Work at the Africa Centre has influenced the WHO's infant feeding guidelines

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A tale of two centres

Two institutes on opposite sides of South Africa are intent on tackling HIV. But they are separated by more than geographical distance, finds Michael Cherry.

Sandwiched between the green Hluhluwe-Umfolozi game reserve and the national motorway running north from Durban is a 435-square-kilometre dustbowl called Umkhanyakude. In the apartheid era it was designated a part of the Zulu homeland, and today each of the small plots is scattered with thatched huts and is home to a family.

Umkhanyakude has one of the highest levels of HIV prevalence in South Africa, peaking at 51% for women aged 25–29, compared with about 30% for pregnant women nationally[1]. These data were collected by researchers at the Africa Centre for Health and Population Studies, a ten-year-old institute housed in an incongruously modern building in the centre of this impoverished region.

"The Africa Centre presents a huge opportunity to do meaningful research in an HIV-stricken area." — Marie-Louise Newell

At the southwestern tip of the African continent, 2,000 kilometres away, lies fair-weathered and affluent Cape Town — another city suffering from the HIV epidemic but home to a rather different research centre. In Cape Town, HIV has spawned a higher incidence of tuberculosis (TB) than in any other city in the world. This disease is the subject of study by researchers at the five-year-old Institute of Infectious Disease and Molecular Medicine (IIDMM), part of the University of Cape Town. Last year, a team there sequenced DNA from the preserved organs of TB victims and showed that the prevalence of a particularly virulent strain originating from southeast Asia has exploded since 1996. This strain is now causing 20% of TB deaths, perhaps because it acquires drug resistance particularly quickly.

Both the Africa Centre and the IIDMM are at the heart of South Africa's battle against HIV and both have received significant funding from Britain's Wellcome Trust medical charity. "Clearly there is some overlap between the two institutions," says Jimmy Whitworth, head of international programmes at Wellcome. But the two also have their differences: the Africa Centre focuses on understanding the health of the local population and the best interventions to help this community, whereas researchers at the IIDMM are interested in understanding HIV on a molecular level and turning that knowledge into clinical practice. And despite the institutes' overlapping remits and the scale of the HIV crisis in South Africa, there is very little collaboration between them.

No one is prepared to say that this remote relationship is holding back research into the country's HIV epidemic. But it is "a cause for regret", says Robert Wilkinson, a senior fellow at the IIDMM who led the TB study, and it is an issue that he and others want to address.

"I don't think that the lack of collaboration is intentional," says IIDMM director Greg Hussey. "The reality is that we tend to collaborate with overseas researchers because, with a few exceptions, they provide our funding."

The Africa Centre was founded by the Wellcome Trust in 1997 and is now part of the University of KwaZulu-Natal (UKZN). About 80% of the institute's running costs — currently US$5 million — are covered by a grant from the trust. The centre faces a difficult balance between the demands of funders — who want high-quality publications in order to justify their support — and the needs and expectations of the poor rural community in which it is based.

Location, location, location

The Africa Centre's location has proved a major barrier to recruiting and retaining senior staff, particularly skilled South Africans who tend to be more interested in working in cities or abroad. Another problem in this regard is that the centre offers no security of tenure; like other Wellcome-funded institutes, all of the staff are on three- to five-year contracts — centre director Marie-Louise Newell is herself on a five-year secondment from University College London in the United Kingdom.

The IIDMM, by contrast, has proved to be a magnet for drawing South Africans abroad back to the country and for attracting foreign talent. The institute was established in 2002 as a virtual entity comprising researchers from departments in the University of Cape Town's science and medical faculties. Two years ago, a new building was completed to house the institute. Its annual budget is approaching US$20

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Clinical practice: the IIDMM is trialing a vaccine against South Africa's dominant HIV subtype.

million, about 40% of which is funded by the university and the rest of which comes from research agencies. The Wellcome Trust has so far supplied more than US$12 million, mostly by funding senior fellowships. Although these are for only five years, the university has agreed to convert them into tenured appointments at their termination, subject to the fellowship recipients' good performance. The combination of the IIDMM's location, its secure and generous funding, world-class facilities and access to HIV patients all serve to attract good researchers.

