

predictive value of screening tests in a representative ante-natal population over time. As would be expected, there is an inverse relationship between the false positivity rate and the positive predictive value of the test. This is largely a function of the prevalence of infection and occurs against the background of steady improvement in the performance of the serological tests. The accuracy of screening serology is currently close to optimal. However, a test result — in terms of being reactive or non-reactive — must constantly be interpreted (as positive or negative) against an estimate of the pre-test probability of infection, as is reflected in the prevalence of HIV in the population from which the individual being tested derives.

Concluding remarks

When the validity of antibody test results is challenged, as should happen from time to time, it is important that this be done with scientific insight and in relation to defined criteria. The choice of the diagnostic test is strongly influenced by the test parameters (sensitivity and specificity), but the interpretation of results is determined by the prevalence of the infection in the population under study.

Cognisance must be taken of the prevalence within the population being tested (the HIV populations in South Africa consist of clusters of differing prevalence¹²), the characteristics of the testing strategy employed, and of the properties of the individual tests themselves.

1. Martin D.J. and Sim J.G.M. (2000). The laboratory diagnosis of HIV infection. *S. Afr. med. J.* 90, 105–109.
2. Anon. (1992). Recommendations for the selection and use of HIV antibody tests. *Wkly Epidemiol. Rec.* 20, 145–149.
3. Department of Health (2000). *Summary Report. National HIV Seroprevalence of Women Attending Antenatal Clinics in South Africa, 1999*. Pretoria.
4. De Cock K.M., Porter A., Kouadio J. et al. (1990). Rapid and specific diagnosis of HIV-1 and HIV-2 infections: an evaluation of testing strategies. *AIDS* 4, 875–878.
5. Celum C.L., Coombs R.W., Lafferty W. et al. (1991). Indeterminate human immunodeficiency virus Type 1 Western blots: seroconversion risk, specificity of supplemental tests, and an algorithm for evaluation. *J. infect. Dis.* 164, 656–664.
6. Behets E., Disasi A., Ryder R.W. et al. (1991). Comparison of five commercial enzyme-linked immunosorbent assays and Western immunoblotting for human immunodeficiency virus antibody detection in serum samples from central Africa. *J. clin. Microbiol.* 29, 2280–2284.
7. Gwinn M., Redus M.A., Granade T.C. et al. (1992). HIV-1 serologic test results for one million newborn dried-blood specimens: assay performance and implications for screening. *J. Acq. Immun. Def. Syndr.* 5, 505–512.
8. Engelbrecht S., de Jager G.J., van Rensburg E.J.

- (1994). Evaluation of commercially available assays for antibodies to HIV-1 in serum obtained from South African patients infected with HIV-1 subtypes B, C, and D. *J. med. Virol.* 44, 223–228.
9. Farzadegan H. (1994). HIV-1 antibodies and serology. *Clin. Lab. Med.* 14, 257–269.
10. McAlpine L., Gandhi J., Parry J.V. and Mortimer P.P. (1994). Thirteen current anti-HIV-1/HIV-2 enzyme immunoassays: how accurate are they?

J. med. Virol. 42, 115–118.

11. Weber B., Moshaghi-Boronjeni M., Brunner M. et al. (1995). Evaluation of the reliability of 6 current anti-HIV-1/HIV-2 enzyme immunoassays. *J. virol. Methods* 55, 97–104.
12. Williams B.G., Gouws E., Colvin M., Sitas F., Ramjee G. and Abdool Karim S.S. (2000). Patterns of infection: using age prevalence data to understand the epidemic of HIV in South Africa. *S. Afr. J. Sci.* 96, 305–312.

Science and HIV/AIDS in South Africa: A review of the literature

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IN ORDER TO ASSESS THE STATE OF scientific knowledge on HIV/AIDS in South Africa, a MEDLINE search was done on HIV- and AIDS-related papers through the National Library of Medicine at the National Institutes of Health in the United States, using HIV, AIDS and South Africa as key words. A total of 466 scientific articles (including editorials and reviews) on HIV/AIDS in South Africa has been published in peer-reviewed journals over the last 17 years. The number published annually has increased rapidly since 1995 (Fig. 1), with 88 appearing in 1999. During the first three months of 2000, 22 papers were published.

