

“CURE” IS NOT A CURE

(The **XXI International AIDS** Conference,
the **V “Towards an HIV Cure”** symposium,
VII 2016, Durban)

(translated from Latvian)

After 16 years the World AIDS conference is back to Durban. Why?
Maybe because S. Africa still has the hardest course of HIV infection in the world. But maybe to recognize its success? E.g., it has driven mother-to-child HIV transmission down to 4%!

(A historical note: AIDS has been in Africa since 1935.)

But globally? Since 2010, new HIV infections have fallen by 6%!

The conference was preceded by several 2 day satellites.

One of them was **the V “Towards an HIV Cure”** symposium.

It had its own scholarship programme. This year there were 2 grantees from the CE Europe.

Nowadays cure research is the most prioritized field of scientific HIV research. Still, some speaker remarked that too much money is spent on vaccines and treatment, not on cure.

The symposium was co-chaired by Nobel prize winner Françoise Barré-Sinoussi from Pasteur institute in Paris.

First, on the misleading **definition**. The word “cure” is just a label, an aspiration. And there are still doubts that “cure” is possible.

There are **2 types of “cure”** researched:

I **“Sterilizing” cure** should completely eliminate HIV from the body.

II **“Functional” cure = undetectable VL without the use of ART = “remission”**.

And remission, according to F. Barré-Sinoussi should be achievable.

Nowadays the following **cure strategies** are investigated:

1. **“Shock and kill”**: shocking HIV out of resting cells and then killing them. Among the shock agents considered are currently used as cancer treatments.
2. **Gene manipulation**: seeking to change a person's cells so that HIV can not infect them. This can be done by altering the genes of a person's immune cells. It would involve extracting CD4T cells and then modifying them.
3. **Stem cell transplants**: they are used to treat life threatening illnesses such as cancer (*e.g., the “Berlin patient”*). Hematopoietic stem cells are the source of all blood cells in the body. Stem cell transplants are a last resort for people with both cancer and HIV. This strategy is not scalable.
4. **Therapeutic vaccines**.

At the same time there are **challenges** related to cure research, e.g.:

- a) There is no clear way to measure the HIV reservoir.
- b) All the strategies carry unknown risks and benefits for potential trial participants.

What about the success in cure field?

American scientists reported that their combination of latency reversing agents: PKC agonist (*gnidimacrini: GM*) and histone deacetylase inhibitor (*thiophenyl benzamide: TPB*) provides a unique and **effective option in reducing the latent HIV-1 reservoir!** (*oral OA3-4*).

Other scientists investigated whether ongoing replication occurs in tissues. They studied 3 individuals who initiated ART shortly after HIV infection and maintained viral suppression for >8 years. As a result – no ongoing HIV replication was detected in tissues compared to peripheral blood, suggesting **cART blocks active HIV replication, including in tissues!** (*o. OA2-5*) (*conf.oral THAA0104LB*)

Th. Ndung'u reported on the *FRESH* study in S.Africa:

A group of young women who were **diagnosed in very early** infection and **immediately given ART** preserved their CD4 counts and the function of cells that HIV normally disrupts. The majority (*19 of 22*) of them never sero-converted, **staying HIV negative** despite having evidence of low levels of HIV infection in cells! (*They are ongoing their ART*).

French researchers pointed out that **vit D deficit** is also associated with disease progression. They concluded that vit D deficiency **participates to the HIV reservoir maintenance** (*poster 41*).

Back to **the conference**.

It gathered >15000 participants. Among them – UN Secretary General Ban Ki-moon, Prince Harry of Wales, Bill Gates, Sir Elton John and Charlize Theron. One could occasionally meet the first inventor of protease inhibitors and other celebrities.

The conference's programme was built from one of the most competitively scored abstract submissions in history: 36% of regular abstract submissions were accepted for presentation.

This was also a big gathering of transgenders, with an amount of sessions devoted to their problems relating to HIV.

992 volunteers helped at the conference. Some of them – from far away countries. Some gathered the airfare asking for donations from their friends (*real and virtual ones*). Volunteers had most different tasks. Some agreed to push disabled PLWHA in their wheelchairs throughout the conference. Some had so many tasks that they had to drink energizers – one was noticed running with his head right into a glass door, and without perceiving it, happily proceeding on. Organisationally, the conference was quite successful. Just we heard rumours that delegates in 3 days time experienced 10 robberies in the city. During the registration for the conference, behind its desks I noticed a lady reading a book "What if There Were no Whites in S. Africa".

The 90:90:90 target (*90% of PLWHA diagnosed, 90% of them on treatment, and 90% of those with undetectable VL by 2020*) is intended to end the AIDS

epidemic by 2030.

