FACT SHEET:
NEW RESEARCH FROM AIDS 2008

This fact sheet highlights a number of important research developments featured in the AIDS 2008 abstract-driven programme. For a complete list of abstracts presented at the conference, please refer to the online Programme-at-a-Glance and/or the CD-ROM distributed to delegates at registration.

TRACK A: Biology and Pathogenesis of HIV

HIV vaccine puzzle grows even more complicated

Failure of a highly touted HIV vaccine in 2007 raised tough questions about the best approach to designing such a vaccine—and even about whether HIV vaccine research should continue [1]. At AIDS 2008, scientists from the Tulane National Primate Research Center in the USA add a new turn to the vaccine maze with evidence that antibodies do not help control simian immunodeficiency virus (SIV) in monkeys (abstract MOAA0101). The results confound expectations in this nonhuman primate model of HIV infection. African green monkeys do not get sick with AIDS diseases despite high and persistent SIV loads (the number of viral copies in a milliliter of plasma). Many theorized that high SIV loads in monkeys reflect low antibody levels—and that correlation implies a role for antibodies in controlling viral load. But in this study monkeys stripped of antibodies by treatment with an anti-antibody agent had the same viral loads and the same CD4-cell counts as monkeys with their antibody forces intact. Some experts questioned the recently failed STEP trial HIV vaccine because it did not try to boost antibody-driven immunity, focusing solely on cell-based immunity instead.

Will antiretrovirals have a long-term impact on the brain?

New diagnoses of HIV-associated neurocognitive disease fell up to 50% after patients started taking potent antiretroviral combinations [2,3], but overall neurocognitive disease prevalence keeps climbing in HIV-infected people. Brain cell research at the University of Hawaii suggests why prevalence of HIV dementia remains so high: Certain antiretrovirals—specifically nucleoside analogs—may upset the balance of mitochondria, the cells' powerhouse (abstract MOAA0103). This cell study found signals of mitochondrial malfunction in neurons (a type of brain cell) exposed to zidovudine (AZT), lamivudine (3TC), and lopinavir/ritonavir (two protease inhibitors) compared with unexposed neurons.

Resistance to antiretrovirals on the rise in China

Most HIV-infected people starting antiretroviral therapy in Asia and Africa use a regimen including two nucleosides (such as zidovudine, didanosine, stavudine, and lamivudine) plus a nonnucleoside (usually nevirapine, sometimes efavirenz). A large study of randomly selected patients starting such a regimen in China charted rising rates of HIV resistance to these two drug classes in 2006-2007 compared with 2004-2005 (abstract TUAA0303). Among patients whose first regimen failed to control HIV replication, 55% ended up with virus resistant to nonnucleosides and 37% with virus resistant to nucleosides—including some nucleosides not used in their regimen. The results underline the need for adherence

counselling to prevent resistance and for second-line regimens based on a protease inhibitor wherever first-line regimens depend on nonnucleosides.

TRACK B: Clinical Research, Treatment and Care

Abacavir studies disagree on heart attack risk

Earlier this year results of a large HIV cohort study stunned HIV physicians and patients with evidence that the nucleoside analogs abacavir and didanosine independently raise the relative risk of myocardial infarction (heart attacks) [4]. Researchers from GlaxoSmithKline, abacavir's maker, analyzed data from 5044 patients in 54 clinical trials and found no heart attack difference between those who took abacavir and those who did not (abstract WEAB0106). But scrutiny of SMART trial [5] results confirmed the earlier cohort study [4], finding a higher risk of cardiovascular disease in people taking abacavir than in those taking other nucleosides (late breaker abstract THAB0305). This SMART analysis suggested abacavir may heighten the risk of heart disease by causing vascular inflammation. Statistical experts will have to scrutinize the three studies for hints on why they reached different conclusions. Possibilities include differences in study populations, length of follow-up, and definitions of myocardial infarction and cardiovascular disease.

Is abacavir/lamivudine weaker against high viral loads?