1983 to 1989

The first scientific paper concerned with HIV/AIDS in South Africa appeared in 1983: a documented report of the first two cases of the acquired immunodeficiency syndrome in male homosexuals identified in South Africa. During the next six years (1984–1989), 46 papers were published on HIV and AIDS in this country. There were several reports describing HTLV-III, HIV, AIDS and AIDS-related conditions in particular risk groups. One hundred and sixty-six cases of AIDS had been seen in South Africa between 1982 and 1988, with a mortality rate of 59%. Of interest was the absence of HIV infection in sex workers, women attending sexually transmitted disease clinics and drug abusers in 1987. Several studies considering the epidemiology of present status and future growth of the AIDS epidemic

were published and one paper reported on the origin of viruses in Africa. Ijsselmuiden *et al.*, in a three-part series published in the *South African Medical Journal* in 1988, emphasized the urgent need for, and proposed steps towards, a comprehensive strategy for the control of HIV infection. In 1988 the first papers appeared on medico-legal issues in caring for people with HIV infection, the impact of AIDS on society, and AIDS education. By the end of 1989, a number of surveillance studies had been presented and confirmed the entry of HIV infection into the heterosexual population in South Africa. While visits by male homosexual patients to HIV clinics reached a plateau in 1989, visits from heterosexual patients started to increase. Although prevalence of HIV was still low in the general population (probably below 0.5%), an alarming increase in the number of AIDS cases in particular risk categories was predicted. In the absence of a vaccine and treatment, an urgent call was made for safer sex practices through education.

1990 to 1994

Of great concern in the early 1990s was

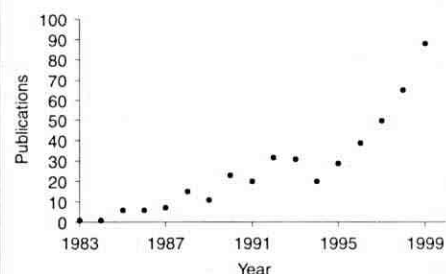


Fig. 1. The annual number of scientific publications, in peer-reviewed journals since 1983, concerned primarily with HIV/AIDS in South Africa.

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the extensive and continuing spread of HIV in urban heterosexual populations, manifested by doubling times of about 8.5 months. HIV data suggested a spread of infection that was far more extensive than the still low numbers of reported AIDS cases. Of an estimated total of 122 951 HIV-infected individuals in South Africa in 1991, 69% were from urban populations, 20% from rural populations and 7% from homosexual men. Data from the National HIV Surveillance Programme showed an increase in the point prevalence of HIV among antenatal clinic attendees from 0.76% in 1990 to 7.6% in 1994 but with wide geographical variation.

Of 125 HIV/AIDS-related papers published during this period, 16% were concerned with social and behavioural research. Most of these dealt with knowledge, beliefs and practices amongst people in particular risk categories, for example, youth, health care workers, sexually transmitted diseases (STD) and family planning clinic attendees. Condom use practices and risk-taking behaviour were reported on in several of these articles. One study was published on the marketing of condoms and microbicides. Nine dealt with ethical issues, such as informed consent and confidentiality, and in two papers the question as to whether or not AIDS should be made a notifiable disease was debated. Seven articles appeared on statistical analysis and modelling of the epidemic. Current, short-term and medium-term predictions of the prevalence of HIV infection were presented. Although the forecasts were tentative, they indicated the seriousness of the HIV epidemic. Using a macro-simulation model, Schall predicted in 1990 that the AIDS epidemic could reach prevalences of 30% in the sexually active population by 2000 to 2005, which is close to the current prevalence amongst women attending ante-natal clinics. Other areas that were well researched at this time include: AIDS-related conditions (12, including Kaposi's sarcoma)*; surveillance and epidemiological studies (12); paediatric AIDS and HIV in children (8); transmission of HIV, mainly through blood transfusion and vertical transmission (6); sexually transmitted diseases and their association with HIV (6); and HIV and dental/oral research (5). The relationship between tuberculosis and HIV was also addressed (4), while several articles dealt with the diagnosis of HIV (4). AIDS education and the evaluation of education programmes was also discussed (5), and

papers appeared on prevention strategies, including infection control and adaptation of the so-called Health Belief Model (3). The association between HIV and dietary and nutritional status was discussed (2), as well as poverty and socio-economic determinants (3). Papers also appeared on migrant labour and HIV (1), traditional healers and ancient beliefs (3), and geographic progression of disease was shown by mapping the AIDS pandemic. With the exception of a study on the genetic analysis of HIV types 1 and 2 mixed infections in India, referring to sequences found in South Africa, very few papers were published on molecular biological or immunological aspects of the disease during this period. There was also a general lack of papers on disease management and care of HIV-infected patients.

