



## WOMEN UNDER HIV SIEGE BOLSTER MICROBICIDE RESEARCH

South African women, facing the brunt of the HIV/AIDS onslaught, are clamouring to help test a cutting-edge microbicide that has already proved effective in preventing HIV infections in animals.

Regarded as being at the forefront of microbicide research worldwide, the trials began in March 2004 and 1 800 women have qualified to take part so far (out of 6 800 targeted for enrolment by September 2005).

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### Queueing up

Dr Sumen Govender, the national clinical study manager, reported unusually long lines of people outside participating clinics in Soshanguve, Pretoria, Isipingo in KwaZulu-Natal and Gugulethu near Cape Town. Just 10 months into the 30-month trial of the seaweed-based gel called Carraguard, recruiters were still drawing large crowds to presentations at church halls, clinics, schools and community centres.

'Many women participating in the previous phase 2 trial (the expanded safety trial) didn't want it to end, they were so into it. It just shows how they view the role of microbicides in the future. It's something that will actually

change their lives and they really value', Govender said.

A major bonus was that hundreds of women had continued into the current phase 3 of the trials, which helped his 120-person team in the field reinforce the vital issue of compliance.

The New York-based Population Council's Centre for Biomedical Research is underwriting this and several other microbicide trials. According to its vice-president, Dr Elof Johansson, prospects for success are 'excellent'.

He told *Izindaba* that globally the only other microbicide that has reached phase 3 clinical trials is a product called Savvy, a detergent that destroys the virus by changing its environment. It is currently being tested in Ghana, while Nigeria will join in the trial later this year (2005).

However, Savvy's major drawback is that, unlike Carraguard, it creates irritation in the vagina.

### Compliance crucial

Both Johansson and Govender admitted that compliance could prove to be the Achilles' heel of the local study, as it is crucial in achieving an acceptable outcome. 'It's based a lot on trust, but we've turned every stone we can, according to the knowledge we currently have,' said Govender.

Clinic counsellors impressed upon participants that they had to use the gel 'each and every time' they had sex. They asked probing, behavioural questions during all follow-up sessions.

Participants receive an extensive briefing beforehand and have to return all used and unused gel dispensers, so that the trial team can take stock of what was given out and what was returned.

### Reason for hope

Govender said the main reason for his optimism was that 'loss to follow-up' levels among trial participants currently stood at less than 3%. 'This stands us in good stead when it comes to women staying in the trial.'

Tools for monitoring behaviour included using a dye that indicated when an applicator had been used, and booklets, pamphlets and posters that were first introduced by community liaison officers at the pre-enrolment stage.

Johansson said the best reason for optimism around the gel was that in animal studies, models that mimicked the HIV infection had proved highly effective in preventing transmission. Results in animals showed that the gel protected monkeys against SIV, rats against herpes simplex, while a special system in which tissue from the human vagina was transplanted into animals had also proved successful. 'All showed that transmission was prevented,' Johansson said.

While the actual mechanism of how the microbicides work remains unknown, clinical trials in a laboratory setting show that Carraguard carries a highly negative charge which repels the highly positively-charged viral



envelope. This deactivates the virus and prevents it from entering the cells.

The gel coats the surface of the vagina and forms a barrier, preventing the cells from moving into the epithelium of the vagina.

Govender emphasised that Carraguard was not a contraceptive or a spermicide, although further work on a dual-purpose gel could emerge should the trials be successful. 'At present our focus is on preventing HIV infection, nothing else,' he said.

Johansson said his centre hoped to begin with three more microbicide gel trials in South Africa next year. These were called Tro2000 – very similar to Buffergel, which changed the pH in the vagina to become unfriendly to the

virus, and Cellulose Sulphate, which bound the virus in a manner similar to Carraguard.

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'It's not always nice to be a world leader in this kind of research because everyone else learns from our mistakes,' he quipped.

## Changing women's lives

He emphasised that an effective microbicide would be the first socially acceptable prophylactic product that women could use themselves.

Condoms were very effective when used consistently and properly.

However, unless they were viewed in 'a more epidemiological way' that took into account the low status and lack of sexual negotiating power of women, their efficacy was dangerously exaggerated.

Govender said his team would begin analysing the data next year and 'hopefully by 2007, give or take a couple of months, we'll have solid results'.

Chris Bateman

## The South African Medical Journal

### 100 years ago:

Sir: The following may be interesting to your readers; Mrs L, age about 40, multipara, had been a patient of mine for several years, during which she had had two miscarriages. Was very neurotic, and frequently complained of bladder trouble, though the urine whenever examined was always normal. She told me that at her last full term labour she had severe fits. In August of this year I attended her in labour in the Maternity Ward of the Kimberley Hospital. Everything was going on very satisfactorily, though labour was progressing rather slowly. The urine was free from albumen the morning labour commenced. In the afternoon I was informed by the nurse that she had had a convulsive attack, but that it was not very prolonged. Half an hour afterwards she had a severe and prolonged eclamptic seizure. I got Dr Briggs to administer chloroform, and easily delivered with forceps. The convulsions at once ceased, and there was no recurrence. Mentioning to Dr Briggs that this was a case of eclampsia without albuminuria, he suggested that it was possibly a case of albuminuria coming on rapidly during labour. To test this, some urine was at once drawn off by catheter, and was found to contain half albumen (sic). Next morning the albumen was greatly diminished, and in two days it was gone. I think the case worthy of record, as, had it not been for Dr Briggs's suggestion, I should certainly have regarded it as non-albuminuric, as at no time previous to labour or even early in labour was albumen present. Yours, etc., ARNOLD H WATKINS.

### 50 years ago: Diagnosis of acute appendicitis

For the past 50 years medical students have been harangued by their teachers on the classic picture of acute appendicitis. In spite of this, mistakes and delay in diagnosis have continued. Many of these have no doubt been due to human failing, but the outstanding reason has been the blind and continued servility of generations of teachers to the concepts of the classic descriptions. One point has from time to time been emphasised by those observers who remain unbound by tradition when it degenerates into rabbinical dogma: the majority of cases of acute appendicitis do fall more or less accurately into the timeworn descriptions, but a very significant minority do not. In this respect figures do not provide any very useful information, but roughly one might say that something like 30% of cases depart in some significant way from the text-book picture of the disease. It is in this group that the vast majority of diagnostic errors occur.