A randomized trial, ACTG A5202, documented a significantly shorter time to virologic failure with abacavir/lamivudine versus tenofovir/emtricitabine when added to efavirenz or atazanavir/ritonavir in patients starting their first regimen with a viral load above 100,000 copies/mL (late breaker abstract THAB0303). People taking abacavir/lamivudine also got grade 3 or 4 side effects significantly faster. But investigators from GlaxoSmithKline, the maker of abacavir and lamivudine, found that a viral load above 100,000 copies/mL did not imperil virologic response or make side effects more likely in six 48-week trials of abacavir/lamivudine (late breaker abstract THAB0304).

Triple antiretroviral regimen falters in 9-country trial

A once-daily regimen combining didanosine (ddI), emtricitabine (FTC), and atazanavir did not control HIV or forestall AIDS as well as twice-daily zidovudine/lamivudine (AZT/3TC) plus once-daily efavirenz in a trial involving previously untreated people in 8 developing countries and the USA (late breaker abstract THAB0404). Failure to stop HIV replication was 77% more likely with ddI/FTC/atazanavir, and AIDS was 3 times more likely than with the other combination. Patients took the protease inhibitor atazanavir without a boosting dose of ritonavir—an acceptable but less popular way to give atazanavir.

Nurses and others step up to ease MD shortage in Africa

Two studies in southern Africa found that nurses and other health professionals can fill many roles traditionally reserved for physicians. So-called task shifting to nonphysicians has gained wide interest as one way to ease acute physician shortages that hamper AIDS care in sub-Saharan Africa. (See the next item for another example of successful task shifting.)
In two large public hospitals in Mozambique, mid-level health personnel cared for 69% of 6006 people starting antiretrovirals, while physicians cared for the other 31% (abstract WEAX0105). Before beginning treatment, the groups were similar in CD4 count, age, gender, and education. After 12 months the groups did not differ in CD4 count or mortality, but the non-MD-treated group was 44% less likely to stop keeping clinic visits and 28% more likely to have their CD4 count measured 6 months after starting therapy.

A study in rural southern Africa compared 427 people starting antiretrovirals in nurse-led primary care clinics and 150 people starting therapy as usual in district hospitals (abstract WEAB0206). All patients were medically stable with a CD4 count above 100 cells/mm^3, and women made up two thirds of each group. People in the nurse-led primary care clinics were

significantly less likely to miss appointments, significantly less likely to die, and significantly more likely to voice satisfaction with medical staff.

How a rural Malawi district met its antiretroviral treatment target
Médecins Sans Frontières reports that task shifting from physicians in a rural Malawi district quadrupled the number of people starting antiretrovirals monthly and helped the district reach its antiretroviral treatment goal (abstract TUAB0303). Malawi's Thyolo district has 600,000 people with HIV infection, including 11,250 who urgently needed antiretrovirals. Shifting antiretroviral care duties away from physicians enabled the district to begin treating an average 400 people monthly in 2007, compared with 100 monthly when only physicians could get patients started on therapy. Almost 12,000 people have now begun antiretrovirals in Thyolo. Task shifting also allowed decentralization of health centers, backed by a community network of 675 volunteers and 9 nurses, who help treat opportunistic infections, refer HIV-infected people to clinics, trace people who miss clinic visits, and offer treatment adherence counseling. (See the preceding item for two more examples of successful task shifting.)

TRACK C: Epidemiology, Prevention and Prevention Research

Should we overhaul HIV prevention strategy?
Repeating an argument they spelled out in *Science* [6], Harvard's Daniel Halperin and colleagues maintain that prevention policies for generalized HIV epidemics—like those in sub-Saharan Africa—remain largely misdirected (abstract TUPDC205). Condom promotion for sex workers can slow epidemics concentrated in the sex industry, and clean needles can stem epidemics concentrated among injecting drug users. But generalized epidemics require more than condom promotion, treatment of other sexually transmitted diseases, or abstinence, Halperin argues. He believes evidence shows prevention in generalized epidemics should focus on male circumcision, family planning, and reduction of multiple sexual partnerships—the last of which contributed to falling HIV rates in Uganda, Kenya, and Zimbabwe.

