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Short items

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

On the importance of doing things properly

II. Glyn Vale and the birth of the "artificial cow"

In a recent poll of British university academics the cracking of the DNA-based genetic code was cited as the most important advance by British scientists during the past 60 years. More surprisingly, voted into eighth-place, just ahead of work on stem cell research, was the development of the so-called "artificial cow". In this project scientists identified from bovine odour the chemicals responsible for attracting tsetse flies and thereby developed a cheap, effective and ecologically friendly means of controlling, or even eradicating, the insect pest.

The workers involved in the project, from Britain's Greenwich University and the Zimbabwe Government's Rekomitjie Research Station in the Zambezi Valley, have made light of the poll, particularly in view of the fact that Greenwich was only constituted as a university in 1992, by which time all of the important early work on the project had been completed.

Nonetheless, that early fieldwork - carried out by Professor Glyn Vale during the 1970s - is worth studying in more detail than is afforded by the press reports, most particularly because it highlights the importance of what might be viewed derisively in some quarters as "blue sky research" – but which should more correctly be termed "fundamental research". As I hope the following analysis will show, the development of the artificial cow emerged almost serendipitously through Vale's efforts to secure the fundamentals of tsetse sampling techniques – an arcane area of research apparently unconnected to the development of tsetse control methods.

Asking questions

Glyn qualified in 1965 with a degree in agriculture from Oxford. Hence when he arrived in the Zambezi Valley later that year, to start working as an entomologist for the Rhodesian Government, he started with the distinct advantage of knowing less than nothing about tsetse flies. He was thus unencumbered with any of the preconceived ideas of tsetse research that had surrounded the field for half a century. Given also a strong aversion to reading, Glyn followed the advice of an earlier Oxford man to: "Start at the beginning … ". He started questioning everything about the way tsetse research was carried out and what it was finding.

The first thing he did not understand was why it was that when men sampled tsetse flies with hand nets they always caught many more male flies than females – despite the fact that laboratory studies, and common sense, indicated quite clearly that females lived much longer than males and ought to outnumber them in the field by a factor of at least two-to-one. The result had been explained in the past by the greater "activity" of male flies.

But Vale wondered whether the sampling system itself might be part of the problem. Perhaps female flies were approaching the men but the men were simply failing to catch them. In his own words he realised that we needed to "improve the efficiency and objectivity of field sampling techniques if we were to resolve important contradictions and anomalies in the behaviour and ecology of tsetse".

Accordingly he started to look at more efficient ways of catching flies and experimented with applying glues to men and to model animals that he towed through tsetse habitat. The model animals were 20 litres metal cans painted black and mounted on pram wheels; they were "led" along through the bush by two men – in the same way as oxen when used as bait for sampling flies.

Vale did find slight improvements in catch but nothing particularly dramatic until the day that he had a model towed through the bush with no accompanying men. And at that point the scales fell from his eyes. Then suddenly there were plenty of female flies caught on the sticky surface. The problem with the "man fly-round" system of tsetse sampling was … well, it was the man. Men repelled tsetse; and they particularly repelled female tsetse - hence the skewed sex ratio.

Visitors to the Zambezi Valley, particularly in those days soldiers on patrol, were openly scornful of the idea that humans could be repellent to tsetse flies. If that were the case why were they bitten so mercilessly all day long? And it was not only visitors who were critical. A letter from a senior official on file in the Tsetse Control Branch questioned the value of the research, suggesting that whereas tsetse might be repelled from landing on a tin can towed through the bush they would not be put off coming to a real live ox - off which they could feed. And, indeed, it had been observed that a greater proportion of female flies could be caught

off stationary or mobile bait oxen than from the normal man fly-round.

The standoff led to the design of a trial to see whether there was any difference between the numbers of tsetse caught off an ox in the absence of men compared to the situation when men were present. But how to catch the flies if no men were present? Happily, by this time, Vale had resurrected and adapted an idea from Kenya of using electrocuting nets to capture tsetse. In an experiment of heroic proportions he made, mostly with his own hands, 12 electric nets each 1.5 meter wide and 3.3 meter high, arranging them in ring to surround an ox and capture automatically any tsetse that approached.

