Evidence of AIDS-related mortality in Mumbai, India

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From an estimated 85 200 HIV-infected individuals in Mumbai in 1997, at least 4120 excess deaths attributed to AIDS occurred among 15–54-year-olds. To prevent repetition of this excess in other parts of India, priority intervention programmes should be instituted quickly because the window of opportunity is closing quickly.

There is disbelief among policy makers, public-health specialists, care providers, and the general public about the magnitude of the HIV epidemic and its consequences in India. The absence of a reliable and efficient health-surveillance system has led to concerns about the impact of the epidemic on demography, economy, and national development. We designed a growth-rate model to analyse data on deaths that occurred between 1987 and 1997 in Mumbai. We used data from the death registry of the Public Health Department of the Mumbai Municipal Corporation, which is fairly reliable and efficient in terms of recording deaths within the city.

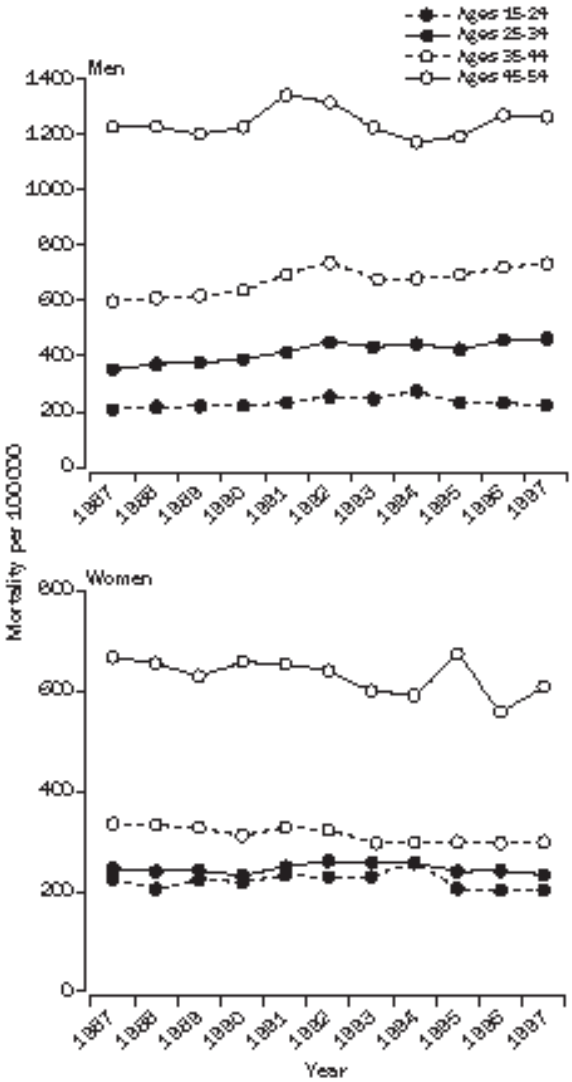
Mumbai has an estimated population of 12 million. Several epidemiological and observational studies carried out during the past 10 years have shown an exponential increase in the prevalence of HIV infection.[1,2] The rates suggest that a large-scale epidemic was introduced among behaviour-based high-risk groups between 1986 and 1990. The main mode of HIV transmission is through the heterosexual route. To estimate the prevalence of HIV infection in Mumbai in 1997, we assumed that there were 60 000 prostitutes, 100 000 incident cases of sexually transmitted disease (STD), and 2·4 million adults (aged 20–30 years) in the general community. The following HIV seroprevalence rates were applied: 45% among prostitutes, 15% among individuals with STDs, and 1·8% in the general community.[2] The general community seroprevalence was taken as that obtained for pregnant women (mainly 20–30 years old) during sentinel surveillance carried out at three sites in Mumbai. We are aware that HIV rates in antenatal populations are generally lower than those among general communities. Use of antenatal seroprevalence rates is therefore likely to underestimate the number of infected adults in the general community. Thus, at least 85 200 people had HIV infection in Mumbai in 1997: 27 000 prostitutes, 15 000 individuals with STDs and 43 200 young adults belonging to the general community.

Year	Number of deaths (number per 100 000 population)		
	Men*	Women*	Total
1987	16 031 (486·8)	7693 (315·9)	23 724 (414·2)
1988	16 567 (495·3)	7576 (303·5)	24 143 (414·3)
1989	16 948 (498·8)	7876 (307·8)	24 824 (416·8)
1990	17 630 (510·9)	7886 (301·0)	25 516 (420·0)
1991	19 397 (553·5)	8440 (313·8)	27 837 (449·4)
1992	20 574 (578·0)	8665 (314·2)	29 239 (462·0)
1993	19 672 (544·1)	8569 (303·1)	28 241 (438·4)
1994	20 245 (551·3)	9005 (310·7)	29 250 (432·3)
1995	20 062 (537·9)	8911 (299·8)	28 973 (432·1)
1996	21 399 (564·9)	8668 (284·5)	30 067 (439·9)
1997	21 800 (566·7)	8968 (287·1)	30 773 (441·4)

* Aged 15–54 years.

