Correspondence

AIDS 2004, **18**:829–835

Coronavirus infection in an AIDS patient

A 30-year-old Chinese man presented in April 2003 to a public hospital in Hong Kong for suspected severe acute respiratory syndrome (SARS). He had been living with HIV (currently at stage CIII) for 5 years and was on highly active antiretroviral therapy (HAART) comprising abacavir 300 mg twice a day, efavirenz 600 mg at night, Kaletra 4 capsules (each capsule contains lopinavir 133.3 mg and ritonavir 33.3 mg) and tenofovir 300 mg twice a day, plus standard *Pneumocystis carinii* pneumonia prophylaxis. He had been on the present HAART regimen since November 2002 and had good drug adherence. His CD4 cell count and viral load were 134 cells/μl and 470 copies/ml [by reverse transcriptase–polymerase chain reaction (PCR), Roche Amplicor], respectively, in February 2003.

The patient gave a one-week history of right-sided chest pain and chills, followed by fever, increasing dry cough and malaise. On admission, he had a fever of 38°C, was mildly tachypnoeic; and his blood pressure was 155/77 mmHg, with a pulse rate of 90/min. The pulse oximetry read 97% while on oxygen 3 l/min. There was no added sound on chest examination. Chest X-ray showed haziness in the right lower zone, with the costophrenic angle being sharp, compatible with consolidation. His white cell count was 6.1×10^9/l, with a significant lymphopenia of 0.4×10^9/l compared with that of 1.2×10^9/l recorded 2 months earlier. Renal and liver function tests, clotting times and creatine kinase level were within normal limits. He was started on pipercillin/tazobactam for empirical treatment of his pneumonia. His fever subsided 24 h later, with a gradual improvement of chest symptoms. His sputum culture revealed commensal organisms only. A work-up for pneumonia, including sputum Gram stain and culture, acid-fast bacilli smear, nasal and throat swabs for the usual viral pathogens did not reveal positive results. His lymphocyte count rose to 1.0 on day 9.

Because of the concurrent SARS outbreak in Hong Kong, a throat swab was taken on day 2 for coronavirus using PCR, which subsequently showed a positive result. The patient was commenced on ribavirin 1200 mg three times a day and prednisolone 25 mg three times a day by mouth from day 7 according to the hospital's standard protocol [1]. He was also covered with lamivudine, to prevent hepatitis flare in view of his hepatitis B surface antigen-positive status. Ribavirin was continued for a total of 20 days, whereas steroid was tailed off over 4 weeks. He tolerated the treatment and remained asymptomatic until day 25 when the fever relapsed (see Fig. 1) and a chest X-ray showed increased right lower zone haziness. Two sputum smears for acid-fast bacilli were positive (taken on days 29 and 30). He was started on anti-tuberculosis treatment and his fever subsided after one day. The first antibodies test for coronavirus on admission was negative, whereas the second titre taken 2 weeks after the onset of symptoms was 1 : 40. Coronavirus PCR tests were repeated for throat and nasal swabs, stool and urine on day 39 and were negative.

This is the first reported case of SARS in an HIV-infected patient. The diagnosis of SARS was made clinically, supported by lymphopenia, positive PCR and serology for SARS-associated coronavirus. Our patient ran a relatively mild course despite his immunocompromised state. There are two possible reasons for this observation. First, the HAART regimen might have protective antiviral effects during the viraemic phase. Kaletra has been found to have some in-vitro activities against coronavirus, and was used as an experimental treatment agent in some hospitals in Hong Kong. The dose of Kaletra used for such purposes was 500 mg twice a day. The viral main proteinase $3CL^{pro}$ was found to control the activities of the coronavirus replication complex [2]. It is unknown whether Kaletra, a combined protease inhibitor, acts on similar targets. Second, the grave prognognosis in

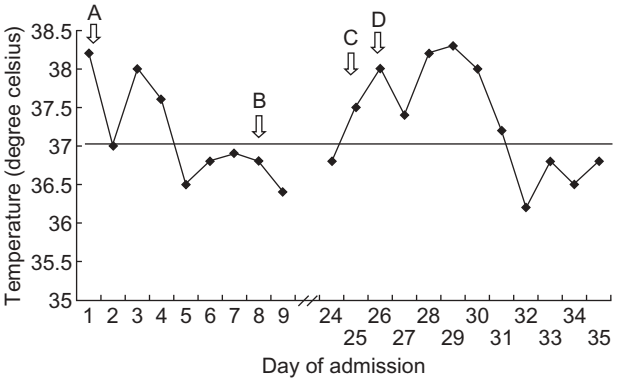

Fig. 1. Temperature of patient. A: Day 1 – patient was started on piperacillin/tazobactam; before admission, patient was given kaletra, abacavir, efavirenz, tenofovir and septrin. B: Day 8 – patient was started on ribavirin, prednisolone and lamivudine. C: Day 25 – patient had recurrence of fever. D: Day 26 – patient was started on anti-tuberculosis medication.

