

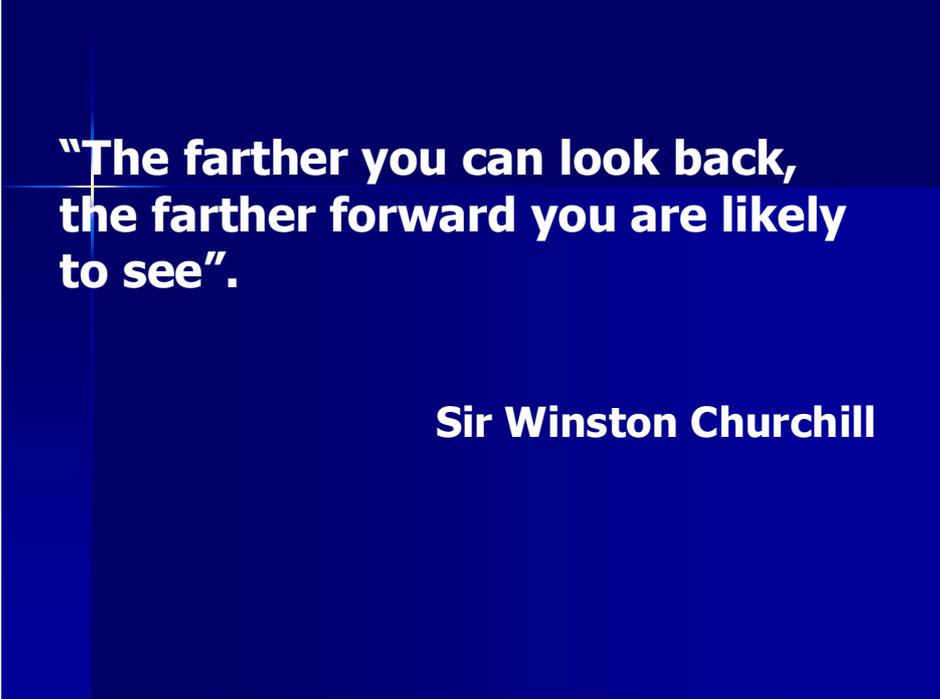
On Women's Health and Rights  
Lectures, Speeches and Statements  
Mahmoud F. Fathalla

## **What does the future hold for the vaginal microbicide field?**

Keynote speech  
Alliance for Microbicides meeting,  
Washington DC, October 6-7, 2009

For the past few years, I have been limiting my travel and speaking engagements. This time, I could not resist the persuasive powers of dear Polly Harrison. I do not think many people can. Also, the subject of the meeting is so close to my heart. It is a pleasure to see and meet many of my old friends, still working on it. As to the Alliance, I happened to be one of the birth attendants around, when it first came to being, and I continued to follow with admiration its good work over the years.

I selected as a topic “What does the future hold for the field of microbicides?”

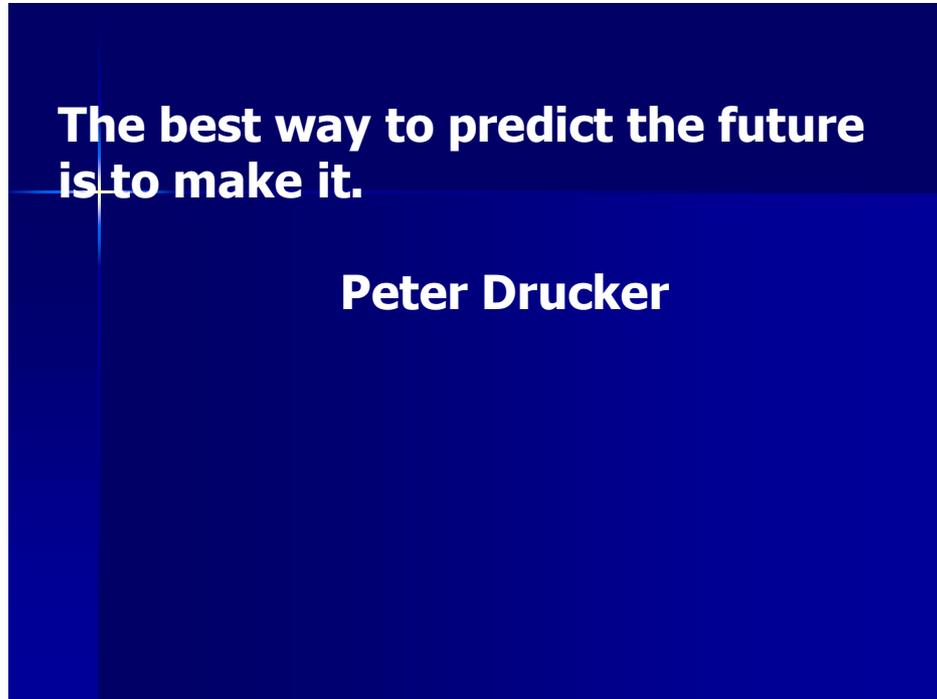


**“The farther you can look back,  
the farther forward you are likely  
to see”.**

**Sir Winston Churchill**

In case some of you may be wondering how an old man qualifies to talk about a future in which he will not be a part, I refer you to a statement made by Winston Churchill in his