Adult death rates adjusted for exponential population growth in Mumbai, India

Modelling of AIDS in high-risk populations is difficult, and epidemics in these groups usually follow patterns very different from those resulting from heterosexual spread (Peter Piot, UNAIDS, Geneva, Switzerland; personal communication). Hence, the growth-rate model is better



Adult mortality per 100 000 population

suited for estimating AIDS mortality than the epidemic model. The annual rate of death among HIV-infected individuals is reported to be 7·3%, and that of clinical tuberculosis to be 8·0% in a prevalent cohort in a natural history study in Mumbai (unpublished data). Thus, an annual mortality rate of 7·3% in the estimated 85 200 HIV-seropositive individuals would predict at least 6220 AIDS-related deaths in 1997.

In a study between October and December, 1998, by the AIDS Research and Control Centre and the Public Health Department of the Mumbai Municipal Corporation, deaths were analysed for the period 1987–97 by age, sex, and cause (table). From census data for 1981 and 1991, the exponential population growth rate was calculated and used to estimate the increase in the adult population each year during 1987–97. The death rate per 100 000 population for 1987, adjusted for annual exponential population growth, was used in the estimation of deaths in subsequent years. Assuming that life expectancy in Mumbai did not change during that decade, the observed number of deaths was substantially greater than the expected number of deaths, starting from 1990. The absolute number of excess deaths in 1997 was 4120 after adjustment for population growth since 1987. These excess deaths accord with the estimated 6220 deaths since many terminally ill people with AIDS return to their villages, where deaths are not recorded in the Mumbai Municipal Corporation death registry. The increasing mortality over the years is significant (χ^2 for trend, $p<0·05$). There were increases in death rates among men aged 25–44 years from 1990 (figure), perhaps representing a disproportionate number of men who had high-risk behaviour and who acquired HIV infection during the initial phase of the epidemic in the late 1980s.

Analysis of causes of death among men and women aged 25–44 years showed that the excess deaths were largely due to tuberculosis and other causes (which include AIDS). Overall, the rates of tuberculosis-related death increased by 70–140% in this population during the 11-year period (data available from investigators). Since tuberculosis is the most common opportunistic infection in AIDS patients in less developed countries,[3-5] a substantial proportion of deaths listed as due to tuberculosis could, in fact, be AIDS associated.

These mortality data confirm that the AIDS epidemic is not only visible, but may be cancelling out the decade-long gains of the health sector in Mumbai.

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Intoxication due to negative canrenone interference in digoxin drug monitoring

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Canrenone and spironolactone caused falsely low readings in a common assay for digoxin (AxSym MEIA) due to negative cross-reactivity. Misleading subtarget concentrations were repeatedly reported, and falsely guided drug dosing resulted in a case of digoxin intoxication.

A 71-year-old man (height 1·80 m, weight 70 kg) with a collum femoris fracture received a total prosthetic replacement which was later removed because of infection and septicaemia. The case was complicated by left-ventricular hypertrophy, liver cirrhosis, and compensated renal failure (serum creatinine 186–292 μmol/L). Intravenous digoxin therapy was started (target concentration 1·5–2·0 μg/L) when a second event of cardiopulmonary decompensation occurred after atrial fibrillation and tachycardia. Heart rate returned to normal, but atrial fibrillation and ventricular extrasystoles were noticed on days 4 and 6. No other potential adverse effects were observed in the non-responsive and ventilated patient. Trough serum concentrations of digoxin measured daily were below target. Dosing was therefore continued once daily, and amounted to 3·8 mg over 11 days. Owing to mechanical failure of our routine monitoring instrument, digoxin was measured on day 10 by two other methods, which gave toxic concentrations of 6·7 μg/L (TDx FPIA, Abbott, Chicago, IL, USA) and 5·7 μg/L (aca, Dade Behring, Marburg, Germany) compared with 0·9 μg/L by our routine assay (AxSym MEIA II, Abbott; figure 1). Digoxin was discontinued after confirmation of the discrepant results the next day. The patient died 4 days later. According to necropsy findings, the cause was multiorgan failure due to septicaemia.

Digoxin-like immunoreactive factor is detectable in serum and plasma during renal and hepatic failure.[1] It can result in falsely high digoxin readings when measured by assays such as the TDx.[2] This factor was therefore suspected of causing the toxic results. However, ultrafiltration, which removes digoxin-like immunoreactive factor, did not decrease the interference significantly. Dilution led to higher results in the MEIA II assay (up to 4 μg/L), which suggested that concentrations in

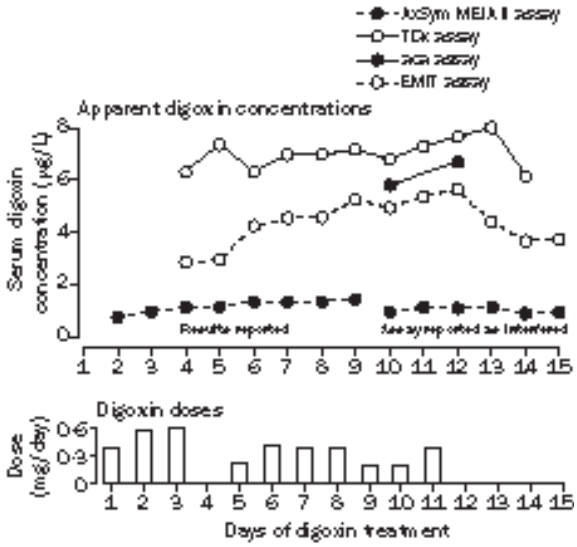

Figure 1: **Dosing of digoxin, and its concentration in serum as measured by four different assays**