in jail when my beloved father died and I was not allowed to attend his funeral. My son was born when I was in jail and I was never allowed to touch him until my release when he was nearly 2 years old. I was banned and even the University of the Witwatersrand would not give me a job at Alexandra Clinic in 1966. The Minister of Justice (*sic*!) denied me the right to study for my Diploma in Public Health at Wits — and even just to go to the library to read journals! I finally left for Edinburgh on an exit permit in 1968, painfully leaving my stepson behind to go to boarding school.

Who can make up for these things? Hundreds of thousands of such things occurred to tens of thousands of people. Millions experienced daily humiliations. Will we ever hear about them? The answer has to be 'no'. And the expressions of regret from the innocent beneficiaries of apartheid are very faint, even in the humane medical profession.

Real transformation remains on the horizon. Doctors can contribute to the process by regarding themselves as Africans and giving their loyalty to Africa, rather than to their pockets. This is the spirit that will create the much-vaunted 'rainbow nation' that does not yet exist.

Costa Gazi
PAC Secretary for Health

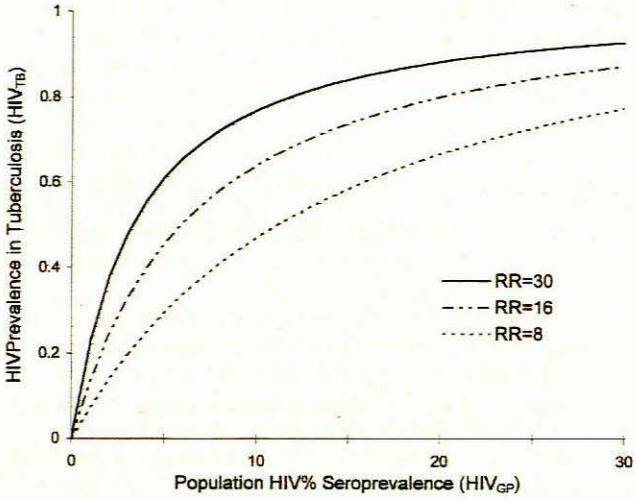
PO Box 12835
Amalinda
5252

HIV-related tuberculosis

To the Editor: Wilkinson and Davies recently described the changing epidemiology and clinical features of tuberculosis in a rural KwaZulu-Natal hospital and related this to a rapid increase in HIV seroprevalence in antenatal clinics in the region.[1] We have also noted an increase in tuberculosis cases at Somerset Hospital, Cape Town, where 21% of admissions of black patients to the general medical wards are now for tuberculosis. Atypical clinical and radiological presentations have also become more common.[2,3]

Some comment is needed on the authors' estimate of the proportion of tuberculosis cases attributable to HIV infection. The authors estimated the attributable fraction (AF) of tuberculosis due to HIV infection using the relative risk (RR) of HIV infection in patients with tuberculosis compared with antenatal women. Ideally, the RR used in the calculation of AF should have been the ratio of incidence of tuberculosis in a cohort with or without HIV infection. Given the difficulty in obtaining such data, the RR for tuberculosis in HIV infection can be derived from the relationship beween HIV_{TB}, the proportion of HIV infection in tuberculosis, and HIV_{GP}, the general population's HIV seroprevalence. Using this relationship (Fig. 1) and assuming that HIV prevalence in antenatal clinics (HIV_{AN}) is equivalent to HIV_{GP}, the calculated RR for tuberculosis in the HIV-positive population in KwaZulu-Natal is 8.5, somewhat higher than the quoted 4.14.

Although it is generally assumed that the RR for tuberculosis in HIV-positive people is constant in different settings, this is unlikely, firstly because of the variation of risk of reactivation with immune status of the individual and



In a defined population, the proportion of tuberculosis cases that are HIV-positive (HIV_{TB}) is given by the ratio of cases of HIV-positive tuberculosis to the total number of cases. (Where HIV_{TB} is the proportion of HIV infection in tuberculosis cases, TB is the tuberculosis incidence rate and HIV_{GP} is the HIV seroprevalence in the general population.

$$HIV_{TB} = \frac{(HIV_{GP} \times TB \times RR)}{(HIV_{GP} \times TB \times RR) + (TB \times (1-HIV_{GP}).}$$

HIV_{TB} is therefore independent of tuberculosis incidence rate (TB) and is a function of HIV_{GP} and RR.