old age: “The farther you can look back, the farther forward you are likely to see.” At least this is what we, old folks, like to believe and try to make younger people believe.



But this is not to say that old age has endowed me with a crystal ball to predict the future. In fact it has left me with a strong belief in an advice given by the late management guru, Peter Drucker: “The best way to predict the future is to make it”

The thrust of my message to you today is that the future of microbicides will be what you will make it to be. I plan to share with you ten propositions, which I hope may help us in making the future for microbicides.

**Microbicides- Making the Future  
Ten propositions**

- **Believe in the beauty of our dream.**

My first proposition is that we continue to believe in the beauty of our dream.

**“The future belongs to those who believe in the beauty of their dreams”**

**Eleanor Roosevelt**

And why is this important for the future of the microbicide field? Eleanor Roosevelt rightly said it: “The future belongs to those who believe in the beauty of their dreams.”

Microbicides are a dream. Looking back, the dream, for many of us, was inspired by the advances of the contraceptive technology revolution. I am old enough to remember the days when a woman had to be completely dependent on her male partner to protect herself from an unwanted pregnancy. With the advent of the contraceptive technology revolution, women for the first time had access to methods that are completely women-controlled. The microbicide dream is that no woman, rich or poor, living in the skyscrapers of Manhattan or in the slums of the less privileged world, will have to be at the mercy of the cooperation of her male partner to protect her health and life, in this pandemic of sexually transmitted infections, including especially HIV. The current HIV preventive strategy: “ABC” **a**bstinence, **b**eing faithful and **c**ondom is not working for women.

### **HIV transmission in intimate partner relationships in Asia**

- Most women are acquiring HIV not because of their own sexual behaviors but because their partners engage in unsafe behaviors.
- More than 90% of women living with HIV acquired the virus from their husbands or from their boyfriends while in long-term relationships.
- At least 50 million women are at risk of acquiring HIV from their intimate partners. These women are either married or are the regular partners of men who engage in higher-risk sexual behaviors.

UNAIDS 2009

Let me share with you from a report very recently released by UNAIDS about: HIV transmission in intimate partner relationships in Asia

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- More than 90% of women living with HIV acquired the virus from their husbands or from their boyfriends while in long-term relationships.
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We speak of intimate partner violence and it is receiving a high level of international and national concern. We should also be speaking, with equal concern, about intimate partner STI/ HIV transmission which, even if less visible, is much more serious.

## Marvelous microbicides

**Intravaginal gels could save millions of lives,  
but first someone has to prove that they work**

Lancet editorial , 27 March 2004

But our dream is still a dream. Yes, microbicides are marvelous. Yes, intravaginal gels could save millions of lives. But, as a Lancet editorial put it in 2004, and still sounds true: “But, first someone has to prove that they work.”

## Microbicides- Making the Future **Ten propositions**

- Believe in the beauty of our dream
- **Make the proof of concept our high priority.**

This leads to the next proposition: we should make the proof of concept the high priority for our field.

We have seen in the past few weeks the excitement in the HIV vaccine field, following the encouraging signals from the Prime/ Boost trial in Thailand. Such signals are what we are looking for.

To say that efficacy trials of HIV vaccines and microbicides have, to date, been disappointing is something of an understatement. Several microbicides have been tested in phase 3 trials. At best, one of the candidates, the polyanion PRO-2000, has been shown to reduce HIV-1 acquisition by 30%. Unfortunately, this result was not statistically significant. At worst, some microbicides have increased HIV-1 infection in recipients.

Nature Medicine 15, 855 - 859 (2009)  
Roadblocks in HIV research: five questions  
Clare Thomas<sup>1</sup>

Where do we stand? This is what Nature Medicine had to say about us in a very recent report:

“To say that efficacy trials of HIV vaccines and microbicides have, to date, been disappointing is something of an understatement. Several microbicides have been tested in phase 3 trials. At best, one of the candidates, the polyanion PRO-2000, has been shown to reduce HIV-1 acquisition by 30%. Unfortunately, this result was not statistically significant. At worst, some microbicides have increased HIV-1 infection in recipients.”  
(Clare Thomas. 2009. Roadblocks in HIV research: five questions. Nature Medicine 15, 855 – 859.)

