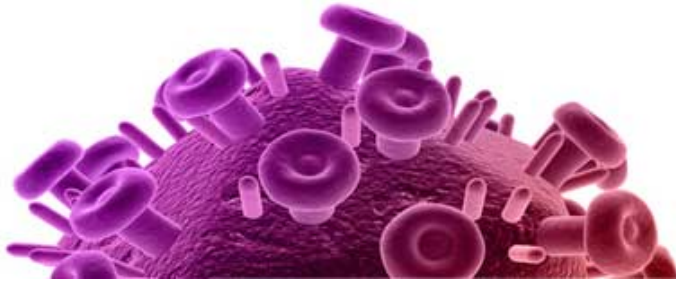


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Online magazine for health professionals and policy makers.

SACEMA • Quarterly

Update on epidemiology from the South African Centre for Epidemiological Modelling and Analysis

Issue 3 September 2010

IN THIS ISSUE

- » [Editorial](#)
- » [What determines the type-specific prevalence of high-risk human papillomavirus \(HPV\) infection? — implications for the impact of vaccination against types 16 and 18](#)
- » [Should we be worrying about Bovine TB?](#)
- » [Can mixed infection explain the high prevalence of TB in crowded areas with high strain diversity and low HIV prevalence?](#)
- » [Short items](#)

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SACEMA Quarterly is an online magazine produced by [SACEMA](#). The aim is to provide regular updates, articles and reviews of developments in quantitative epidemiology. The intention of the magazine is to present this work in a way that it will be accessible to the lay-person and to the interested health professional and policy-maker.

Editorial

John Hargrove

With effect from 1 July 2010 I have stepped down as Director of SACEMA. I shall continue to work as a Senior Research Fellow, focussing on my research in the area of tsetse and trypanosomiasis biology and control. The Director's position has been filled by Dr Alex Welte, who has moved to Stellenbosch from the Computational and Applied Mathematics (CAM) at the University of the Witwatersrand. Alex is no stranger to SACEMA having been involved from the earliest days and he made a huge contribution to our early development in helping to secure major international funding. There is every reason to be extremely optimistic about an exciting future for SACEMA under Alex Welte's leadership and I am sure you will all join me in wishing Alex well as the head of this organisation over the coming years.

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What determines the type-specific prevalence of high-risk human papillomavirus (HPV) infection? — implications for the impact of vaccination against types 16 and 18

Johannes A. Bogaards and Johannes Berkhof



Cervical cancer is the second most common cancer among women worldwide, with an annual incidence of approximately half a million cases. Over 80% of these occur in developing countries. It is firmly established that persistent infection with one of the so-called high-risk human papillomavirus (hrHPV) types is a prerequisite for the development of cervical cancer. Estimating the impact

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of HPV vaccination on the reduction in the rate of cervical cancer requires an understanding of the determinants that govern the prevalence of the various hrHPV types prior to vaccination. The fact that hrHPV is sexually transmitted partly explains the age-specific patterns in hrHPV prevalence data and the geographic variation in hrHPV infection risk. However, it is unclear why some high-risk types are more widespread than others.

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Should we be worrying about Bovine TB?

Wayne M. Getz



tourism.

Given the enormous burden that the current HIV/AIDS and TB epidemics have imposed on rural areas in the eastern and central provinces of South Africa, how much attention should the National and Provincial governments be paying to zoonotic diseases such as bovine TB (BTB) in these areas? The answer lies not only in the extent to which BTB poses an additional burden on human health in the region, but also on the degree to which it threatens food security, exacerbates poverty, and threatens conservation and green

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Can mixed infection explain the high prevalence of TB in crowded areas with high strain diversity and low HIV prevalence?

Doreen Mbabazi & Rachid Ouifki



the proportion of mixed infection in these areas. To investigate the impact of these parameters, a mathematical model was developed for TB transmission dynamics that accounts for mixed infection.

There are many different strains of TB. If there happen to be many strains circulating in a population, then individuals could be infected with more than one strain at a time which we define as mixed infection. This article focuses on the question whether mixed infection can explain the high prevalence of TB in some areas with overcrowding, low HIV prevalence and a high diversity in TB strains. The aim was to identify the factors that characterize mixed infection and investigate their impact on both the prevalence of TB and

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Short items

By the editors

Here we present short articles on recent publications, conference announcements and reports related to the work of SACEMA.

