The low-down on HIV/Aids worldwide

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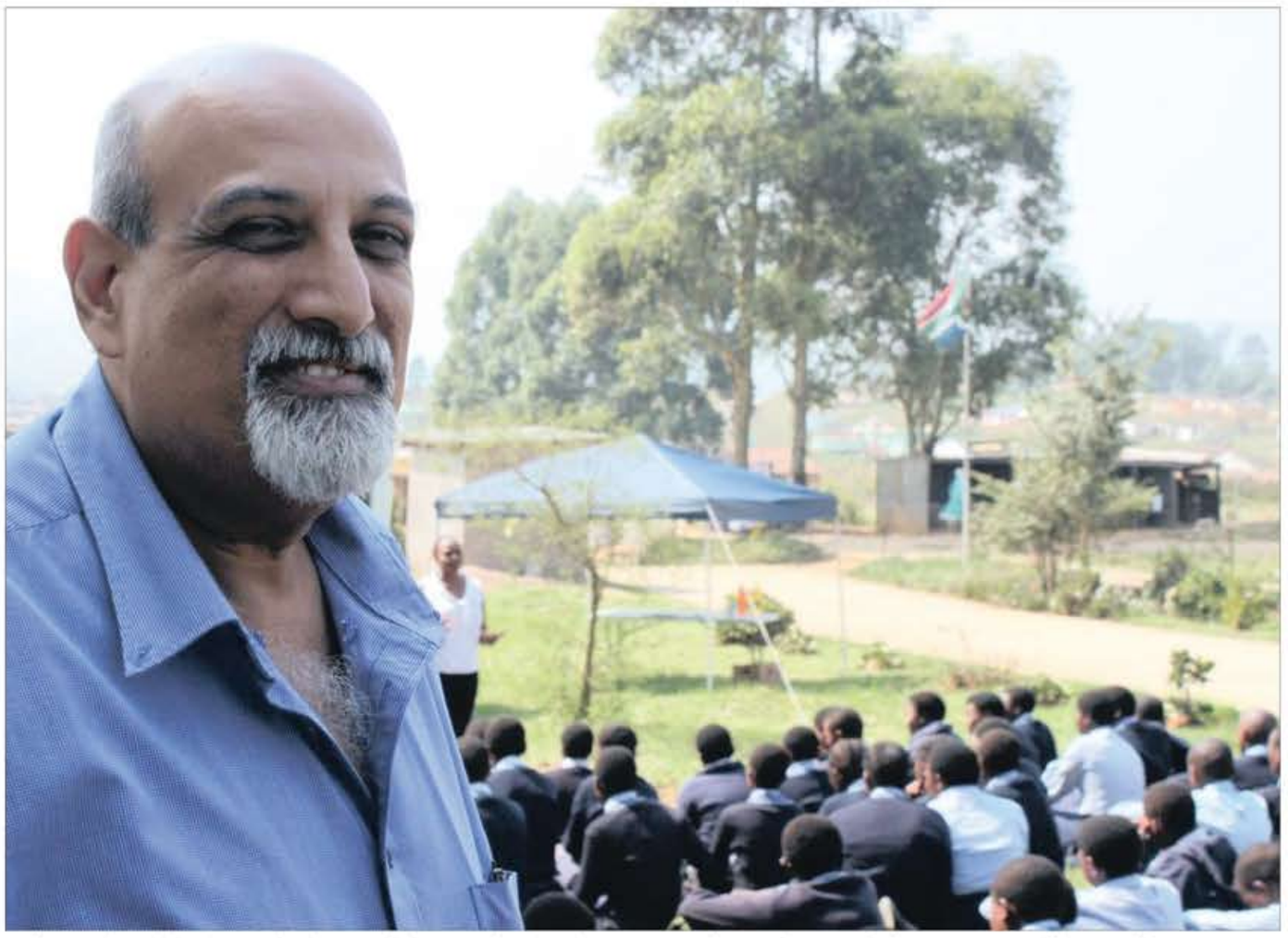
Professor Salim Abdool Karim, the director of the Centre for the Aids Programme of Research in SA, unpacked some jargon about the virus with ***Kamcilla Pillay*** *before next month's International Aids Conference in Durban*



Professor Salim Abdool Karim, the director of the Centre for the Aids Programme of Research in South Africa (Caprisa), will be one of the experts at next month's International Aids conference.