The bad news did not put me off. For one thing, from the beginning we never thought that developing an effective safe and acceptable microbicide will be an easy task, scientifically, ethically and economically.

**The probability of a thing happening is inversely proportional to its desirability.**

Gumperson's law

Our field has been so far under the curse of Gumperson's law: "The probability of a thing happening is inversely proportional to its desirability."

But this should not put us off. From the beginning, we never thought that developing an effective safe and acceptable microbicide will be an easy ride. We knew that the road will be bumpy.

But we were encouraged by the mood of "We will do" and "yes, we can" in this great country. A friend once told me about the American definition of the difference between the possible and the impossible: the possible is what we do now; the impossible is what takes some more time.

I must declare to this distinguished audience that I am an optimist and there is nothing I can do about it. I guess that when the powers that be are assembling the genes for our DNA, the Human Pessimism Gene is sometimes out of stock. Rather than delaying their conception, some people like me are allowed to get away without it. The difference between an optimist and a pessimist is that the pessimist sees the difficulty in every opportunity; the optimist sees the opportunity in every difficulty. I see an opportunity in the setbacks which the field had suffered.

**Success is the result of  
good judgment;**

**Good judgment is the result of  
experience;**

**Experience is the result of  
bad judgment.**

I concede that we may have made some bad judgments. True, success is the result of good judgment; but good judgment is the result of experience; and experience is the result of bad judgment. We must seize the opportunity to revisit our previous judgments, to get the experience to make good judgments.

## **Microbicides- Making the Future Ten propositions**

- Believe in the beauty of our dream
- Make the proof of concept our current priority
- **Follow the logic path**

This leads to my next proposition: follow the logic path. It may sound like a Buddhist teaching, but it is not. I borrow this nice term from our honorable Chair, Neal Nathanson. This is how he puts it:

## Logic Path

If an extensive trial has shown a particular product to be ineffective, we should learn as much as possible from this failure. One way to learn would be to re-visit all of the preclinical studies done on the product, possibly add some additional ones, and to use the information to set a threshold that a future candidate product would have to exceed, to justify expensive clinical trials.

**Neal Nathanson** (Personal communication)

“If an extensive trial has shown a particular product to be ineffective, we should learn as much as possible from this failure. One way to learn would be to re visit all of the pre-clinical studies done on the product, possibly add some additional ones, and to use the information to set a threshold that a future candidate product would have to exceed, to justify expensive clinical trials.”

## **Microbicides- Making the Future Ten propositions**

- Believe in the beauty of our dream
- Make the proof of concept our high priority
- Follow the logic path
- **Involve the community in our clinical trials**

There was another hard lesson to learn from past experience, and that leads to another proposition. We need involvement and support of communities in our clinical trials. Without it, failures can lead to a backlash.

## **Aftermath of the Failed cellulose Sulphate trial**

- **"Medical research trial guinea pigs contract HIV"**
- **"'Guinea pig' story on HIV prevention worrying "**
- **"HIV clinical trials in SA need to be vigorously policed"**

**Press coverage in South Africa press**

It was hurting to read the unjustified and I think unfair press coverage in South Africa press in the aftermath of the closure of the Cellulose sulphate trial: "Medical research trial guinea pigs contract HIV"; "'Guinea pig' story on HIV prevention worrying "; "HIV clinical trials in SA need to be vigorously policed". I hope that, never again, we will see this coverage.

## Microbicides- Making the Future Ten propositions

- Believe in the beauty of our dream
- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- **Beware of donor fatigue**

The next proposition is: Beware of donor fatigue. Donor fatigue is real. Ask those of us who have been in the contraceptive research and development field for so long. In previous incarnations, in a long career, I have been on both sides of the fence. I was on the receiving side, and I worked with the giving side. I can tell you, first hand, that donors are not to be relied upon as faithful partners. Their love is not sustainable. They can be distracted by other beautiful causes coming in their way, and there is no shortage of beauties competing for attention in the global health field.

## Microbicides- Making the Future Ten propositions

- Believe in the beauty of our dream
- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- Beware of donor fatigue
- **Think: public sector;**  
**Act: private sector**

The next proposition is about the public and private sectors. Private- Public sector partnerships are now a buzz word in the field of international health, and will continue to be needed for the future of the microbicide field. We need to think public sector and to act private sector. The private sector thinks of doing well; the public sector thinks of doing good. The private sector will go where it smells money. The public sector goal is to develop products that are affordable and can be delivered in low resource settings. But we must learn to act Private sector. The private sector act is a pro-choice act. It will have no sense of guilt in immediately aborting a product development lead that does not appear to be promising. They know that money saved is money gained.