$$HIV_{TB} = \frac{(HIV_{GP} \times RR)}{1+HIV_{GP}\ (RR-1).)}$$

Fig. 1. Plots of HIV prevalence in tuberculosis versus general population HIV seroprevalence are shown for three groups at differing RRs for the development of active tuberculosis — Hlabisa patients with an RR of 8, Cape Town patients with an RR of 16 and AIDS patients exposed during a tuberculosis outbreak with an RR of 30.

hence the stage of the epidemic in the population and, secondly, because of the varying risk of transmission of tuberculosis from and to HIV-infected adults, depending on behavioural and socio-economic factors. At Somerset Hospital, a new diagnosis of HIV infection was made in 45% (CI 32 - 58%) of black women admitted with tuberculosis in 1995 - 1996. During this period, the antenatal HIV prevalence for this population group was 4.7% (CI 2.5 - 6.9%). Fig. 1 shows a plot of HIV_{TB} versus HIV_{GP} for KwaZulu-Natal with an RR of 8, for Cape Town where the RR obtained using the formula is 16 and for AIDS patients with an RR of 30, calculated during a tuberculosis outbreak.[4] The Cape Town analysis was limited to black females between the ages of 14 and 49 years with a new diagnosis of tuberculosis, for whom the HIV_{AN} should best approximate the HIV_{GP}. Patients with prior known HIV-positive status were excluded from the analysis to avoid referral bias from local HIV clinics. It should be noted that all curves show an initial steep slope which moderates with increasing seroprevalence. This non-linear relationship illustrates why tuberculosis patients act as a sentinel group for HIV early in the epidemic, all the more so if the RR for tuberculosis in HIV-positive patients is high. The initial steepness of the curves, however, should caution us that inaccuracies in HIV_{GP} will be reflected as large changes in RR calculated with the formula, especially when HIV_{GP} is < 20%. Calculation of attributable risk further amplifies any inaccuracies in the measured RR inherent in this type of analysis.

Both the tuberculosis incidence rate and the RR associated with HIV infection in KwaZulu-Natal are similar to other reports from Africa.[5] In contrast the high RR of the Cape Town urban black population may indicate a significant amount of horizontal transmission. Combined with a background tuberculosis incidence rate that is already the highest in Africa, we can expect an increase in HIV-related tuberculosis in Cape Town that is unprecedented in the global HIV epidemic to date.

Finally, we would like to emphasise the point made by Wilkinson and Davies, that national notifications have not increased in recent years.[6] The lack of culture facilities in most areas of South Africa, the high rate of smear-negative cases and the atypical presentation in advanced HIV infection are probable causes of underreporting. However, it must also be questioned whether the widespread underreporting is a manifestation of the crisis of morale and manpower in our health care system. Studies such as that of Wilkinson and Davies complement routine notification, but should not be a substitute for it. Population attributable fraction and RR may be considered abstruse, but accurate measurement of these parameters is important for projection of the impact of the HIV/tuberculosis epidemic in South Africa.

Robin Wood
Chris Hudson

Department of Medicine
Somerset Hospital
Green Point
Cape Town

1. Wilkinson D, Davies GR. The increasing burden of tuberculosis in rural South Africa — impact of the HIV epidemic. *S Afr Med J* 1996; **87:** 447-450.
2. Wood R, O'Keefe EA, Maartens G. The changing pattern of transmission and clinical presentation of HIV infection in the Western Cape region of South Africa. *S Afr J Epidemiol Infect* 1996; **11:** 96-98.
3. Post FA, Wood R, Pillay GP. Chest radiographic appearance of pulmonary tuberculosis relates to the degree of HIV immunosuppression. *Tuberc Lung Dis* 1995; **76:** 518-521.
4. Tuberculosis outbreak among persons in a residential facility for HIV-infected persons — San Francisco. *MMWR* 1991; **40:** 649-652.
5. Bermejo A, Veeken H, Berra A. Tuberculosis incidence in developing countries with high prevalence of HIV infection. *AIDS* 1992; **6:** 1203-1206.
6. Report of the review of the tuberculosis control programme of South Africa. *Epidemiological Comments* 1996; **23:** 2-19.