Q: What is the significance of July's conference?

A: The Aids 2016 conference is an opportunity to take a cold and hard look at what it is really going to take to bring about the "end of Aids as a public health threat" – the UNAids 2030 vision.

The conference will be the perfect stage to generate new ideas on how to reach this noble goal – it will be an opportunity to create, once again, a common purpose focused on achieving this important goal. It is no easy goal.

Q: What do you think is its importance for the man in the street? What is his takeaway?

A: A combination of scientific discoveries and the political will to make treatment and prevention options available will allow people to lead healthy lives.

Q: Could you take me through the history of the origins and history of HIV.

A: Acquired immunodeficiency syndrome (Aids) is the world's most devastating epidemic in the history of humankind.

Since the first reported cases of Aids in 1981, more than 70 million people have been infected with the human immunodeficiency virus (HIV). HIV is a retrovirus that causes Aids and is spread from mother to child, through blood contamination and through sex. When spread, HIV specifically enters, infects and grows in the human body's cells that have a CD4 receptor. After HIV multiplies in a CD4+ cell, the cell dies – releasing hundreds of new HIV into the body.

This process leads to the systematic destruction and loss of CD4+ cells over a period of years. During this period, which is on average about seven years, the person is asymptomatic with HIV infection, but is infectious, thereby creating the conditions for the efficient spread of this virus. After a period ranging from a year to many years, the CD4+ cell numbers drop to low levels and the person is then unable to develop a proper immune response, that is immune deficiency.

This immunodeficiency state makes the person susceptible to various opportunistic infections and malignancies, which signal the onset of Aids.

In an attempt to discover the origin of HIV, samples have been collected from a number of primate species. Comparisons between different HIV and simian immunodeficiency virus

(SIV) gene sequences indicate that HIV was transmitted to humans from African green monkeys, chimpanzees and sootey mangabeys in central and west Africa.

It has been estimated that this interspecies transmission event occurred at some time around the 1900s.

These chimpanzee SIV isolates have all been obtained from equatorial west Africa and this is probably the region where a human first became infected with an ancestral HIV. HIV transmission and spread can be tracked by analysing genetic sequence diversity.

Molecular epidemiology studies have shown that the first epidemic in South Africa in homosexual men in the 1980s was associated with subtype B. This subtype is rarely found in Africa but is common in North America and Europe, implying that HIV first entered South Africa from another continent. In contrast, the second HIV epidemic in the heterosexual population was associated with subtype C.

This subtype is dominant in southern Africa and it is therefore likely that the second epidemic originated from regional spread from other countries in Africa and was not a consequence of the first epidemic.

The explosive spread of subtype C infection in South Africa in the early 1990s was in fact a result of multiple introductions of HIV into the country. An analysis of the phylogenetic relationship between viruses shows that South African viruses are interspersed among sequences from Zambia, Malawi, Botswana and Zimbabwe.

Q: HIV/Aids treatment and finding a vaccine?

A: HIV treatment provision is a key component of any country's Aids strategy. Not only is antiretroviral therapy (ART) life-saving, but it also has the potential to prevent HIV transmission. For example, the use of antiretrovirals has reduced mother-to-child transmission of HIV to the point where a global plan has been developed for the elimination of new HIV infections among children.

The scale-up of antiretroviral therapy globally has surpassed expectations with coverage of treatment reaching 17 million people at the end of 2015, more than 3 million of whom are in South

Africa. However, more than half of all people living with HIV are still in need of treatment, many of whom do not know their HIV status.

The advances in HIV treatment and recent advances in the use of antiretrovirals for HIV prevention have created a newfound optimism that it may be possible to control the HIV epidemic.

Q: What are some of the challenges (societal and medical) when it comes to finding prevention tools?

A: Despite substantial increases in knowledge of what works in preventing HIV infection, and resources for their implementation, the virus continues to spread.