Closer looks at two acyclovir trials that failed to ward off HIV
In the past year two big placebo-controlled trials showed that suppressing herpes simplex virus type 2 (HSV-2) with acyclovir did not help prevent HIV infection [7,8]—a surprising result because HSV-2 doubled or tripled HIV risk in earlier population-based studies. At AIDS 2008, researchers from both trials take a closer look at factors that may explain the disappointing outcomes.

A study that randomized 821 HSV-2-positive but HIV-negative female bar and hotel workers to acyclovir or placebo found almost exactly the same HIV risk in the two groups (abstract THAC0303) [7]. Overall HIV incidence measured 4.27 diagnoses per 100 person-years, but among 16- to 19-year-olds, incidence reached 10.3 per 100 person-years. Numerous factors independently heightened the risk of HIV infection: younger age, getting paid for sex, drinking alcohol, getting injections outside the clinic, and recent gonorrhea.

A trial involving 1358 women in southern Africa and 1814 men who have sex with men (MSM) in Peru and the USA found equivalent risks of HIV infection among people randomized to acyclovir and those randomized to placebo (abstract THAC0301) [8]. Yet overall risk of genital ulcers and risk of HSV-2-positive genital ulcers fell significantly among acyclovir takers. Notably, though, these risk reductions were always greatest in the US MSM, followed by Peruvian MSM, then by African women. And only US MSM had a significant drop in HSV quantity in genital ulcers.

Further findings on protective benefit of male circumcision

In the past few years three randomized trials found that circumcision lowers the risk of HIV infection in heterosexual men, but not necessarily in their female sex partners [9-11]. At AIDS 2008 one of the three trial groups [10] showed that the protective effect for circumcised men lasts at least 42 months and may get stronger with time (late breaker abstract THAC0501). Studying men in another of the three randomized trials [9], researchers showed for the first time that circumcision lowers the risk of *Trichomonas* infection and high-risk human papillomavirus (HPV) infection in sexually active men (late breaker abstract THAC0502). These findings suggest why women with circumcised partners run a lower risk of certain infections besides HIV. HPV is a critical factor in development of cervical cancer.

Higher infant death risk with formula versus breast feeding

Although strict formula feeding lowers HIV transmission risk from mothers to infants, it is often impractical in sub-Saharan Africa because it costs too much and it suggests a woman has HIV infection. A study of formula versus breast feeding in HIV-infected women from Uganda's rural Rakai district recorded a significantly higher HIV rate in breastfed infants than in formula-fed infants at 6 weeks of age (13% versus 4%) (abstract THAC0406). But 1 year after birth, overall death risk was 50% lower in the 226 breastfed infants than in the 84 formula-fed infants. HIV-free survival did not differ between the two groups at 1 year.

Can unsafe sex be safe? Insights on Swiss Commission advice

Earlier this year the Swiss Federal Commission on HIV/AIDS raised a ruckus by suggesting sex without condoms may pose no realistic risk of HIV transmission from people with an undetectable viral load and no sexually transmitted infections [12]. This communication touched off an intense and ongoing international debate. At AIDS 2008 a multistudy analysis involving 5161 heterosexual couples could neither confirm nor refute the Swiss estimate that HIV transmission risk per sex act falls below 1 in 100,000 for a person with an undetectable viral load (late breaker abstract THAC0505). On Sunday at 15:45, the Swiss Commission will hold a satellite meeting to discuss the scientific issues involved with outside experts, and will open the controversy to public debate (SUSAT41-HIV Transmission Under ART).

Condom-induced erectile dysfunction boosts risk of unsafe sex

Dutch men who have sex with men who reported condom-induced erectile dysfunction (COINED) were almost 7 times more likely to plan unprotected anal intercourse with casual partners than were men without erectile dysfunction, according to results of a 435-man study in an Amsterdam cohort (abstract THPDC205). Although rates of unprotected anal intercourse were similar with casual partners (18%) and steady partners (17%), COINED did not boost the risk of planned unprotected anal intercourse with steady partners. Because COINED influenced intentions to use condoms before casual sex, the researchers caution that "intention-based prevention strategies will probably not be able to address this problem and alternative strategies should be applied."

