirms that some proactive interventions are able to affect attitudes regarding sexuality and, in many cases, appreciably diminish the likelihood of early sexual debut.^{115,124,127,137,144,145,150-156} By addressing etiologic factors, primary prevention and sustained behavioral change can be achieved. In fact, research from CDC recently indicated that the level of sexual activity in the adolescent population is declining^{157,158} and other recent studies indicate that the majority of sampled 13- to 17year-old adolescents in America had not commenced sexual involvement.¹⁵⁹ The importance of addressing the primary sexual behavior of adolescents is highlighted by CDC: one of the national health objectives for 2010 developed by the US Department of Health and Human Services is "to increase...the proportion of adolescents in grades 9-12 who have never had sexual intercourse."157

The potential benefit of increasing the proportion of adolescents who have not had intercourse and promoting partner reduction is not limited to western nations. A publication by the US Agency for International Development (USAID) gives evidence for changes in sexual behavior and STD rates that have occurred in association with a "social vaccine" program¹⁶⁰ that was implemented nationally in Uganda. This program included widespread, intensive public health education, which addressed myths and misinformation, a primary focus on advocating delayed sexual debut and partner reduction, and risk reduction through condom use for HIV discordant couples and those having multiple sexual partners.^{115,160} Reported

changes occurring in association with this national program include the number of women reporting multiple sexual partners fell from approximately 20% in 1989 to 2.5% in 2000¹⁶¹; in one district, the rates of 13- to 16year-old adolescents involved in sexual activity declined from nearly 60% in 1994 to less than 5% by 2001¹⁶⁰; and, during approximately the same period of time, national HIV prevalence steadily declined from about 30% in 1992,^{162,162} to an estimated 5% in 2001.¹⁶⁰

Many authors have concluded that sexual behavior modification provides the most consistent explanation for the HIV decline in Uganda^{160,163-168}; more specifically, the evidence suggests that "behavior change, as distinct from condom adoption"¹¹⁶ has been the primary factor responsible for the marked reduction.^{115,116,160} Condom promotion was not a dominant program element in Uganda:^{160,169} ever-use of condoms remained low with only 16% of women in 2000 reporting that they had ever had sex involving condoms,¹⁶⁰ and a study of the general population in one district of Uganda found that only 4.4% reported consistent condom use.¹¹⁰ In addition, Dr Vinand Nantulya, an Ugandan infectious disease specialist and government adviser who has been involved in a Harvard School of Public Health study of the Uganda experience, recently commented on the general attitude toward condoms in his country by stating, "Ugandans never really took to condoms."¹⁶¹ Although condom use with nonregular partners has increased in Uganda in the past half decade, the primary behavioral modification in that country was summarized by the authors of the USAID report who concluded that in association with the concerted public initiatives to modify lifestyle, Ugandan men "were less likely to have ever had sex (in the 15- to 19year-old range), more likely to be married, ...and less likely to have multiple partners."¹⁶⁰

The situation in Uganda contrasts starkly with other African nations such as Zimbabwe and Botswana. In these countries there were extensive initiatives promoting condom use and, compared with Uganda, there were higher rates of both condom sales and reported use; nonetheless, HIV prevalence in these countries is among the highest in the world.^{6,160,161,170} There is an unprecedented 55.6% HIV prevalence among pregnant women aged 25 to 29 years in urban Botswana and current infection rates in Zimbabwe suggest that by 2020 there will be a 30% loss to the workforce because of AIDS.^{170,171}

Comment

Given the current STD pandemic, it is imperative that physicians begin to reevaluate STD prevention and management strategies. Escalating worldwide rates of these infections, their potentially devastating short- and long-term sequelae for infected individuals, and the economic and social impacts of these infections make STD prevention a critical issue. Although risk-reduction strategies and treatment of existing infection are important, the stark ineluctable reality is that to promote optimal, life-long health, primary prevention of infection must be promoted. The success of prevention programs that address primary sexual behavior suggests that serious deliberation of strategies promoting delayed sexual debut and partner reduction is warranted.