## Microbicides- Making the Future **Ten propositions**

- Believe in the beauty of our dream
- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- Beware of donor fatigue
- Think: public sector; act: private sector
- **Continue the search for Mrs McCormick**

The next proposition; continue the search for Mrs McCormick. Looking for Mrs McCormick, as some of you may remember, was a slogan for a fundraising campaign for microbicides in the early 1990s. It was inspired by the story of Mrs. Katharine McCormick, the philanthropist who, together with Margaret Sanger in 1951 supported and motivated a set of eminent scientists to create a safe, effective and easy to use oral contraceptive pill. We still need a Mrs McCormick, perhaps less for her money but more for sustained advocacy for our field by women.

## Microbicides- Making the Future **Ten propositions**

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- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- Beware of donor fatigue
- Think: public sector; act: private sector
- Continue the search for Mrs McCormick
- **Tap the potential of science in developing countries**

To make the future of this field, we need all the resources we can mobilize. The scientific community in the South is a resource that we should tap for infusing new blood in our field. Developing countries are where the problem is and where the action will be.

Capacity building and infrastructure strengthening should be organized and resourced on a long-term basis, not just for the duration of a finite research program, so that the sustainability of benefits is assured.

IWGM Workshop on North-South International Collaboration in Microbicide Research, 24 April, 2006 in Cape Town, South Africa

Let me quote from the report of IWGM Workshop on North-South International Collaboration in Microbicide Research, in April, 2006 in Cape Town:

“Capacity building and infrastructure strengthening should be organized and resourced on a long-term basis, not just for the duration of a finite research program, so that the sustainability of benefits is assured.”



**Microbicides- Making the Future**  
**Ten propositions**

- Believe in the beauty of our dream
- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- Beware of donor fatigue
- Think: public sector; act: private sector
- Continue the search for Mrs McCormick
- Tap the potential of science in developing countries
- **Collaborate, collaborate and collaborate**

My next proposition is a plea for collaboration.

## HIV/STI Prevention R & D of Microbicide and PrEP Candidates

- **12** microbicide and PrEP candidates in clinical trials (including **6** ARV-based HIV prevention candidates)
- **39** clinical trials: **25** Ongoing- **14** Planned and funded
- **3** clinical candidates not currently in trials
- **6** microbicide candidates in advanced preclinical development
- Other ongoing and planned studies

Alliance for Microbicide Development, September 09

This is the September pipeline for microbicides I received in the Alliance news:

12 microbicide and PrEP candidates in clinical trials (including 6 ARV-based HIV prevention candidates)

39 clinical trials: 25 Ongoing- 14 Planned and funded

3 clinical candidates not currently in trials

6 microbicide candidates in advanced preclinical development

Other ongoing and planned studies.

This rich pipeline gives hope, but it also calls for collaboration, if we want, given the available resources, to see one or more products reaching the end of this crowded pipeline.

**When spider webs unite, they can halt even a lion.**

**African proverb**

There is power in collaboration. An African proverb says: “When spider webs unite, they can halt even a lion.” If we want to halt that virus through the development of microbicides, we need to unite.

## **Microbicides- Making the Future Ten propositions**

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- Make the proof of concept our high priority
- Follow the logic path
- Involve communities in our clinical trials
- Beware of donor fatigue
- Think as public sector; act as private sector
- Continue the search for Mrs McCormick
- Tap the potential of science in developing countries
- Collaborate, collaborate and collaborate
- **Keep the spirit of the ALLIANCE alive**

My last proposition to you is to keep the spirit of the Alliance alive.

**“In 1997, the Rockefeller Foundation asked us to do something special and distinctive, in effect to create a “microbicide field.” At that time, as many of us remember, there was little interest in microbicides, as science or as a public health need; paltry funding; and almost no interaction across the relevant disciplines and sectors.**

**Polly Harrison**

As Polly Harrison put it: “In 1997, the Rockefeller Foundation asked us to do something special and distinctive, in effect to create a “microbicide field.” At that time, as many of us remember, there was little interest in microbicides, as science or as a public health need; paltry funding; and almost no interaction across the relevant disciplines and sectors.”

The Alliance may not continue to exist physically, but let the spirit of the Alliance continue to live in us and with us.

**Coming together is a beginning;  
keeping together is progress;  
working together is success.**

Henry Ford

I want to leave you with one last message, a quotation ascribed to Henry Ford. The Alliance has made us come together; let us keep together; and above all work together. This will be the success which will define the future for the microbicide field,