> *"A mix of behavioural, biomedical and structural HIV prevention actions is likely to be needed"*

The inability to curb the epidemic in many settings is due to the inability to implement proven HIV prevention strategies at the necessary scale and magnitude to those who need it most, and not recognising the link between HIV prevention and broader development needs.

Prevention efforts have generally targeted whole communities or those who are HIV negative.

There is a steady shift in prevention efforts from a narrow focus on HIV uninfected persons to a more effective continuum of prevention that includes those who are uninfected, recently infected, infected but asymptomatic as well as those with advancing HIV disease and on antiretroviral therapy.

There is also a shift towards the provision of combination prevention. A single HIV prevention intervention is unlikely to be able to alter the epidemic trajectory as HIV epidemics in communities are complex and comprise a mosaic of different risk factors and different routes of transmission.

Hence, a mix of behavioural, biomedical and structural HIV prevention actions is likely to be needed to alter the course of the HIV epidemic.

The combination of HIV prevention interventions needed will vary depending on cultural context, the population targeted and the stage of the epidemic.

Q: Why are the rates of HIV infection so high among adolescent women?

A: Several factors contribute to the increased vulnerability of young women in acquiring HIV. In sub-Saharan Africa, adolescent girls and young women tend to acquire HIV infection at a much earlier age than their male peers.

This age-sex disparity in infection is a consequence of young girls partnering with men who are about 5 to 10 years older than themselves and already living with HIV. In some cases, women, particularly those from impoverished backgrounds, engage in transactional sex and form relationships with older men for financial and social security.

In addition to choosing a sexual partner who may already be infected with HIV, early sexual debut and gender-based violence have also been shown to impact on the vulnerability of adolescent girls and young women in acquiring HIV infection.

Q: Take me through the history of vaccine development. Do you think there will be a viable, affordable one available in the next 20 years?

A: The quest for an HIV vaccine started soon after the first cases of Aids were reported in 1981. This evolving field has experienced many disappointments and some rare successes, underscoring the complex challenges in finding a safe and efficacious product.

Early efforts, focused on experiences in developing vaccines for other viral infections and included the use of attenuated forms of the virus; vector-based products; protein-based and nucleic acid-based vaccines.

The initial focus on simple viral proteins to elicit an antibody response, not surprisingly with hindsight, had limited success. The focus then turned to vector-based products and eliciting an effective cellular immune response by stimulating anti-HIV CD8+ T-cells.

The STEP & amp; Phambili trials of an adenovirus 5 vector vaccine against HIV revealed in 2008 that cellular immune response vaccines are complicated and may actually increase the risk of HIV infection.

In 2009, the RV144 trial demonstrated modest (31%) preventive efficacy for an HIV vaccine regimen comprising ALVAC-HIV (vCP1521) and clade B/E gp120 Env protein (AIDSVAX B/E) in Thai volunteers, and while there was a lukewarm response to the initial findings, subsequent sub-group analysis of the data re-energised the vaccine field. Significantly, for the first time, correlates of protection in a study in humans were identified.

Antibodies against the V1V2 region of the HIV envelope were most likely the mechanism by which the vaccine prevented HIV infection.

This important finding is the basis of the Caprisa 256 monoclonal antibody which also targets the V1V2 region of the HIV envelope.

The Caprisa 256 antibody, which is from a KwaZulu-Natal woman, is highly potent against HIV and is currently in production at the US National Institutes of Health Vaccine Research Centre.

The Thai trial findings led to a strengthening of the HIV vaccine effort with scientists, governments, pharmaceutical companies, funders, and community groups all joining to form the Pox-Protein Public-Private Partnership (P5) partnership, one of the most ambitious vaccine initiatives in HIV vaccine research.

Q: For many, the subject of HIV and Aids is cloaked in acronyms, medical jargon and stigma. What do you think medical experts need to keep in mind when it comes to communicating with lay people on the condition?

A: It is important that scientific experts are accessible to speak to the media or with communities. Answers must be simplified and medical and scientific jargon thoroughly explained.

It is important to demystify science and to translate research and the impact it is having on people and their lives.