References

- 1. Piot P. Introduction. Br Med Bull 2001;58:3-5.
- Michaud CM, Murray CJ, Bloom BR. Burden of disease—implications for future research. JAMA 2001;285:535-9.
- Short C. Secretary of State for International Development. Presentation at the International Conference on HIV/AIDS Prevention, London, February 2002.
- 4. Lamptey PR. Reducing heterosexual transmission of HIV in poor countries. BMJ 2002;324:207-11.
- 5. Gayle HD, Hill GL. Global impact of human immunodeficiency virus and AIDS. Clin Microbiol Rev 2001;14:327-35.
- Centers for Disease Control. The global HIV and AIDS epidemic, 2001. MMWR Morb Mortal Wkly Rep 2001;50:434-9.
- 7. Cernescu C. Romanian HIV-AIDS epidemic after a decade of evolution. Rom J Virol 1999;50:5-15.
- Ghys PD, Bazant W, Monteiro MG, Calvani S, Lazzari S. The epidemics of injecting drug use and HIV in Asia. AIDS 2001; 15(5 Suppl):S91-9.
- Kalichman SC, Kelly JA, Sikkema KJ, Koslov AP, Shaboltas A, Granskaya J. The emerging AIDS crisis in Russia: review of enabling factors and prevention needs. Int J STD AIDS 2000;11: 71-5.
- 10. Fears of an Eastern European explosion of HIV epidemic are being realized. Aids Alert 2002;17:19-20 3.
- Chen XS, Gong XD, Liang GJ, Zhang GC. Epidemiologic trends of sexually transmitted diseases in China. Sex Transm Dis 2000; 27:138-42.
- Cohen MS, Ping G, Fox K, Henderson GE. Sexually transmitted diseases in the People's Republic of China in Y2K: back to the future. Sex Transm Dis 2000;27:143-5.
- Eberstadt N. The future of AIDS. American Enterprise Institute for Public Policy Research. Washington (DC): Foreign Affairs, Council on Foreign Relations; Nov/Dec 2002.
- Lemke D. Man no be God: Bushdoctor in Cameroon. Lincoln (NE): Writers Club Press; 2001.
- Genital HPV infection. 2001. In CDC: STD Prevention [Government website]. [cited 14 December 2002]. Available at: URL: http:///www.cdc.gov/nchstp/dstd/Fact_Sheets/FactsHPV.htm.
- Health Canada. Population and Public Health Branch. STD Epi Update, Bureau of HIV/AIDS, STD and TB Update Series 2000.
- Sellors JW, Karwalajtys TL, Kaczorowski J, Mahony JB, Lytwyn A, Chong S, et al. Incidence, clearance and predictors of human papillomavirus infection in women. CMAJ 2003;168:421-5.
- Collins S, Mazloomzadeh S, Winter H, Blomfield P, Bailey A, Young LS, et al. High incidence of cervical human papillomavirus infection in women during their first sexual relationship. BJOG 2002;109:96-8.
- Rosenfeld WD, Vermund SH, Wentz SJ, Burk RD. High prevalence rate of human papillomavirus infection and association with abnormal papanicolaou smears in sexually active adolescents. Arch Pediatr Adolesc Med 1989;143:1443-7.