- Unintended consequences: on the importance of doing things properly. I. Jean Humphrey and the ZVITAMBO Trial
- Modelling the potential impact of age-targeted early HIV treatment initiation in South Africa

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Should we be worrying about Bovine TB?

Wayne M. Getz | *Professor of Environmental Science at the University of California, Berkeley, and Extraordinary Professor at the University of Pretoria. Areas of interest: quantitative population biology; theoretical, movement and disease, ecology and epidemiology; TB, HIV, and anthrax epidemiology.*

Bovine tuberculosis (BTB) is a chronic disease caused by *Mycobacterium bovis*, a bacterial pathogen that is part of the *Mycobacterium tuberculosis* complex that causes clinical tuberculosis (TB) in humans and other mammals. Notably these include cattle around the world, badgers in Britain, deer in North America, possums in New Zealand and a comprehensive array of wildlife throughout Africa, including buffalo, rhino, antelope, big cats, and monkeys. BTB is transmitted primarily via aerosol pathways, but also through alimentary routes including saliva, intrauterine and milk consumption pathways.

Given the enormous burden that the current HIV/AIDS and TB epidemics have imposed on rural areas in the eastern and central provinces of South Africa, how much attention should the National and Provincial governments be paying to zoonotic diseases such as bovine TB (BTB) in these areas? The answer lies not only in the extent to which BTB poses an additional burden on human health in the region, but also on the degree to which it threatens food security, exacerbates poverty, and threatens conservation and green tourism.

History of BTB in South Africa

BTB was introduced from Europe into South Africa during the 18th and 19th centuries through the importation of infected cattle. It was first detected in South Africa in cattle in 1880. Evidence of BTB transmission to wildlife was obtained in 1929, when the disease was detected in the Eastern Cape in kudu and common duiker. The economic impacts of BTB in cattle became increasingly severe over the 20th century leading to the implementation of a national BTB control and eradication program in 1969. As a result, by 1995, less than 1% of cattle in commercial herds were infected with BTB. Today, however, the prevalence of BTB in both cattle in rural communities and wildlife in conservation areas remains uncertain.

BTB was first diagnosed in African buffalo in the Kruger National Park (KNP) in 1990, where it was found to occur along its southern boundary. Further sampling during the 1990s revealed that BTB was increasing in prevalence in the southern sectors of KNP while spreading northwards. An analysis of outbreak patterns and BTB strain types suggested that BTB was most likely transmitted

to buffalo from cattle in the southeast corner of KNP some time between 1950 and 1960 (1). At the start of the new millennium, the invasion of BTB into KNP had led to unusually high levels of prevalence in African buffalo (5–45% depending upon on region), compared with white-tailed deer in Michigan (0–4%). Thus African buffalo in KNP provided an ideal system to study the disease ecology of BTB. Motivating questions for such a study include the impact of the disease on the demography of focal species such as buffalo and rhino; how movement of animals may affect the spread of disease; the impact of the disease on predator populations that feed on diseased prey, such as lion; and the impact that predators may have in cleansing diseased herds by preferentially preying on sick animals.

Studying BTB in KNP

Funded by the US National Science Foundation, we undertook such a study in KNP, from 2000–2006. The study built on data that had been collected by KNP scientists through park-wide lethal sampling in 1991–1992 and in 1998, which determined the BTB prevalence via a combination of macroscopic examination of the lungs, histopathology and culture techniques (2). To assess how the movement of sick individuals contributes to the spatial spread of BTB, collars were placed emitting very high frequency (VHF) radio signals on approximately 160 individuals. This allowed recording of the movement of each collared animal between one to several times per week. In addition, from November 2000 to July 2006, 1053 buffalo (593 different individuals) were captured and blood samples were taken to estimate prevalence, while either placing collars on individuals, removing collars from individuals, or just monitoring the current status of previously tested individuals.

Disease status was determined using the interferon-gamma (IFN γ) BOVIGAMTM assay that, unlike skin tests, does not require confining or recapturing animals 48–72 hours later. The IFN γ test is quite reliable, with a specificity (proportion correctly identified as negative) of 99% and sensitivity (proportion correctly identified as positive) of 85%. The high specificity, together with the lack of any evidence that infected buffalo recover from BTB, made it reasonable to assume that positive individuals remained positive for the duration of the study. Thus BTB-negativity was regarded as a variable that could change its value only once – from negative to positive – when evaluating the status of individuals every 6–12 months over a six-year period.