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young patients with SARS might be related to the excessive immune response to the new virus. Cytokine dysregulation may account, at least partly, for the severity of clinical disease [3]. The defective cellular immunity in HIV infection could paradoxically be a protective factor in some patients. The plausibility of these explanations has yet to be confirmed. On the other hand, it could be argued that if Kaletra was active against coronavirus, it should have prevented the infection in the first place. Finally, HIV and coronavirus co-infection may carry other deleterious consequences. The precipitation of tuberculosis by steroid is a cause for concern [4]. There is also the potential risk of prolonged viral shedding in HIV infection if the clearance of coronavirus is ineffective. Furthermore, the mild symptoms of SARS in HIV patients may go unnoticed, making public health control of SARS difficult.

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'DOTS' and 'DOT' for delivering antiretroviral therapy in resource-poor countries

Liechty and Bangsberg [1] made the case that the enthusiasm for HIV directly observed treatment (DOT) programmes is premature, and they show that there is little evidence as yet that DOT for antiretroviral drugs improves virological, immunological or clinical outcomes. The enthusiasm for HIV DOT stems from the experience of tuberculosis control programmes, in which the direct observation of treatment is promoted as one part of an overall strategy for tuberculosis control. Criticism of HIV DOT may be valid, but it misses the point and detracts from the overall message that the strategy for tuberculosis control might be a useful model on which to base a strategy for delivering antiretroviral therapy.

The overall aim of tuberculosis control is to reduce mortality, morbidity, and transmission of the disease, while preventing the development of drug resistance. The main intervention is standardized combination chemotherapy provided under direct observation, at least during the initial phase of treatment, to all identified sputum smear-positive tuberculosis patients, the main sources of infection. The framework for effective tuberculosis control incorporates a global strategy called 'directly observed treatment, short course' (DOTS) (Table 1) [2]. DOT is just one component of this policy package. Other components, such as a quality assured diagnostic service, uninterrupted supply of drugs and a standardized monitoring

Table 1. Five components of the DOTS strategy.

- Sustained political commitment
- Access to quality-assured sputum microscopy
- Standardized short-course chemotherapy for all cases of tuberculosis under proper case management conditions, including direct observation of treatment
- Uninterrupted supply of quality-assured drugs
- Recording and reporting system enabling outcome assessment of all patients and assessment of overall programme performance

DOTS, Directly observed treatment, short course.

and evaluation system are also essential to the strategy of achieving the global targets for tuberculosis control: an 85% cure rate and a 70% case detection rate for new cases of smear-positive pulmonary tuberculosis [2]. A similar strategy for delivering antiretroviral drugs has been successfully tested in small projects in resource-poor countries [3], and this may provide a simple, structured, safe and effective way of providing a high technology intervention to places where it is most needed, such as in sub-Saharan Africa [4].

DOT versus self-administered treatment in the context of tuberculosis control has also been the subject of extensive debate, particularly about what approach improves treatment adherence. The randomized controlled trials in South Africa and Pakistan [5,6], which showed that DOT was no more effective than self-administered treatment, have been widely used to throw doubt on the effectiveness of this observed therapy approach. However, in the trials it is important to note that all alternative options for treatment care processes were associated with high default rates and poor treatment outcomes. This suggests that the debate around DOT should be broadened, and there is in fact a growing appreciation that DOT is not just about watching patients take their medication [7]. It is more about making life acceptable for tuberculosis patients during their treatment, and finding creative ways of helping patients complete their treatment successfully. DOT should be conceptualized as a broad package of support to the patient, within the framework of a chronic care model [7]. DOT, therefore, may vary in terms of what the package contains and the context in which the package is being implemented. A similar concept of HIV DOT would seem reasonable when considering the provision of life-long antiretroviral drugs to patients with HIV/AIDS. Nevertheless, as Liechty and Bangsberg [1] pointed out, a broader concept of DOT still needs to be evaluated, so that practice and policy is based on sound evidence.