- 20. Rosenfeld WD. Sexually transmitted diseases in adolescents: update 1991. Pediatr Ann 1991;20:303-12.
- 21. Beutner RR. Human papillomavirus infection. J Am Acad Dermatol 1989;20:113-23.
- Campion MJ, Singer A, Clarkson PK, McCance DJ. Increased risk of cervical neoplasia in consorts of men with penile condylomata acuminata. Lancet 1985;1:943-6.
- Oriel JD. Natural history of genital warts. Br J Vener Dis 1971; 47:1-13.
- Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. N Engl J Med 1998;338:423-8.
- Crum CP. The beginning of the end for cervical cancer? N Engl J Med 2002;347:1703-5.
- 26. Franceschi S. Human papillomavirus: a vaccine against cervical carcinoma uterine. Epidemiol Prev 2002;26:140-4.
- Human papillomaviruses and cancer. 2001. In: Cancer Information Services [a National Cancer Institute website]. [cited 25 March 2002]. Available at: URL:http://cis.nci.nih.gov/fact/3_20.htm.
- Rice PS, Cason J, Best JM, Banatvala JE. High risk genital papillomavirus infections are spread vertically. Rev Med Virol 1999;9:15-21.
- Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med 2003;348:518-27.
- 30. Piketty C, Darragh TM, Da Costa M, Bruneval P, Heard I, Kazatchkine MD, et al. High prevalence of anal human papillomavirus infection and anal cancer precursors among HIV-infected persons in the absence of anal intercourse. Ann Intern Med 2003;138:453-9.
- Chang JY, Lin MC, Chiang CP. High-risk human papillomaviruses may have an important role in non-oral habits-associated oral squamous cell carcinomas in Taiwan. Am J Clin Pathol 2003; 120:909-16.
- 32. Centers for Disease Control. Genital HPV Infection. Atlanta (GA): National Center for HIV, STI and TB Prevention, Division of Sexually Transmitted Diseases Prevention; 2001.
- Hemminki K, Dong C. Cancer in husbands of cervical cancer patients. Epidemiology 2000;11:347-9.
- 34. Picconi MA, Eijan AM, Distefano AL, Pueyo S, Alonio LV, Gorostidi S, et al. Human papillomavirus (HPV) DNA in penile carcinomas in Argentina: analysis of primary tumors and lymph nodes. J Med Virol 2000;61:65-9.
- 35. Rusk D, Sutton GP, Look KY, Roman A. Analysis of invasive squamous cell carcinoma of the vulva and vulvar intraepithelial neoplasia for the presence of human papillomavirus DNA. Obstet Gynecol 1991;77:918-22.
- 36. Gillison ML, Koch WM, Capone RB, Spafford M, Westra WH, Wu L, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst 2000;92:709-20.
- 37. Mork J, Lie AK, Glattre E, Hallmans G, Jellum E, Koskela P, et al. Human papillomavirus infection as a risk factor for squamous-cell carcinoma of the head and neck. N Engl J Med 2001;344:1125-31.
- Frisch M, Glimelius B, van den Brule AJ, Wohlfahrt J, Meijer CJ, Walboomers JM, et al. Sexually transmitted infection as a cause of anal cancer. N Engl J Med 1997;337:1350-8.
- 39. Orjuela M, Castaneda VP, Ridaura C, Lecona E, Leal C, Abramson DH, et al. Presence of human papilloma virus in tumor tissue from children with retinoblastoma: an alternative mechanism for tumor development. Clin Cancer Res 2000;6:4010-6.
- Hughes JP, Garnett GP, Koutsky L. The theoretical population-level impact of a prophylactic human papilloma virus vaccine. Epidemiology 2002;13:631-9.

- Sharma DC. HPV vaccine trial may take place in India. Lancet Oncol 2002;3:649.
- 42. Koutsky LA, Ault KA, Wheeler CM, Brown DR, Barr E, Alvarez FB, et al. A controlled trial of a human papillomavirus type 16 vaccine. N Engl J Med 2002;347:1645-51.
- Corey L, Handsfield HH. Genital herpes and public health: addressing a global problem. JAMA 2000;283:791-4.
- Nahmias AJ, Lee FK, Beckman-Nahmias S. Sero-epidemiological and -sociological patterns of herpes simplex virus infection in the world. Scand J Infect Dis Suppl 1990;69:19-36.
- 45. Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK, et al. Herpes simplex virus type 2 in the United States, 1976 to 1994. N Engl J Med 1997;337:1105-11.
- 46. Anagrius C, Hallen A, Moi H, Persson E. Prevention of sexually transmitted diseases and abortions—the present situation for medical care of sexually transmitted diseases in Sweden. Semin Dermatol 1990;9:190-3.
- Corbett EL, Steketee RW, ter Kuile FO, Latif AS, Kamali A, Hayes RJ. HIV-1/AIDS and the control of other infectious diseases in Africa. Lancet 2002;359:2177-87.
- Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: a meta-analysis. J Infect Dis 2002;185:45-52.
- 49. Smith JS, Herrero R, Bosetti C, Munoz N, Bosch FX, Eluf-Neto J, et al. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. J Natl Cancer Inst 2002;94:1604-13.
- Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labor. N Engl J Med 1991;324:1247-52.
- Stanberry LR, Spruance SL, Cunningham AL, Bernstein DI, Mindel A, Sacks S, et al. Glycoprotein-D-adjuvant vaccine to prevent genital herpes. N Engl J Med 2002;347:1652-61.
- 52. Navarro C, Jolly A, Nair R, Chen Y. Risk factors for genital chlamydial infection. Can J Infect Dis 2002;13:195-207.
- Gaydos CA, Howell MR, Pare B, Clark KL, Ellis DA, Hendrix RM, et al. *Chlamydia trachomatis* infections in female military recruits. N Engl J Med 1998;339:739-44.
- 54. Buve A, Weiss HA, Laga M, Van Dyck E, Musonda R, Zekeng L, et al. The epidemiology of gonorrhoea, chlamydial infection and syphilis in four African cities. AIDS 2001;15(4 Suppl): S79-88.
- Wallin KL, Wiklund F, Luostarinen T, Angstrom T, Anttila T, Bergman F, et al. A population-based prospective study of *Chlamydia trachomatis* infection and cervical carcinoma. Int J Cancer 2002;101:371-4.
- Turner CF, Roger SM, Miller HG, Miller WC, Gribble JN, Chromy JR, et al. Untreated gonococcal and chlamydial infection in a probability sample of adults. JAMA 2002;287:726-33.
- 57. Workowski KA, Levine WC. Sexually transmitted diseases treatment guidelines 2002. Centers for Disease Control and Prevention. MMWR Recomm Rep 2002;51:1-78.
- 58. Wiesenfeld HC, Lowry DL, Heine RP, Krohn MA, Bittner H, Kellinger K, et al. Self-collection of vaginal swabs for the detection of *Chlamydia*, gonorrhea, and trichomoniasis: opportunity to encourage sexually transmitted disease testing among adolescents. Sex Transm Dis 2001;28:321-5.
- 59. Schachter J. Chlamydial infections. West J Med 1990;153:523-34.
- Patrick DM. Chlamydia control: components of an effective control strategy to reduce the incidence of *Chlamydia trachomatis*. Can J Human Sex 1997;6:143-9.
- Genuis SJ. Risky sex: the onslaught of sexually transmitted disease. Edmonton (Canada): KEG Publishing; 1992.
- 62. Meeker M. Epidemic: how teen sex is killing our kids. Washington (DC): Lifeline Press; 2002.