The analysis of this data suggested that BTB had a negligible effect on the demography of buffalo in KNP (3). Using a Cox proportional hazard model for mortality, the data suggested that being BTB positive was likely to increase mortality rates by not more than 2% per year. Further, though BTB positive females appeared slightly less often to have calves at their sides, no differences could be detected in calving rates in high and low BTB areas of prevalence. This is not to say that in times of severe stress – such as during an extended drought, which did not occur during the study period – infected animals would not succumb earlier and in greater numbers from BTB infection. But during normal periods, it seems that the primary affect of BTB in the African buffalo is that it constitutes a relatively large and active reservoir for the enzootic maintenance of *M. bovis* in the ecosystem, with continuous spill over effects to other species.

The impact of BTB on other species in KNP is not known, although various researchers have suggested its potential to do harm, especially to predators that feed on BTB infected buffalo. In the described study, it could not be demonstrated that lion preferentially kill sick animals, although BTB certainly kills lions in KNP, but also with no discernable impact on lion populations (4). A primary concern, however, is spill over from buffalo back to cattle. Buffalo originating in KNP

have been found to wander beyond the park boundary. It is also believed that BTB can spread from buffalo back to livestock indirectly by small wild and domestic mammals, raising concerns about the impact of BTB on humans in the same environment. It also has economic implications since it restricts trade of affected cattle and wildlife species and has, in fact, spawned a thriving industry for the ranching of certified disease-free African buffalo.

BTB in KZN

In addition to KNP, considerable concern exists for the spread of BTB in the buffalo population in KwaZulu-Natal's Hluhluwe-iMfolozi park (HiP). BTB was first detected in a black rhino in this park in 1970. In 1986 BTB was confirmed to be prevalent in HiP buffalo, with the source attributed to local cattle mixing with buffalo before the park was fully fenced in the 1960s. Many small-scale farmers neighbouring HiP live under impoverished conditions and rely solely on livestock for their food and financial security. They also have limited access to animal and human healthcare services. Thus the introduction and spread of BTB into HiP could have a devastating impact on the health and well-being of livestock and humans if it is not contained.

A study by Claire Geoghegan, PhD student at University of Pretoria, investigated BTB in rural communities neighbouring HiP, by measuring the prevalence of both brucellosis (another food-borne zoonoses that causes abortion or premature calving of recently infected animals) and BTB in community cattle, as well as surveying over a thousand households to assess their resilience to threats from zoonotic disease and agricultural disasters. In collaboration with scientists from Onderstepoort Veterinary School, the degree to which milk storage and souring processes mitigate or exacerbate the threat of BTB infection is assessed.

Burden on human health

If BTB infections spread to cattle, then humans become at risk due to their close-association with sick animals during herding and milking. Also individuals, particularly children, the elderly, malnourished, and immunocompromised, risk alimentary infection through ingestion of bacteria in milk and dairy products. BTB has been isolated in dairy products throughout Africa, and children given raw milk are particularly at risk of developing infection in lymph nodes, a common condition in Europe in the 19th century prior to widespread pasteurisation of milk (5).

Infections of BTB through consumption of infected meat and milk often lead to extra-pulmonary TB that is much more likely to go undiagnosed and unreported than the more usual pulmonary TB. Also BTB is resistant to eleven of the most cost-effective and accessible front line drugs, and is thus more difficult and expensive to treat (6). To top this, TB is a major opportunistic disease of individuals infected with HIV, resulting in a prevalence of 80% in HIV patients in KwaZulu-Natal. Thus the co-occurrence of *M. bovis* and HIV in the rural communities presents a considerable threat that needs to be investigated and monitored.

So, yes, we should be worrying about bovine tuberculosis in South Africa. It is only through studies like those discussed here that we can begin to evaluate the importance of widespread testing and control for bovine TB in rural areas in South African, and the rest of sub-Saharan Africa.

[Back to Top](#)

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- [Editorial: Changing of the Guard at SACEMA](#)
- [What determines the type-specific prevalence of high-risk human papillomavirus \(HPV\) infection? — implications for the impact of vaccination against types 16 and 18](#)
- [Should we be worrying about Bovine TB?](#)
- [Can mixed infection explain the high prevalence of TB in crowded areas with high strain diversity and low HIV prevalence?](#)
- [Short items](#)

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- [Issue 2 June 2010](#)
- [Issue 1 April 2010](#)
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- [Issue 3 September 2009](#)
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