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Stable drug supply and distribution in an integrated healthcare delivery system, but unconfirmed need for daily witnessed dosing

We agree with Dr Harries that future large-scale antiretroviral treatment programmes in resource-poor settings would do well to emulate several aspects of the directly observed treatment, short course (DOTS) strategy; specifically the consolidation of multilateral political support, development of reliable diagnostic systems, assured drug supply, and infrastructure for comprehensive outcome assessment.

We suggest caution, however, with respect to the role of daily witnessed dosing. Although this is only a single component of the DOTS strategy, it has been promoted as a centrepiece of such programmes [1,2]. Dr Harries acknowledges appropriate skepticism regarding the attributable impact of witnessed dosing on improving tuberculosis treatment outcomes. Others, however, have argued that witnessed dosing is an indispensable component of DOTS programmes [3,4]. Witnessed dosing of HIV antiretroviral therapy is complicated by the need for lifelong treatment, daily medication dosing, and the consequent impact on individual rights in the setting of a highly stigmatizing disease. For these reasons, we suggest that witnessed dosing is the most problematic element in the large-scale expansion of HIV treatment access in resource-poor settings based on the DOTS model. Otherwise, we entirely agree with Dr Harries that HIV treatment programmes should be conceptualized as a broad package of support to the patient, within the framework of a chronic care model similar to that of existing tuberculosis programmes.

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Political and socioeconomic instability: how does it affect HIV? A case study in the Democratic Republic of Congo

Five years ago, we reported a low and stable HIV prevalence in selected population groups, despite the poor environment and political instability, in the Democratic Republic of Congo (DRC) [1]. Since then, the central government has lost control of almost one third of the country and war is waging across DRC [2,3]. We hereby report to what extent the ongoing conflict could impact on the stability of HIV prevalence reported in our previous study.

From March to May 2002, we conducted HIV serosurveys in four major cities: Kinshasa, Mbuji-Mayi, Lubumbashi, located in the government-held areas, and Kisangani, under the control of the rebels, Rwandan and Ugandan armies. Convenient sampling was obtained among pregnant women attending antenatal clinics, tuberculosis patients, clinic outpatients, blood donors, sexually transmitted infection (STI) patients, sex workers and internally displaced people (IDP). After informed consent, 3090 individuals, 2201 women (72.1%) and 889 men (28.8%), were screened for HIV antibody by a rapid assay (Abbott Determine HIV-1/2; Abbott Laboratory, Tokyo, Japan) or a commercial enzyme-linked immunosorbent assay (Organon Technika, Belgium). All reactive specimens were discriminated and confirmed by a line immunoassay (Innolia HIV-1/2; Innogenetics, Ghent, Belgium).

Comparing our data with those obtained in the previous study (Table 1), we found that in Kinshasa, the prevalence rates in pregnant women, tuberculosis patients, sex workers, STI patients and blood donors had not changed significantly. Similar trends were observed among pregnant women and tuberculosis patients in Mbuji-Mayi. However, HIV prevalence among outpatients in Kinshasa has decreased significantly ($\chi^2 = 6.3$, $P = 0.01$).

The reasons for these results remain unclear, but one could assume that the pattern of healthcare-seeking behaviour may have changed as a result of increased poverty and insecurity. Impoverished individuals rarely find the money needed to pay for health services. The pattern of service delivery has also changed: medical services have been eroded over decades of mismanagement and in many communities they collapsed completely during the war.

These trends could also be associated with the change in risk behaviour caused by a limitation of movements and a decrease in social life. The purchasing power of Congolese civil servants has declined steadily, and public sector wages are not paid regularly [2,4], forcing men to change their behaviour by limiting their access to commercial sex workers and other partners.

When stratified by age groups, our data show some decline in HIV prevalence rates (although not statistically significant) in those under 20 years: pregnant women, from 3% in 1997 to 1.7% in 2002; outpatients from 37.5% in 1997 to 16% in 2002; and STI patients from 20% in 1997 to 7.4% in 2002. Recent infections among young people (15–24 years) could have decreased over time, maybe suggesting a change in risk behaviour [5,6].

With respect to sex issues, data from tuberculosis patients showed that women under 25 years constituted 70% of HIV infections ($\chi^2 = 7.5$, $P = 0.005$). Although the rape of women and girls had been reported in Kisangani [7], in our study, the rate of HIV infection in pregnant women was 3.6%, lower than the 4.5% reported in 1997 [8]. In addition, an HIV prevalence of 3.4% among pregnant women in Lubumbashi contrasts with the level of 9% reported in the 1999 sentinel survey [8].