- Munger K. The role of human papillomaviruses in human cancers. Front Biosci 2002;7:d641-9.
- 64. Kadow JF, Regueiro-Ren A, Weinheimer SP. The role of viruses in human cancer development and antiviral approaches for intervention. Curr Opin Investig Drugs 2002;3:1574-9.
- Anttila T, Saikku P, Koskela P, Bloigu A, Dillner J, Ikaheimo I, et al. Serotypes of *Chlamydia trachomatis* and risk for development of cervical squamous cell carcinoma. JAMA 2001;285: 47-51.
- Mayor S. Human papilloma-virus classified as carcinogenic. BMJ 1996;313:70.
- Moscicki AB, Hills N, Shiboski S, Powell K, Jay N, Hanson E, et al. Risks for incident human papillomavirus infection and low-grade squamous intraepithelial lesion development in young females. JAMA 2001;285:2995-3002.
- Vezina C, Steben M. Genital herpes: psychosexual impacts and counselling. Can J Cont Med Ed 2001;13:125-37.
- Silber TJ. Mental health aspects of sexually transmitted diseases in adolescents. In: Greydanus DE, Wolraich ML, editors. Behavior pediatrics. New York: Springer-Verlag; 1992. p. 381-6.
- Clarke P, Ebel C, Catotti DN, Stewart S. The psychosocial impact of human papillomavirus infection: implications for health care providers. Int J STD AIDS 1996;7:197-200.
- 71. Rosemberg SK. Sexually transmitted papillomaviral infection in men: an update. Dermatol Clin 1991;9:317-31.
- Campion MJ, Brown JR, McCance DJ, Atia W, Edwards R, Cuzick J, et al. Psychosexual trauma of an abnormal cervical smear. BJOG 1988;95:175-81.
- Voog E, Lowhagen GB. Follow-up of men with genital papilloma virus infection: psychosexual aspects. Acta Derm Venereol 1992; 72:185-6.
- VanderPlate C, Aral SO. Psychosocial aspects of genital herpes virus infection. Health Psychol 1987;6:57-72.
- Vezina C, Steben M. Psychosexual impacts of human papillomavirus. Can J Cont Med Ed 2001;13:139-53.
- Health Canada. Population and Public Health Branch. Infectious syphilis in Canada. STD Epi Update, Bureau of HIV/AIDS, STD and TB Update Series 2002.
- Centers for Disease Control. Congenital syphilis—New York City, 1986-1988. MMWR Morb Mortal Wkly Rep 1989;38:825-9.
- Kaul D, Patel JA. Clinical manifestations and management of pediatric HIV infection. Indian J Pediatr 2001;68:623-31.
- Walker N, Schwartlander B, Bryce J. Meeting international goals in child survival and HIV/AIDS. Lancet 2002;360:284-9.
- Meyers TM, Pettifor JM, Gray GE, Crewe-Brown H, Galpin JS. Pediatric admissions with human immunodeficiency virus infection at a regional hospital in Soweto, South Africa. J Trop Pediatr 2000;46:224-30.
- Whitley RJ, Arvin AM. Herpes simplex infections. In: Remington JS, Klein JO, editors. Infectious diseases of the fetus and newborn infant. 4th ed. Philadelphia: WB Saunders; 1995. p. 354-76.
- Puranen M, Yliskoski M, Saarikoski S, Syrjanen K, Syrjanen S. Vertical transmission of human papillomavirus from infected mothers to their newborn babies and persistence of the virus in childhood. Am J Obstet Gynecol 1996;174:694-9.
- Rice PS, Mant C, Cason J, Bible JM, Muir P, Kell B, et al. High prevalence of human papillomavirus type 16 infection among children. J Med Virol 2000;61:70-5.
- Tseng CJ, Liang CC, Soong YK, Pao CC. Perinatal transmission of human papillomavirus in infants: relationship between infection rate and mode of delivery. Obstet Gynecol 1998;91:92-6.
- 85. Armbruster-Moraes E, Ioshimoto LM, Leao E, Zugaib M. Detection of human papillomavirus deoxyribonucleic acid sequences in amniotic fluid during different periods of pregnancy. Am J Obstet Gynecol 1993;169:1074.
- Armbruster-Moraes E, Ioshimoto LM, Leao E, Zugaib M. Presence of human papillomavirus DNA in amniotic fluids of