The institute's mission is to translate molecular laboratory research into the clinic and it is having some of its greatest impact in African initiatives to develop vaccines against TB and HIV. Virologist Carolyn Williamson, now a principal investigator at the IIDMM, was central to the initial elucidation of the virus's diversity in South Africa. In 1999, her group showed that the country's epidemic is dominated by a strain of HIV known as subtype C, whereas in the developed world subtype B is dominant[2]. This suggested that vaccines developed against foreign strains might not work well in South Africa.

The big picture

One of the Africa Centre's main achievements, meanwhile, are its HIV surveillance data. These represent one of the few precise estimates of HIV prevalence in South Africa, because they are collected by visiting and testing everyone in a household rather than, more typically, by testing pregnant women who attend antenatal clinics. In one study, the researchers compared their surveillance figures with those from an antenatal survey in the same region and confirmed that HIV prevalence was similar across the data sets in almost all age groups. But according to the surveillance figures, women aged 15–19 had an HIV prevalence that was only half that suggested by the antenatal survey. This disparity has been attributed to the fact that some of the cohort are not yet sexually active[3].

Another widely acclaimed accomplishment of the centre is a study on HIV transmission during breast-feeding. Previous studies estimated that breast-feeding is associated with a 10–20% probability of HIV transmission, so the World Health Organization (WHO) formerly recommended feeding infants with formula milk as a first choice, where it was safe to do so. But as in much of Africa, most women in Umkhanyakude lack access to clean water and cannot safely avoid breast-feeding, although many supplement it with formula or solid food. Previous studies had not distinguished between transmission risks from exclusive breast-feeding and this type of mixed feeding.

The centre's study showed that, in this rural setting, exclusive breast-feeding is a much better strategy. Babies who received breast milk and formula were nearly twice as likely to acquire HIV — and when mixed with solids, the risk was almost 11 times higher[4]. One reason for this is that infant formula and solid food can cause microscopic damage to cells lining a baby's immature gut, helping HIV to enter the body, says author Nigel Rollins of UKZN. The study helped prompt the WHO to refine its infant feeding guidelines earlier this year, so that exclusive breast-feeding is the default option where feeding with infant formula alone is not possible or safe.

"It might well be possible to develop concrete plans for collaboration." — Robert Wilkinson

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While the Africa Centre has focused on means of HIV transmission in the local community, Williamson's group at the IIDMM set to work developing vaccines against the dominant subtype C. The team surveyed HIV from newly infected patients and selected genes that best represented South African subtype-C strains[5]. The idea is that individuals immunized with vaccines containing genes from dominant local viruses are more likely to recognize and launch an immune response when infected by one of them. The IIDMM is now carrying out one arm of a clinical trial in Cape Town of an HIV vaccine that includes these genes, funded by the International AIDS Vaccine Initiative. The results of this trial should be available by the end of the year.

Building on this work, the HIV vaccine-development group at the institute, headed by Anna-Lise Williamson, recently developed two new, refined vaccines incorporating additional subtype-C genes and modifications to make them more potent[6]. These will go into clinical trials next year — the first HIV vaccines developed in Africa to enter trials.

Dual aspect

The Africa Centre presents a huge opportunity to do meaningful research in an HIV-stricken area, says Newell, and some researchers are hopeful that the relationship between the two institutes could yet blossom. Populations studied by the Africa Centre could prove an ideal testing ground for interventions developed at the IIDMM. "An obvious area of collaboration is the clinical testing at the Africa Centre of candidate vaccines that were developed at the IIDMM," says Lynn Morris of the National Institute for Communicable Diseases in Johannesburg. And, says Wilkinson, "it might well be possible to develop concrete plans for collaboration in the future."

As yet, there are no firm plans for such a partnership. But perhaps in time the 2,000 kilometres between Umkhanyakude and Cape Town will be bridged. ■

Michael Cherry is *Nature*'s contributing correspondent in South Africa.

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