TRACK D: Social, Behavioural and Economic Science

Another HIV risk for drug-using women: coerced sex with police officers

A study of 287 women arrested for drug use in St. Louis, Missouri, disclosed that 78 of them (27%) had sex with a police officer, often as a result of coercion (abstract THPDD202). Of the 78 women who had sex with a policeman, 26% said they were raped and 55% said they had sex because the officer promised not to arrest them in return—but not all the cops kept that promise. Almost all women who had sex with a policeman, 96%, did so with an officer on duty, and 74% had sex with one officer more than once. Only 53% of women who had sex with a police officer always used a condom in such encounters. Drug-using women run a high risk of HIV infection because of both sexual relations and drug behaviours.

Migration to, and deportation from, USA affect HIV risk in Mexicans

Two studies from the host country for AIDS 2008 detailed how migration from Mexico to the United States—and back again—affect the risk of getting infected with HIV.

A survey of 1056 injecting drug users in Tijuana, just across the border from California, found that deportation from the USA independently quadrupled the risk of HIV infection among male drug injectors (abstract TUAD0205). Among women, three factors independently boosted HIV risk—younger age, lifetime syphilis infection, and living longer in Tijuana. Among men, independent risk factors were high syphilis bacterium levels, being arrested because of injection track marks, and having more injecting partners.

Another study involved 364 male migrants living in rural or urban California (abstract TUAD0203). Needle sharing and low condom use decreased significantly after migration to the US, but three HIV risk factors became significantly more frequent—sex with a sex worker, sex work by the migrant himself, and sex while under the influence of drugs or alcohol.

TRACK E: Policy and Political Sciences

Enforcing drug patents does not spread antiretroviral technology

Contrary to statements by the World Trade Organization and the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS) [13], a study of 25 developing countries found no evidence that enforcing intellectual property rights on drugs (patents) improved the flow of antiretroviral drug technology (abstract MOPDE206). The study did find that drug company initiatives promote transfer of second-line antiretroviral technology. But companies aimed 80% of such initiatives at only two countries—India and South Africa.

Making HIV transmission a crime does more harm than good

Laws that criminalize HIV transmission—or even the possibility of transmission—often assume the guise of human rights legislation, according to three reports from Africa, Europe, and Central Asia (abstracts WEAE0101, WEAE0102, and WEAE0103). Western African countries put 10 such laws on the books since 2005, usually mandating broad disclosure and "duty-to-warn" obligations. Some laws make it a crime for a mother to transmit HIV to her infant. A southern African rights group says lack of evidence that such laws prevent HIV transmission has not diminished support of certain "model legislation" by the US Agency for International Development (USAID). A survey of 53 nations in Europe [14] and Central Asia found most HIV transmission prosecutions involve already marginalized people, such as migrants from other countries. One rights group calls on UNAIDS and other global health agencies to take a stand against criminalizing HIV transmission.

More drug arrests do not lower injecting drug use rate

"Increasing hard-drug arrest rates did not predict falling IDU [injecting drug use] prevalence . . . a result inconsistent with criminal deterrence theory." That conclusion emerged from a statistical comparison of heroin and cocaine possession arrest rates and IDU prevalence in 96 large US urban areas (abstract TUAE0202). Separate analyses using different statistical methods yielded no evidence supporting the notion that putting hard drug users behind bars lowers prevalence of injecting drug use. Getting people to stop injecting drugs should affect HIV rates in areas where IDUs help drive the epidemic, but these results suggest throwing them in jail seems an unlikely remedy.

References

1. National Institute of Allergy and Infectious Diseases. Immunizations are discontinued in two HIV vaccine trials. 21 September 2007. (http://www3.niaid.nih.gov/news/newsreleases/2007/step_statement.htm)

2. Brodt HR, Kamps BS, Gute P, et al. Changing incidence of AIDS-defining illnesses in the era of antiretroviral combination therapy. AIDS. 1997;11:1731-1738.