pregnant women with cervical lesions. Gynecol Oncol 1994;54: 152-8.

- Cordon-Cardo C. Virus linked to pediatric eye tumor. Van Nuys (CA): National Cervical Cancer Coalition; 2001 Research bulletin.
- Buka SL, Tsuang MT, Torrey EF, Klebanoff MA, Bernstein D, Yolken RH. Maternal infections and subsequent psychosis among offspring. Arch Gen Psychiatry 2001;58:1032-7.
- Low-Beer D, Stoneburner RL, Mukulu A. Empirical evidence for the severe but localized impact of AIDS on population structure. Nat Med 1997;3:553-7.
- McIlhaney JS Jr. Sexually transmitted infection and teenage sexuality. Am J Obstet Gynecol 2000;183:334-9.
- Genuis SJ, Genuis SK. The dilemma of adolescent sexuality, I: the onslaught of sexually transmitted diseases. J Soc Obstet Gynecol Can 1993;15:552-65.
- 92. Wald A, Langenberg AG, Link K, Izu AE, Ashley R, Warren T, et al. Effect of condoms on reducing the transmission of herpes simplex virus type 2 from men to women. JAMA 2001;285: 3100-6.
- Genuis SJ, Genuis SK. Orgasm without organisms: science or propaganda? Clin Pediatr 1996;35:10-7.
- Giovannelli L, Campisi G, Lama A, Giambalvo O, Osborn J, Margiotta V, et al. Human papillomavirus DNA in oral mucosal lesions. J Infect Dis 2002;185:833-6.
- Edwards S, Carne C. Oral sex and the transmission of viral STIs. Sex Transm Infect 1998;74:6-10.
- Oncale RM, King BM. Comparison of men's and women's attempts to dissuade sexual partners from the couple using condoms. Arch Sex Behav 2001;30:379-91.
- 97. Macaluso M, Kelaghan J, Artz L, Austin H, Fleenor M, Hook EW 3rd, et al. Mechanical failure of the latex condom in a cohort of women at high STD risk. Sex Transm Dis 1999;26:450-8.
- Warner L, Clay-Warner J, Boles J, Williamson J. Assessing condom use practices: implications for evaluating method and user effectiveness. Sex Transm Dis 1998;25:273-7.
- de Vincenzi I. A longitudinal study of human immunodeficiency virus transmission by heterosexual partners. European Study Group on Heterosexual Transmission of HIV. N Engl J Med 1994;331:341-6.
- Hausser D, Michaud PA. Does a condom-promoting strategy (the Swiss STOP-AIDS campaign) modify sexual behavior among adolescents? Pediatrics 1994;93:580-5.
- 101. Catania JA, Coates TJ, Stall R, Turner H, Peterson J, Hearst N, et al. Prevalence of AIDS-related risk factors and condom use in the United States. Science 1992;258:1101-6.
- Weisman CS, Plichta S, Nathanson CA, Ensminger M, Robinson JC. Consistency of condom use for disease prevention among adolescent users of oral contraceptives. Fam Plann Perspect 1991; 23:71-4.
- 103. Kegeles SM, Adler NE, Irwin CE Jr. Sexually active adolescents and condoms: changes over one year in knowledge, attitudes and use. Am J Public Health 1988;78:460-1.
- 104. Genuis SJ, Genuis SK. Dealing with the AIDS epidemic: quo vadis? J Soc Obstet Gyncol Can 1995;17:219-23.
- 105. Madhok R, McCallum AK, McEwan R, Bhopal RS. Students' knowledge and behavior concerning safer sex: a UK study. J Am Coll Health 1993;42:121-5.
- Tyden T, Olsson S, Bjorkelund-Ylander C. Female university students in Sweden: sex, contraception and STDs. Adv Contracept 1991;7:165-71.
- 107. Herlitz C. Condom use due to the risk of AIDS: trends in the general population of Sweden. Scand J Soc Med 1992;20:102-9.
- 108. Catania JA, Binson D, Docini MM, Stall R, Choi KH, Pollack LM, et al. Risk factors for HIV and other sexually transmitted diseases and prevention practices among US heterosexual adults: changes from 1990 to 1992. Am J Public Health 1995; 85:1492-9.