1995 to 2000

The rising trend in HIV prevalence rates continued during this period and this was matched by an increase in scientific output (Fig. 1). The prevalence of HIV infection amongst women attending ante-natal clinics reached 23% in 1998, with the highest prevalence in KwaZulu-Natal (32%) and the lowest in the Western Cape (5.2%). On the basis of the ante-natal surveys and certain assumptions, it was estimated that 3.6 million South Africans were infected with the HI virus in 1998, up from an estimated 1.7 million in 1995. Of particular concern for public health is the high prevalence amongst young women, aged 15 to 25 years.

A total of 293 papers was published during this period. South Africa joined the global effort to develop an effective AIDS vaccine and there was a substantial increase (24) in the number of papers on genetic, immunological and molecular biological aspects. Studies were done to assess the correlation between HIV RNA levels, CD4 counts and the risk of progression to AIDS or death. With limited resources for diagnosis and management of the disease, absolute CD4 counts are used to monitor disease progression and institute prophylaxis against opportunistic infections. Genetic analyses were performed to determine HIV-1 subtypes in different risk groups in South Africa. Subtype B viruses were associated with homosexual transmission and subtype C with heterosexual transmission, suggesting two separate epidemics. Neutralization of HIV subtypes and the implications for vaccine formulations were discussed.

Compared to the previous period there was a decrease in the proportion of

papers on surveillance and epidemiology (14/293). Almost one quarter of all papers published during this period were concerned with tuberculosis (31) and other HIV/AIDS-related illnesses (38), including *Pneumocystis carinii* pneumonia, cancers, streptococcal diseases, meningitis and others. Nine papers were concerned with the association between sexually transmitted diseases and HIV; disease management and assessment of care for patients infected with HIV were also addressed (11). Social aspects were still well researched (21) and included assessment of knowledge, attitudes and sexual behaviour, children requiring social services, impact of HIV on quality of life and barriers to condom use. Thirteen papers dealt with ethics, informed consent, confidentiality and voluntary testing, and whether AIDS should be made a notifiable disease. Most of the papers on transmission of infection were concerned with determinants of mother-to-child transmission such as breastfeeding, antibody levels of the mother and mode of delivery (12/17). The others discussed transmission through anal sex, blood transfusions and exposure of health-care workers, such as forensic medical personnel, to blood and traumatized bodies. Diagnosis and testing received attention (13), including an evaluation of several antibody assays and rapid tests, dried blood spots and use of the polymerase chain reaction. Frequency of testing and diagnosis was also discussed. There was an increase in the number of papers dealing with prevention and public health interventions. Six papers were concerned with HIV in relation to sexual education and the evaluation of such programmes. Of the other papers on prevention (15), there were two on microbicide research, one on AIDS programmes at the workplace, on antiretroviral drugs for pregnant mothers and the cost-effectiveness of preventing mother-to-child transmission (5), on child-feeding practices and a plea for dried milk formula (2), and a paper on the universal precautions for prevention. A number of papers were concerned with paediatric HIV and AIDS (15), dealing mainly with morbidity and mortality in children infected with HIV. Papers were published on adult mortality (6), including a study on the survival differences between the two independent epidemics of heterosexual and homosexual infection in South Africa. Although there were no papers on direct treatment of HIV in South Africa, the treatment of sexually transmitted diseases, tuberculosis and HIV-related cancer continued to

*Figures in brackets indicate the number of papers.

receive attention (13). Papers were also published on nutrition (3), socio-demographic impact and demographic modelling (2), HIV and infertility (1), hormonal contraception and HIV (1), HIV amongst intravenous drug users (1), pharmacokinetics, in particular antiretroviral drug activity (1), whether South Africa should be preparing for vaccine trials and new prospects in vaccine research (2), geographical presentation of HIV heterogeneity and proximity to roads in a rural district in South Africa (1), and the origin of HIV (1). There was a general lack of papers on population dynamics and risk factors such as migrancy and circumcision, which may play an important role in transmission of HIV in South Africa. Only one paper on each of these topics appeared in the literature during this period.

Conclusion

A substantial literature exists covering many aspects of HIV/AIDS and related diseases in South Africa. These include social, behavioural, epidemiological, clinical and molecular studies. During the first period covered in this review, 1983 to 1989, the focus of the scientific research was on men who have sex with men and on AIDS. However, several papers discussed the likely impacts of the epidemic and warned of the threat posed by HIV/AIDS to South Africa.