However, the high HIV prevalence observed among IDP (7.1%) is in line with most other findings, showing that collective violence and consequent population movements are likely to increase the vulnerability of this population to the further spread of HIV [9,10]. As reported by Leroy *et al.* [11], the prevalence of HIV-1

Table 1. HIV prevalence per population groups and per city and comparison with the 1997 data in Kinshasa and Mbuji-Mayi.

	2002			1997			
Population groups	No. tested	HIV n (%)	95% CI	No. tested	HIV n (%)	χ^2	*P*
Pregnant women							
Kinshasa	582	17 (3%)	(1.6–4.7)	511	16 (3.1)	0.14	0.7
Mbuji-Mayi	318	14 (4.4%)	(1.4–7.0)	300	19 (6.3)	0.7	0.37
Lubumbasha	203	7 (3.4%)	(2.5–7.4)				
Kisangani	164	6 (3.6%)	(1.4–7.8)				
Tuberculosis patients							
Kinshasa	248	53 (21.7%)	(16.4–27.0)	200	50 (26)	2.14	0.10
Mbuji-Mayi	170	39 (23%)	(20.0–37.9)	60	16 (28)	0.7	0.4
Lubumbashi	106	30 (28.3%)	(16.9–30.0)				
Kisangani	35	10 (28.5%)	(14.6–46.3)				
Clinical outpatients							
Kinshasa	175	61 (34.8%)	(27.8–42.4)	63	33 (52)	6.3	0.01
Lubumbashi	58	30 (51.7%)	(38.2–65.0)				
Kisangani	60	18 (30%)	(18.8–43.2)				
Blood donors							
Kinshasa	295	4 (1.3%)	(0.4–3.4)	321	10 (3.1)	0.65	0.47
Lubumbashi	138	5 (3.6%)	(1.2–8.3)				
STI patients							
Kinshasa	203	18 (8.8%)	(5.3–13.7)	214	26 (12.1)	1.19	0.21
Lubumbashi	6	7 (11.5%)	(4.7–22.2)				
Female sex workers							
Kinshasa	162	38 (23.4 %)	(16.6–33.5)	100	29 (29)	1.52	0.21
Internally displaced people							
Lubumbashi	112	8 (7.1%)	(3.1–13.6)				

CI, Confidence interval; STI, sexually transmitted infection.

in pregnant women from rural areas in Kigali, Rwanda, was higher than expected (24%) and was attributed to rape and displacement during the genocide.

Although our research included two sites used in the 1997 study, no clear trend emerged regarding the HIV epidemic in these population groups. The low and stable HIV prevalence observed in urban area may hide a high and growing problem in vulnerable groups [12,13]. The selection bias, which excluded rural populations who do not have access to healthcare services, could explain the limitations of the study in assessing the overall situation [14,15]. However, the high prevalence of HIV among IDP shows that population groups (used in sentinel surveys), and traditional methods are not appropriate to evaluate the effect of insecurity and political instability on the HIV situation in DRC.

A comprehensive study that includes other vulnerable groups should be carried out at national level to determine the reasons behind the low and stable seroprevalence. Persisting insecurity, military movement and civilian displacement seem to be linked to the high seroprevalence observed in some population groups. National authorities are urged to establish an enabling environment for the implementation of effective and sustainable HIV/AIDS prevention and care programmes.

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HIV optimism does not explain increases in high-risk sexual behaviour among gay men in Scotland

Elford *et al*. [1] found that HIV optimism could not explain the increase in high-risk sexual behaviour among gay men in London. There was a similar increase in risk among Scottish gay men between 1999 and 2002 [2], and we investigate here whether HIV optimism can explain this.

We compared rates of unprotected anal intercourse (UAI) with casual partners and the levels of HIV optimism in cross-sectional bar-based surveys of gay men in Scotland's two largest cities: Glasgow and Edinburgh (1999: $N = 2498$, response rate 77.5%; 2002: $N = 1734$, response rate 62.0%) [3,4]. HIV optimism was measured using two single-item scales (optimism 1: 'I am less worried about HIV infection now that treatments have improved'; and optimism 2: 'I believe that new drug therapies make people with HIV less infectious'). Men who agreed or strongly agreed with the items were categorized as optimistic and men who disagreed or strongly disagreed were categorized as not optimistic. 'Unsure' was included as a category in 1999, but men who responded 'unsure' or who had not answered these in either survey were excluded from the analyses (sample size: 1999 $N = 1694$, 2002 $N = 1489$).