Sub-Saharan African countries are moving quickly to the recommended Treat All (p. THPEB057).

But the Australian state NSWales has made a significant progress towards ending the HIV epidemic by 2020.

The situation now is the following:

- Worldwide: 57% : 46% : 38%
- E&S Africa; 56% : 54% : 45%
- Asia & Pacific: 64% : 41%
- W&C Europe and N America: 89% : 59% : 47%

- E Europe, C Asia, W&C Africa are falling far behind these regions! And without major changes and investments, the 90:90:90 target is not achievable.

Only 22 countries have adopted WHO 2015 treatment guidelines (*ART for every HIV-diagnosed person*). The biggest gap between diagnosis and treatment is especially large in Asia, Pacific, W Europe and N America.

These were the numbers presented by the UNAIDS Executive Director M. Sidibe in his Progress Report.

One of the most important messages brought by the conference was PARTNER study results. They showed **zero** linked **HIV transmissions** from >58000 individual times that **sero-different couples (both straight and gay)** had **sex without condoms, provided the VL of the HIV+ partner is undetectable**. Neither the presence of STIs nor likely viral load blips between tests had any impact in enabling transmission. These results also challenge criminalisation laws in many countries (*including the U.S.A.*) that continue to imprison people.

Adherence is still a problem to many.

Challenges with daily oral medication have stimulated the development of long-acting injectable (LAI) ART. **Cabotegravir + rilpivirine injection every 4 or 8 weeks has shown an effective VL control** in people switched from their daily oral ART regimens. American and British scientists discovered that these patients prefer the LAI ART to daily oral regimens due to practical and emotional benefits: it is more discreet, helps in managing stigma and has less possibility of others discovering one's HIV status (o. THAB0204).

As we know, **ART simplification** brings less side effects, reduces pill burden, and is financially favourable to the budget.

Argentinian scientists (*CARDEL trial*) proved that a dual therapy (DTG/lamivudine) produces rapid virologic suppression (*with a favourable safety/tolerability profile*) in HIV+, treatment-naïve individuals, thus showing that **this dual therapy is as effective as the traditional triple one** (o.FRAB0104LB)

One of the conference side events was a community lecture on a preventive HIV **vaccine**. This vaccine has shown a ~50% effectiveness. During the lecture it was stressed that ART is becoming too expensive, so we are never going away without a vaccine.

On the other hand, at another meeting it was mentioned that too much money is being spent on vaccines with no results as of yet. (*Some American vaccine specialist who works for the government confessed that his salary is ¼ mln. \$/yearly*).

Now, on life- styles.
One of the most significant clinical challenges in HIV is a decline in bone mineral density (BMD), suggesting a tendency towards osteoporosis/and fracture. German and Nigerian scientists compared moderate intensity aerobic (*MIA*) exercises and **progressive resistance exercises (PRE)**. Their conclusion is that **the highest positive change factor for BMD** occurred with the PRE group of patients on ART. Importantly, ART should not be commenced without complementary exercises (*considering its observed adverse effects on BMD*)! (*p. THPEBO82*).

Interestingly, there has been the first controlled alcohol administration experiment to assess whether level of objective intoxication differs by HIV serostatus. Researchers discovered that **blood alcohol concentration (BAC) was significantly lower among HIV+ participants**. Viral load and taking ART were not significantly associated with BAC. So, contrary to predictions, HIV+ participants attained BACs that were 6-7% lower than their HIV- counterparts (*p. THPEB083*).

During the conference one had to conclude that **anti- smoking campaigns** (*also in connection with HIV*) have their results. Indeed, very few conference delegates were seen smoking!

Until recently, **PLWHA** were completely excluded from life insurance in Switzerland. After a sobering feedback, the Swiss AIDS Federation established a cooperation with an insurance broker. By interposing him, several insurers agreed to make a **life insurance contract**. This may pose a good example to other insurers (*p. TUPED382*).

As usual at the World AIDS conferences, the Global Village gives relaxing moments. The daily morning rave seeks to reconnect people with their bodies, a human drive towards a healthier, more energized and more integrated you. Many participants joined this rave.

But nobody (*except one local boy*) could repeat the vibey moves of Afro- zumba dancers, accompanied by Zulu drummers. Especially, that the girls were kicking upwards a straight leg past their heads!

For a joyous remark at the end, here comes a quote (*“Journal of Viral Eradication”, July, 2016*):

“...tremendous improvements in life expectancy of PWA have been observed, and in some cohorts, **life expectancy is greater** than in the general population..”

Inseparably yours - A.Kalnins - AGIHAS