The experiment was a simple one. An ox would be tethered at the centre of the ring of nets and would stand there for three hours – either by itself, or with three men standing next to it. Any fly that approached the ox would be caught on the electric net and fall onto a plastic sheet coated with glue. If the critics were correct, the numbers of flies approaching the ox should not be reduced by the presence of the men – perhaps they might even be enhanced if the men were also seen as food by the flies. In the event, the results were as unequivocal as they were astounding; when the men were absent the catch increased by factors of 1.4 for *G. m. morsitans* Westwood and 3.0 for *Glossina pallidipes* Austen. Vale's point about the repellent effect of men was proven beyond any shadow of a doubt and all questions regarding the desirability of the research were summarily despatched.

Importance of odour

But there was a very important twist in the ox's tale … On every day when the experiment was carried out the vast majority of the flies was caught on those electric nets that were downwind of the ox. This suggested very strongly to Vale that odour must be a factor in the flies detecting the ox; indeed it even seemed possible that the olfactory stimulus might be more important than the visual. How could Vale find out?

It was one of the blessings of those bygone days that the one thing that was in plentiful supply was manpower, and Vale got men to dig a pit large enough to house a large ox – induced to walk into the cavern by the prospect of fresh green fodder and perhaps also by the cool and the absence of tsetse! When the pit was duly covered with a metal roof topped with soil, and the door closed, Vale was able to use a fan to provide at the surface the olfactory stimulus provided by an ox, but with no attendant visual stimulus. Flies were caught on an electric net placed just downwind of the pit's air vent. A series of experiments then demonstrated that roughly 80% of the flies arriving at an ox could be attributed to the olfactory stimulus.

Substitution of the ox with sheep, goats, donkeys and a variety of wild ungulates demonstrated that the number of flies caught increased as a quasi-linear function of the mass of the animal. For Vale, who was never scared off by matters of scale, it was a logical next step to have constructed a pit large enough to house six oxen – and found that the catch just kept increasing, apparently linearly, with dose. Within two years he had constructed a pit capable of housing the Rekomitjie Research Station's entire livestock herd and it was possible then to catch in excess of 14,000 tsetse flies in a three-hour period.

Now the potential pay-off was obvious - from what had started as a piece of fundamental research to establish the basis of an improved sampling system for tsetse. If the chemicals responsible for the olfactory attraction could be identified it might be possible, by their use in sufficient quantities, to attract and kill enough tsetse flies to have the basis of a very efficient method of tsetse control. This was particularly evident to Vale because of his knowledge of the known facts of tsetse population dynamics. Female tsetse produce only one offspring at a time, at approximately 10 day intervals. Simple calculations show, therefore, that no tsetse population can grow if the adult female death rate exceeds about 3.5 per day. With the huge numbers of flies that could now be caught this seemed a very easy target.

In some senses the rest is history. A hunt was started for the active chemicals in ox odour. Carbon dioxide had already been shown to be a component – but by itself it attracted <5% of the number coming to an ox. Acetone emerged as the next component, suggested on general grounds rather than through any smart analytical procedure.

Greenwich University's involvement in the programme started after Zimbabwe gained independency in 1980 and Professors Hall and Torr have worked with Vale ever since. Their collaboration saw the identification of 1-octen-3-ol as a further component of the odour. Following the demonstration in Kenya that ox urine was also an attractant, workers in Kenya and the Zimbabwe-Greenwich partnership independently came to the conclusion that the active components were 4-methylphenol and 3-propylphenol.

Armed with four chemicals (carbon dioxide could not be used, for practical reasons) it has been shown possible to eradicate populations of tsetse flies using just four odour-baited, insecticide-treated "targets" per square kilometre. The targets are simple pieces of black and blue cotton mounted on a pivot. The system is simple, effective and relatively cheap, and ecologically attractive in that it makes minimal impact on other insects. As such it ought to be attractive also to the accountants who, increasingly, control scientists' research. In their excitement over the cost implications, however, they would do well to remember that the system had its origins in apparently arcane fundamental research and in Glyn Vale's insistence on doing things properly.