To the Editor: I read with great interest the paper by Wilkinson and Davies[1] describing the increasing burden of HIV-related tuberculosis. The importance of their message is beyond any doubt. I would like to add two points. Firstly, the authors seem to be unaware of my previous report,[2] which, as far as I am aware, is the first study on the impact of the HIV epidemic on tuberculosis in rural South Africa. Of much more importance, however, is the fact that both surveys[1,2] point in the same direction.

Directly observed therapy (DOT) was started at Emmaus Hospital, Bergville District, KwaZulu-Natal, in 1987.[3] A survey from 1987 through 31 July 1995, showed a 3.7-fold caseload increase, i.e. in excess of Hlabisa's. Smear positivity rate was much higher — 91% without known or suspected HIV and 64% with HIV. The HIV status was tested in consenting patients in whom, on a clinical basis, there was a suspicion of their being immunodepressed. They represented 11.2% of all tuberculosis patients enrolled for DOT between 1 August 1994 and 31 July 1995. The proportion of HIV seropositivity was 71.4%, i.e. in excess of 55% at Hlabisa in 1995. The overall mortality rate increased over the years from 3% in 1987 to 11% during the last year of the survey. The overall tuberculosis reactivation rate was 13.7%; the estimated prevalence of drug resistance was 6%. (No figures concerning same are reported from Hlabisa.) The RR of HIV infection with tuberculosis was 5.1; the attributable fraction where tuberculosis was attributable to HIV was 0.80. At Hlabisa the latter two values were 4.14 and 0.76, respectively.

In conclusion, the similarities between both reports are striking, and confirm the magnitude of the problem of HIV-related tuberculosis in rural South Africa. I also agree with the authors that DOT is the most cost-effective management of tuberculosis.

L-J van Bogaert

University of Transkei
Umtata, E Cape

1. Wilkinson D, Davies GR. The increasing burden of tuberculosis in rural South Africa — impact of the HIV epidemic. *S Afr Med J* 1997; **87:** 447-450.
2. Van Bogaert LJ. Treatment of tuberculosis in developing countries. *Lancet* 1995; **346:** 1099-1100.
3. Westaway MS, Conradie PW, Remmers L. Supervised out-patient treatment for tuberculosis: evaluation of a South African treatment programme. *Tubercle* 1991; **72:** 140-145.

Dr Wilkinson replies: We are grateful for the interest in our work shown by your correspondents. We did not quote Van Bogaert's work as the results are probably biased and should be interpreted cautiously. If HIV testing is limited to patients in whom immunosuppression is suspected, reported HIV seroprevalence will most probably be high. Indeed only 11.2% of patients seem to have been tested: it is therefore not possible to draw conclusions about the HIV status of other patients, and further analysis should be undertaken cautiously. We have previously reported the data requested.[1]

The formulas used by Wood and Hudson are not referenced and we are not sure that all their assumptions hold. However, we did state in our paper that our estimate of the population attributable risk percentage was probably conservative and we gave reasons and justification for this. We need to be cautious about drawing broad assumptions from referral settings, as it is very difficult to be sure what the source population really is and how unbiased patient selection is. It is not clear what criteria are used for admitting patients with suspected tuberculosis to Somerset Hospital. It is also not clear if there are substantial differences in tuberculosis transmission rates between Cape Town and KwaZulu-Natal. In a large community-based study of the molecular epidemiology of tuberculosis transmission[2] we showed that approximately 45% of new cases of smear-positive tuberculosis were probably recently transmitted, which is a higher proportion than that shown by Warren *et al*. in Cape Town.[3] We await with interest unbiased, population-based data from Cape Town that document accurately the extent of the impact of HIV infection on tuberculosis.

1. Wilkinson D, Pillay M, Davies GR, Sturm AW. Resistance to antituberculosis drugs in rural South Africa: rates, patterns, risks, and transmission dynamics. *Trans R Soc Trop Med Hyg* 1996; **90:** 692-695.
2. Wilkinson D, Pillay M, Lombard C, Davies GR, Sturm AW. Molecular epidemiology and transmission dynamics of *Mycobacterium tuberculosis* in rural Africa: results from a large, population-based study. *Trop Med Int Health* 1997 (in press).
3. Warren R, Hauman J, Beyers N, *et al*. Unexpectedly high strain diversity of *Mycobacterium tuberculosis* in a high-incidence community. *S Afr Med J* 1996; **86:** 45-49.