- 109. Bankole A, Darroch JE, Singh S. Determinants of trends in condom use in the United States, 1988-1995. Fam Plann Perspect 1999;31:264-71.
- 110. Ahmed S, Lutalo T, Wawer M, Serwadda D, Sewankambo NK, Nalugoda F, et al. HIV incidence and sexually transmitted disease prevalence associated with condom use: a population study in Rakai, Uganda. AIDS 2001;15:2171-9.
- 111. Rojanapithayakorn W, Hanenberg R. The 100% condom program in Thailand. AIDS 1996;10:1-7.
- 112. Hanenberg RS, Rojanapithayakorn W, Kunasol P, Sokal DC. Impact of Thailand's HIV-control programme as indicated by the decline of sexually transmitted diseases. Lancet 1994;344: 243-5.
- 113. Pisani E, Garnett GP, Grassly NC, Brown T, Stover J, Hankins C, et al. Back to basics in HIV prevention: focus on exposure. BMJ 2003;326:1384-7.
- 114. Alary M, Mukenge-Tshibaka L, Bernier F, Geraldo N, Lowndes CM, Meda H, et al. Decline in the prevalence of HIV and sexually transmitted diseases among female sex workers in Cotonou, Benin, 1993-1999. AIDS 2002;16:463-70.
- 115. Shelton AJ, Halperin DT, Nantulya V, Potts M, Gayle HD, Holmes KK. Partner reduction is crucial for balanced "ABC" approach to HIV prevention. BMJ 2004;328:891-4.
- Green EC, Conde A. Sexual partner reduction and HIV infection. Sex Transm Infect 2000;76:145.
- 117. Kilmarx PH, Palanuvej T, Limpakarnjanarat K, Chitvarakorn A, St Louis ME, Mastro TD. Seroprevalence of HIV among female sex workers in Bangkok: evidence of ongoing infection risk after the "100% condom program" was implemented. J Acquir Immune Defic Syndr 1999;21:313-6.
- 118. Nelson KE, Celentano DD, Eiumtrakol S, Hoover DR, Beyrer C, Suprasert S, et al. Changes in sexual behavior and a decline in HIV infection among young men in Thailand. N Engl J Med 1996;335:297-303.
- 119. Paz-Bailey G, Kilmarx PH, Supawitkul S, Chaowanachan T, Jeeyapant S, Sternberg M, et al. Risk factors for sexually transmitted diseases in northern Thai adolescents: an audiocomputer-assisted self-interview with noninvasive specimen collection. Sex Transm Dis 2003;30:320-6.
- 120. Thato S, Charron-Prochownik D, Dorn LD, Albrecht SA, Stone CA. Predictors of condom use among adolescent Thai vocational students. J Nurs Scholarsh 2003;35:157-63.
- Lertpiriyasuwat C, Plipat T, Jenkins RA. A survey of sexual risk behavior for HIV infection in Nakhonsawan, Thailand, 2001. AIDS 2003;17:1969-76.
- 122. Stammers T, Ingham R. For and against: doctors should advise adolescents to abstain from sex. BMJ 2000;321:1520-2.
- 123. Stuart-Smith S. Teenage sex. BMJ 1996;312:390-1.
- 124. Kay LE. Adolescent sexual intercourse: strategies for promoting abstinence in teens. Postgrad Med 1995;97:121-7, 132-4.
- 125. Genuis SJ, Genuis SK. Adolescent sexual involvement: time for primary prevention. Lancet 1995;345:240-1.
- 126. Genuis SJ, Genuis SK. The dilemma of adolescent sexuality: part IV—dealing with the challenge. J Soc Obstet Gyncol Can 1994; 16:1343-59.
- 127. Sonenstein FL, Pleck JH, Ku LC. Levels of sexual activity among adolescent males in the United States. Fam Plann Perspect 1991; 23:162-7.
- 128. Wasserheit JN. Effect of changes in human ecology and behavior on patterns of sexually transmitted diseases, including human immunodeficiency virus infection. Proc Natl Acad Sci U S A 1994;91:2430-5.
- Santelli JS, Brener ND, Lowry R, Bhatt A, Zabin LS. Multiple sexual partners among U.S. adolescents and young adults. Fam Plann Perspect 1998;30:271-5.