John Hargrove, November 2010

Treatment as prevention: the discussion continues

In the first edition of the SACEMA Quarterly (March 2009) Brian Williams provided a discussion on the various arguments for and against the in a Lancet article suggested approach of 'treatment as prevention' of HIV (early treatment of HIV infected individuals will prevent transmission of the virus) (1). As this 'test-and-treat' strategy continues to be the topic of – often heated – debate, another article was devoted to this issue, focusing on how feasible and realistic this approach is (2). Recently a letter has been published in the Lancet, indicating that the costs of eliminating HIV in South Africa have been underestimated (3). The appearance of this piece merely indicates that more research needs to be done on the cost-effectiveness of this approach. Keeping in mind that is very difficult to answer what the costs are for the society in terms of e.g. lives and productivity lost.

While the debate continues, there is also time to celebrate the achievements up till now: The AIDS scientist Dr. Julio Montaner has won the Albert Einstein World Award of Science for his pioneer wok on this life-saving concept of treatment as prevention (4). The British Colombia Centre for Excellence in HIV/AIDS, under the leadership of Dr. Montaner is currently implementing this strategy in a pilot project to Seek and Treat for Optimal Prevention of HIV/AIDS (STOP HIV/AIDS). As a direct result of this work, the province has already seen a decrease in new HIV diagnoses and a reduction in HIV related morbidity and mortality. Dr. Montaner aims to help prioritize treatment as prevention around the globe and bring vital life-saving therapies to the low- and middle-income countries where they are needed most urgently. Dr. Montaner is keen to work with SACEMA on developing a feasibility study in South Africa to test the idea of treatment as prevention and Dr. Viviane Dias Lima (who works closely with Dr. Montaner) will be coming to spend some time at SACEMA.

References:

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2. Williams BG. Stopping HIV: Treatment as prevention. SACEMA Quarterly, issue April 2010. [http://www.sacemaquarterly.com/magazines.php?page=detailview&p_id=14&d_id=42] Accessed 10 November, 2010.
3. Wagner B, Blower S. Costs of eliminating HIV in South Africa have been underestimated. Lancet. 376(9745):953-954.
4. Dr. Julio Montaner named 2010 recipient of the "Albert Einstein" World Award of Science (press release, 3 November 2010) [http://www.cfenet.ubc.ca/news/releases/dr-julio-montaner-named-2010-recipient-albert-einstein-world-award-science] Accessed 12 November, 2010.

Concurrent sexual partnerships and the HIV epidemic in Africa

The notion that concurrent sexual partnerships (having more than one partner at the same time) are especially common in sub-Saharan Africa and explain the region's high HIV prevalence is accepted by many as conventional wisdom. A systematic review that was recently published was conducted to question this theory. The quantitative and qualitative evidence offered by the principal proponents of the concurrency hypothesis was evaluated and the mathematical model they use to establish the plausibility of the hypothesis analysed. They find that research supporting the concurrency hypothesis "either finds no correlation or has important limitations." In addition, they charge that the mathematical models used "require unrealistic assumptions about frequency of sexual contact, gender symmetry, levels of concurrency, and per-act transmission rates." Quantitative evidence cited to support the concurrency theory is unconvincing, the authors charge, because it excludes demographic and health surveys and other data that find *low* concurrency in Africa. Proponents of concurrency "make broad statements about non-African concurrency based on very few surveys, report data incorrectly, report data from studies that have no information about concurrency as though they supported the hypothesis, report incomparable data and cite unpublished or unavailable studies." The researchers maintain that supportive qualitative data is often "irrelevant" because they do not compare Africa with other regions. They conclude by saying that promoters of the concurrency hypothesis have failed to establish that concurrency is unusually prevalent in Africa or that the kinds of concurrent partnerships found in Africa produce more rapid spread of HIV than other forms of sexual behaviour. The authors urge policy makers to "turn attention to drivers of African HIV epidemics that are policy sensitive and for which there is substantial epidemiological evidence."

Reference: Sawers L, Stillwaggon E. Concurrent sexual partnerships do not explain the HIV epidemics in Africa: a systematic review of the evidence. J Int AIDS Soc. 2010;13:34.