3. Sacktor N, Lyles RH, Skolasky R, et al. HIV-associated neurologic disease incidence changes: Multicenter AIDS Cohort Study, 1990-1998. Neurology. 2001;56:257-260.

4. D:A:D Study Group. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. Lancet. 2008;371:1417-1426. (http://www.cphiv.dk/portals/0/files/DAD%20Position%20statement%20Lancet_CROI%20Abstract%202008.pdf)

5. Strategies for Management of Antiretroviral Therapy (SMART) Study Group, El-Sadr WM, Lundgren JD, Neaton JD, et al. CD4+ count-guided interruption of antiretroviral treatment. N Engl J Med. 2006;355:2283-2296. (http://content.nejm.org/cgi/content/abstract/355/22/2283)

6. Potts M, Halperin DT, Kirby D, et al. Public health. Reassessing HIV prevention. Science. 2008;320:749-750.

7. Watson-Jones D, Weiss HA, Rusizoka M, et al. Effect of herpes simplex suppression on incidence of HIV among women in Tanzania. N Engl J Med. 2008;358:1560-1571. (http://content.nejm.org/cgi/content/full/358/15/1560)

8. Celum C, Wald A, Hughes J, et al, the HPTN 039 Protocol Team. Effect of aciclovir on HIV-1 acquisition in herpes simplex virus 2 seropositive women and men who have sex with men: a randomised, double-blind, placebo-controlled trial. Lancet. 2008;371:2109-2119. (www.thelancet.com/journals/lancet/article/PIIS0140673608609204/fulltext content.nejm.org/cgi/content/full/358/15/1560).

9. Auvert B, Taljaard D, Lagarde E, et al. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005;2(11):e298. (http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020298)

10. Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369:643-656.

11. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369:657-666.

12. Mascolini M. Controversy over Swiss statement on safe sex without condoms. World AIDS News. 2 February 2008. (http://www.iasociety.org/Admin/Element.aspx?article=True&elementId=10747)

13. TRIPS material on the WTO website. (http://www.wto.org/english/tratop_e/trips_e/trips_e.htm)

14. Global Network of People Living with HIV/AIDS Europe. Criminalisation of HIV transmission in Europe. (http://www.gnpplus.net/criminalisation/index.shtml)

Guide to Key Abstract Studies in 5 Tracks at AIDS 2008

TRACK A: Biology and Pathogenesis of HIV			
Author	*Abstract No.*	*Site*	*Key findings*
Gaufin	MOAA0101	USA	Antibodies did not control SIV in monkeys, a finding that runs against prevailing theory and raises new questions about developing an HIV vaccine.
Kim	MOAA0103	USA	Antiretroviral-related damage of mitochondria in certain brain cells may explain a persistently high rate of neurocognitive disease in people otherwise responding well to therapy.
Liao	TUAA0303	China	Climbing rates of resistance to first-line antiretroviral regimens underline the need for better adherence counseling and potent second-line regimens.

TRACK B: Clinical Research, Treatment and Care			
Author	*Abstract No.*	*Site*	*Key findings*
Hernandez Lundgren	WEAB0106 THAB0305 **(Late Breaker)**	International International	Analysis of 5000 clinical trial participants contradicted an earlier finding that abacavir raises the relative risk of heart attacks. Heart disease rates in the SMART trial were higher among people taking abacavir than among those taking other drugs in this class.
Sax Pappa	THAB0303 **(Late Breaker)** THAB0304 **(Late Breaker)**	USA International	In a randomized trial, risks of virologic failure and side effects were higher among people starting abacavir plus lamivudine with a viral load above 100,000 copies/mL than in those starting tenofovir plus emtricitabine. Analysis of six earlier trials found no higher risk of virologic failure in people with a viral load above 100,000 copies/mL who began a regimen including abacavir plus lamivudine.
Campbell	THAB0404	International	A once-a-day regimen of didanosine,