During the period 1990 to 1994, it started to become clear that the heterosexual epidemic was rapidly exceeding the homosexual epidemic in scale and importance and the focus of attention changed in this direction. The number of papers dealing with social and behavioural aspects of the epidemic increased steadily and important studies were published on the epidemiology and likely future growth of the epidemic; predictions were made then, that have proved to be depressingly accurate.

The third period under consideration, 1995 to 2000, has seen an increase in research on all fronts but in particular there has been a dramatic increase in the number of papers dealing with the molecular biology of the virus, on aspects of vaccine research, and an increase in interest in AIDS-related diseases and in particular tuberculosis.

While the accumulated knowledge is substantial, there are still many areas in which little or no research has been done. Given the magnitude of the threat that HIV/AIDS poses, it may be useful to consider some of these in the hope that -

researchers will begin to investigate some of these areas.

It is important to develop effective, sustainable community-based interventions which will limit and, we hope, reduce the spread of infection. At the time of writing there seemed to be few large-scale attempts to manage the epidemic, although one such attempt is described in this issue (see page 351). Research is clearly urgently needed that focuses on the development and thorough evaluation of intervention programmes.

Relatively little attention has been given to the development of detailed demographic models that can be used to forecast the future course of the epidemic, to examine the likely impacts that different kinds of intervention might have (including vaccines, increased condom use, management of sexually transmitted diseases, behaviour change programmes, media campaigns and so on), and to provide a sound basis on which to plan the nation's response to the epidemic. We know, for example, that over the next 10 years or so we are likely to see a 20-year drop in life expectancy and an increase by a million or more in the number of orphans. What is less clear is how the socio-economic impact of the epidemic will vary geographically, how it will vary among people in different social classes, and what the effect will be on different industries.

While increasing attention and greater resources are being devoted to vaccine research, an important aspect of this is the preparation of communities amongst which vaccine trials can be conducted. It is often forgotten that before such trials can be conducted, several years have to be spent not only educating communities about vaccine research but also collecting baseline data that are essential for the effective planning and execution of such trials. While one such study is currently under way in Hlabisa, in rural KwaZulu-Natal, more are needed.

The levels of infection have reached quite extraordinary dimensions and it is becoming almost inevitable that ways will have to be found to make antiretroviral therapies widely available. Although the main problem of giving antiretrovirals is cost, issues such as medical supervision, compliance and drug resistance are also of great concern. There is an encouraging body of research on immune boosters and nutritional aspects of the disease and work in this direction should be considerably strengthened. It is clear that consid-

erably more attention has to be given to therapeutic options for the future.

Given that a vaccine is unlikely to be available for a long time and that therapeutic drugs are unlikely to be available to everyone, it is essential that research into the behavioural aspects of the epidemic be strengthened. It is now widely accepted that effective behaviour change involves changing peer and community norms of behaviour but little is known about how this can best be achieved; research into such areas, including gender violence, is urgently needed. It is now being suggested that voluntary counselling and testing would have a significant impact but there is no research on this issue in South Africa and anecdotal evidence suggests that revealing one's HIV status, even to those closest to you, can be dangerous.

While prevention of vertical transmission has received considerable attention, no work has been done on post-exposure prophylaxis for rape victims. Given the high incidence of rape in South Africa, this too needs urgent attention.

While there is an increasing body of evidence to show that male circumcision is protective, no work has been done in this area, either to investigate the magnitude of the effect or to consider the social implications of such practices.

Finally, and most surprising, there has been an almost complete lack of scientific work on the relation between migrancy and HIV apart from one study in Hlabisa. It can be argued that one of the most important driving forces of the epidemic in southern Africa is the century-old system of oscillating migration, which both serves to put people at risk of infection and, when they become infected, to spread the epidemic widely and rapidly.

While the scientific community has responded to the challenges of HIV/AIDS in South Africa with an impressive body of scientific literature, much still has to be done. Probably the greatest need is to develop a strong, well-directed and well-funded programme of research that brings together social, clinical, biomedical and molecular scientists as well as policy makers and planners to provide the support that will be needed if we are to deal with the epidemic effectively and save what we can from an otherwise disastrous situation.

A bibliography of the references used to write this review can be accessed on the *South African Journal of Science* web site: www.nrf.ac.za

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