- Greenberg J, Magder L, Aral S. Age at first coitus: a marker for risky sexual behavior in women. Sex Transm Dis 1992;19: 331-4.
- 131. Genuis SJ, Genuis SK. Teen sex: reality check. Edmonton (Canada): Winfield House Publishing; 2002.
- 132. Cohen MW. Adolescent sexual activity as an expression of nonsexual needs. Pediatr Ann 1995;24:324-9.
- 133. Hawkins JD, Catalano RF, Kosterman R, Abbott R, Hill KG. Preventing adolescent health-risk behaviors by strengthening protection during childhood. Arch Pediatr Adolesc Med 1999; 153:226-34.
- Jorgensen SR, Potts V, Camp B. Project taking charge: six month follow-up of a pregnancy prevention program for early adolescents. Fam Relations 1993;42:401-6.
- Weinstein M, Thornton A. Mother-child relations and adolescent sexual attitudes and behavior. Demography 1989;26:563-77.
- 136. Santelli JS, DiClemente RJ, Miller KS, Kirby D. Sexually transmitted diseases, unintended pregnancy, and adolescent health promotion. Adolesc Med 1999;10:87-108.
- 137. Small SA, Luster T. Adolescent sexual activity: an ecological risk-factor approach. J Marriage Fam 1994;56:181-92.
- 138. Hillis SD, Anda RF, Felitti VJ, Marchbanks PA. Adverse childhood experiences and sexual risk behaviors in women: a retrospective cohort study. Fam Plann Perspect 2001;33: 206-11.
- 139. Santelli JS, Lowry R, Brener ND, Robin L. The association of sexual behaviors with socioeconomic status, family structure, and race/ethnicity among US adolescents. Am J Public Health 2000; 90:1582-8.
- 140. Blum RW, Beuhring T, Shew ML, Bearinger LH, Sieving RE, Resnick MD. The effects of race/ethnicity, income, and family structure on adolescent risk behaviors. Am J Public Health 2000; 90:1879-84.
- 141. Resnick MD, Bearman PS, Blum RW, Bauman KE, Harris KM, Jones J, et al. Protecting adolescents from harm: findings from the National Longitudinal Study on Adolescent Health. JAMA 1997; 278:823-32.
- 142. Rosenthal SL, Von Ranson KM, Cotton S, Biro FM, Mills L, Succop PA. Sexual initiation: predictors and developmental trends. Sex Transm Dis 2001;28:527-32.
- Ellen JM, Adler N. Sexual initiation and developmental changes. Sex Transm Dis 2001;28:533-4.
- 144. Young EW, Jensen LC, Olsen JA, Cundick BP. The effects of family structure on the sexual behavior of adolescents. Adolescence 1991;26:977-86.
- 145. Fergusson DM, Lynskey MT. Alcohol misuse and adolescent sexual behaviors and risk taking. Pediatrics 1996;98:91-6.
- 146. Halpern-Felsher BL, Millstein SG, Ellen JM. Relationship of alcohol use and risky sexual behavior: a review and analysis of findings. J Adolesc Health 1996;19:331-6.
- 147. Strunin L, Hingson R. Alcohol, drugs, and adolescent sexual behavior. Int J Addict 1992;27:129-46.
- 148. Shafer MA, Boyer CB. Psychosocial and behavioral factors associated with risk of sexually transmitted diseases, including human immunodeficiency virus infection, among urban high school students. J Pediatr 1991;119:826-33.
- 149. Ammann AJ. Preventing HIV. BMJ 2003;326:1342-3.
- Vincent ML, Clearie AF, Schluchter MD. Reducing adolescent pregnancy through school and community-based education. JAMA 1987;257:3382-6.