In 1999, 177 men (10.5%) reported UAI with casual partners compared with 268 (18.0%) in 2002 ($P < 0.001$). Most men were not optimistic, but HIV optimism did increase between the surveys. In 1999, 235 men (13.9%) agreed with optimism 1 compared with 345 (23.2%) in 2002 ($P < 0.001$); and 129 men (7.6%) agreed with optimism 2 compared with 186 (12.5%) in 2002 ($P < 0.001$). Overall, optimistic men were more likely to report UAI with casual partners than men who were not optimistic. For optimism 1, 19.6% of optimistic men (113/578) reported UAI with casual partners compared with 12.8% of men who were not optimistic (332/2599; $P < 0.001$). For optimism 2, the corresponding percentages were 21.1% (66/313) versus 13.2% (379/2864; $P < 0.001$).

The unadjusted odds of UAI with casual partners were significantly higher in the 2002 survey compared with 1999, and among optimistic men compared with men who were not optimistic (Table 1). When entered into multivariate logistic regression, controlling for confounding factors, both survey year and optimism 1 remained significant; with no significant interaction between the two ($P = 0.7$; Table 1).

The analysis was repeated separately for men who had had an HIV test and those who had not. Never-tested men who engaged in UAI, by not knowing their own HIV status, were doing so with partners who may have been of discordant antibody status. However, even among tested men, only 20% always knew their casual partner's status, demonstrating that the majority of these men also engaged in non-concordant UAI. There were no significant differences in optimism between tested and never-tested men; HIV testing levels did not change between 1999 and 2002. The unadjusted odds of UAI with casual partners were significantly higher in the 2002 survey and among optimistic men for both groups (Table 1). When the multivariate models were run separately for tested and never-tested men, only the year of survey remained significant (Table 1). There

Table 1. Unprotected anal intercourse with casual partners, survey year and HIV optimism: unadjusted and multivariate logistic regression.

	Unadjusted			Multivariate[a]		
	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*
UAI with casual partners: all men (N = 3177)						
Survey 2002	1.89	1.54–2.31	< 0.001	1.80	1.46–2.23	< 0.001
HIV optimism 1 – agree	1.66	1.31–2.10	< 0.001	1.36	1.03–1.80	0.03
HIV optimism 2 – agree	1.75	1.31–2.35	< 0.001	1.37	0.96–1.94	0.08
UAI with casual partners: tested men (N = 1690)						
Survey 2002	1.70	1.31–2.20	< 0.001	1.65	1.26–2.16	< 0.001
HIV optimism 1 – agree	1.58	1.16–2.16	0.004	1.41	0.98–2.03	0.07
HIV optimism 2 – agree	1.62	1.08–2.42	0.019	1.31	0.81–2.11	0.3
UAI with casual partners: never-tested men (N = 1467)						
Survey 2002	2.15	1.54–2.99	< 0.001	1.99	1.40–2.82	< 0.001
HIV optimtimism 1 – agree	1.87	1.30–2.70	0.001	1.41	0.90–2.22	0.1
HIV optimism 2 – agree	2.10	1.37–3.24	0.001	1.51	0.89–2.59	0.1

[a]Multivariate logistic regression included age, social class, qualification level, city and frequency of bar use (frequency of bar use was significant in each model, $P < 0.01$).HIV optimism 1 statement: 'I am less worried about HIV infection now that treatments have improved'.
HIV optimism 2 statement: 'I believe that new drug therapies make people with HIV less infectious'.

was a significant interaction between survey year and optimism 1 for never-tested men [odds ratio (OR) 0.43, 95% confidence interval (CI) 0.20–0.94, $P < 0.05$]. Therefore, whereas the percentage of never-tested men reporting UAI with casual partners increased between 1999 and 2002, the rate of increase was greater among those who were not optimistic than among those who were.

As has been found elsewhere [5], the majority of Scottish gay men were not optimistic. Optimistic men were more likely to report high-risk sexual behaviour than men who were not optimistic; an association that has been reported elsewhere [6–8]. However, both the year of survey and being 'less worried about HIV infection now that treatments have improved' were significantly and independently associated with sexual risk in the multivariate analysis. If HIV optimism alone explained the increase in sexual risk, either the year of survey would not have remained significant or there would have been a significant interaction between year and optimism. In fact, the survey year remained significant after controlling for optimism and other confounding factors, and for the study groups as a whole there were no significant interactions between the survey year and optimism. Where there was an interaction, among never-tested men, the rate of increase was actually higher among men who were not optimistic than among those who were.

Our results strongly suggest that HIV optimism cannot explain the recent increase in high-risk sexual behaviour among Scottish gay men; supporting the earlier findings for men in London [1]. Priority should be given to identifying other factors related to increased sexual risk.

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