	(Late Breaker)		emtricitabine, and atazanavir (without ritonavir) did not control HIV or prevent AIDS as well as zidovudine plus lamivudine and efavirenz in this 9-country trial.
Gimbel-Sherr	WEAX0105	Mozambique	Nonphysicians did as well as physicians in caring for AIDS patients, a result suggesting one remedy for the MD shortage in Africa.
Humphreys	WEAB0206	Southern Africa	AIDS patients in nurse-led primary care clinics had a lower risk of dying than patients cared for in district hospitals, a result underscoring the feasibility of "task shifting" in HIV epicenters.
Massaquoi	TUAB0305	Malawi	Shifting antiretroviral care duties away from physicians enabled a rural district to quadruple the number of people starting therapy.

TRACK C: Epidemiology, Prevention and Prevention Research			
Author	*Abstract No.*	*Site*	*Key findings*
Halperin	TUPDC205	International	Global HIV prevention may be failing because it applies tactics developed for concentrated epidemics to generalized epidemics, argues a team of HIV experts.
Watson-Jones Sanchez	THAC0303 THAC0301	Tanzania Peru, South Africa, USA, Zambia, Zimbabwe	HIV prevention researchers identify several factors that may explain why treating herpes with acyclovir did not prevent HIV infection in a large, placebo-controlled trial. Authors of a placebo-controlled trial in which treating herpes with acyclovir failed to prevent HIV infection detail differences in acyclovir's impact on three populations studied.
Bailey Auvert	THAC0501 **(Late Breaker)** THAC0502 **(Late Breaker)**	Kenya South Africa	Extended follow-up in one of three trials establishing that circumcision lowers HIV risk in heterosexual men found that protective effect lasts at least 42 months and may grow stronger with time. Further study of another circumcision trial population determined that the procedure lowers the risk of two other sexually transmitted pathogens in men.
Kagaayi	THAC0406	Uganda	Compared with formula feeding,

			breastfeeding by HIV-infected mothers raised the risk of HIV transmission 6 weeks after birth but lowered the risk of all-cause infant mortality at 1 year.
Attia	THAC0505 **(Late Breaker)**	International	Review of studies involving over 5000 heterosexual couples could not confirm or refute a negligible HIV transmission risk from people with an undetectable HIV load and no sexually transmitted infections. Swiss experts had claimed that risk was exceedingly low when suggesting unprotected sex may be safe in such couples.
Davidovich	THPDC205	Netherlands	Condom-induced erectile dysfunction in Dutch gays inflated the likelihood of planned unprotected anal intercourse 7 times.

TRACK D: Social, Behavioural and Economic Science

Author	*Abstract No.*	*Site*	*Key findings*
Cottler	THPDD202	USA	More than 25% of women arrested for drug use reported sex with a police officer, often as a result of coercion.
Strathdee	TUAD0205	Mexico	Deportation from the US to Mexico quadrupled the risk of HIV infection among injecting drug users in Tijuana.
Sanchez	TUAD0203	California, Mexico	Migration from Mexico to California made three HIV risk factors more likely, but two risk factors became less likely after migration.

TRACK E: Policy and Political Sciences

Author	*Abstract No.*	*Site*	*Key findings*
Wilson	MOPDE206	International	Protecting drug patents did not promote antiretroviral technology transfer, as claimed by the World Trade Organization, in this 25-country study.
Pearshouse	WEAE0101	Western Africa	Western African countries passed 10 laws since 2005 making HIV transmission a crime, including mother-to-child transmission.
Clayton	WEAE0102	Sub-Saharan Africa	HIV transmission laws in southern Africa often ignore factors such as

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			whether safe sex is practiced or HIV status is disclosed, according to this rights group analysis.
Hows	WEAE0103	Europe, Central Asia	A survey of 53 European and Central Asian countries found that most prosecutions for HIV transmission involve already marginalized groups.
Friedman	TUAE0202	USA	Arresting more people for hard drug use did not lower rates of injecting drug use across the USA, a finding that contradicts criminal justice theory.