- 151. Blake SM, Simkin L, Ledsky R, Perkins C, Calabrese JM. Effects of a parent-child communications intervention on young adolescents' risk for early onset of sexual intercourse. Fam Plann Perspect 2001;33:52-61.
- Sieving RE, McNeely CS, Blum RW. Maternal expectations, mother-child connectedness, and adolescent sexual debut. Arch Pediatr Adolesc Med 2000;154:809-16.
- 153. Griffin GC. Condoms and contraceptives in junior high and high school clinics: what do you think? Postgrad Med 1993;93:21-3 26-8, 37-8.
- 154. Howard M, McCabe JB. Helping teenagers postpone sexual involvement. Fam Plann Perspect 1990;22:21-6.
- 155. Hubbard BM, Giese ML, Rainey J. A replication study of reducing the risk, a theory-based sexuality curriculum for adolescents. J Sch Health 1998;68:243-7.
- 156. Kirby D, Barth RP, Leland N, Fetro JV. Reducing the risk: impact of a new curriculum on sexual risk-taking. Fam Plann Perspect 1991;23:253-63.
- 157. Centers for Disease Control. Trends in sexual risk behaviors among high school students—United States, 1991-2001. MMWR Morb Mortal Wkly Rep 2002;51:856-9.
- 158. Centers for Disease Control. Trends in sexual risk behaviors among high school students—United States, 1991-1997. MMWR Morb Mortal Wkly Rep 1998;47:749-52.
- Ford K, Sohn W, Lepkowski J. American adolescents: sexual mixing patterns, bridge partners, and concurrency. Sex Transm Dis 2002;29:13-9.
- 160. Hogle J, Green EC, Nantulya V, Stoneburner R, Stover J. What happened in Uganda? Declining HIV prevalence, behavior change, and the national response. Washington (DC): US Agency for International Development, Office of HIV/AIDS, Bureau of Global Health; 2002.
- 161. Allen A. Sex change. New Republic 2002;226:14-5.
- Uganda tackles AIDS from the very top down. AIDS Alert 1999; 14(8 Suppl):3-4.
- 163. Kilian AH, Gregson S, Ndyanabangi B, Walusaga K, Kipp W, Sahlmuller G, et al. Reductions in risk behaviour provide the most consistent explanation for declining HIV-1 prevalence in Uganda. AIDS 1999;13:391-8.
- 164. Whitworth JA, Mahe C, Mbulaiteye SM, Nakiyingi J, Ruberantwari A, Ojwiya A, et al. HIV-1 epidemic trends in rural south-west Uganda over a 10-year period. Trop Med Int Health 2002;7:1047-52.
- Grulich AE, Kaldor JM. Evidence of success in HIV prevention in Africa. Lancet 2002;360:3-4.
- 166. Mbulaiteye SM, Mahe C, Whitworth JA, Ruberantwari A, Nakiyingi JS, Ojwiya A, et al. Declining HIV-1 incidence and associated prevalence over 10 years in a rural population in south-west Uganda: a cohort study. Lancet 2002;360:41-6.
- 167. Okware S, Opio A, Musinguzi J, Waibale P. Fighting HIV/AIDS: is success possible? Bull World Health Organ 2001;79:1113-20.
- Buve A, Bishikwabo-Nsarhaza K, Mutangadura G. The spread and effect of HIV-1 infection in sub-Saharan Africa. Lancet 2002; 359:2011-7.
- Nantulya VN. HIV/AIDS prevention: policy and program context of Uganda's success story. Presentation to USAID, Washington, DC, February 5, 2002.
- Adetunji J, Meekers D. Consistency in condom use in the context of HIV/AIDS in Zimbabwe. J Biosoc Sci 2001;33:121-38.
- 171. Fact list. AIDS: Focus on Africa. CMAJ 2002;167:529.