Research Article

Effective Vaccine against and Immunotherapy of the HIV: Scientific Report and Ethical Considerations from Cameroon[1]

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ABSTRACT

In this paper, the scientific results, of biomedical research on a therapeutic vaccine for HIV carried out by V. Anomah Ngu since the 1990s in Cameroon are presented and some relevant ethical considerations and implications raised. The initial results of the research were first orally presented to the Cameroon Academy of Sciences on 2 December 1999 in a paper titled: '**Vaccines for the HIV: Past Efforts and Future Prospects'**. The problematic that set off the research was the puzzle as to why the natural HIV infection provokes immune responses that fail to kill and eliminate the virus from the body. The intuitive hypothesis of the research was the conviction that the key to an effective vaccine against the infection lay in identifying, understanding and eliminating the reason for this failure. Given the gravity of the HIV/AIDS, especially in sub-Saharan Africa and other poor regions of the world, some of the ethical imperatives motivating the research include finding a simple and effective vaccine that can be cheaply and affordably produced, using traditional rather than high technology methods. A candidate vaccine that fits this description has been discovered through V. Anomah Ngu's research. The vaccine, tentatively named VANHIVAX, has so far been tested on a very limited scale (on HIV-positive persons) in Cameroon with what we consider very hopeful and promising results.

Key words: HIV/AIDS, therapeutic vaccine, VANHIVAX, Cameroon

RÉSUMÉ

Le présent article présente les résultats scientifiques de la recherche biomédicale menée au Cameroun depuis les années 90 par V. Anomah Ngu sur un vaccin thérapeutique contre le VIH. Il soulève également quelques questions éthiques pertinentes et explore leurs implications. Les premiers résultats de cette recherche ont, pour la première fois, été présentées oralement à l'Académie des sciences du Cameroun le 2 décembre 1999. Ce fut dans un article intitulé '**Vaccins contre le HIV: chemin parcouru et à parcourir'**. Il était question, dans cette recherche, de comprendre pourquoi l'infection naturelle au VIH provoque des réponses immunitaires qui ne réussissent pas à tuer et éliminer le virus du corps. L'hypothèse intuitive était que le chemin vers un vaccin efficace contre l'infection passe par l'identification, la compréhension et l'élimination de la cause de cet échec. Au regard de la gravité du VIH/SIDA surtout en Afrique au Sud du Sahara et dans d'autres régions pauvres du monde, certains des impératifs éthiques qui motivaient la recherche étaient la recherche d'un vaccin simple et efficace pouvant être fabriqué et vendu à moindre coût au moyen d'une technologie traditionnelle plutôt qu'une technologie de pointe.Un vaccin potentiel remplissant ces conditions a été découvert grâce aux travaux de V. Anomah Ngu. Ce vaccin provisoirement dénommé VANHIVAX a déjà été testé à très petite échelle (sur des personnes séropositives) au Cameroun avec des résultats qui nous semblent très prometteurs.

Mot clés: VIH/SIDA, vaccin thérapeutique, VANHIVAX, Cameroun

[1]Le présent article a été présenté pour la première fois au Cinquième Congrès mondiale sur la Bioéthique organisé à Imperial College, Londres, Royaume-Uni, du 21 au 24 septembre 2000 avec pour titre *Effective vaccine against and immunotherapy of the HIV: Scientific report and ethical considerations from Cameroon (Ngu, V. A. and G. B. Tangwa (2000). Fifth World Congress of Bioethics, Imperial College, London, UK.*Les aspects scientifiques de l'article ont été traités par V. Anomah Ngu ; Godfrey B. Tangwa s'est occupé des aspects éthiques.

PART ONE: GENERAL AND ETHICAL CONSIDERATIONS

Introduction

In pre-colonial Africa, access to healthcare, in general, and treatment of illness, in particular, was within the reach of all and sundry, irrespective of social or economic status (Tangwa 1999). Prophylactic medicines, whenever they were prepared, and wherever they were available, were freely distributed to all and sundry and it was inconceivable that a sick person could present before a healer and fail to get treatment for any reason other than, perhaps, the acknowledged incompetence of the particular healer for the particular illness, in which case the patient was usually referred to a more knowledgeable or more competent colleague in the domain. The only necessary and sufficient condition for accessing medical treatment in traditional Africa was, thus, the simple fact of being ill and in need of treatment. Moreover, the whole community felt concerned when anyone was ill, and all available resources, both personal and communal, were mobilised in search of a cure, because health was considered, quite rightly, as the value of all values, the value that makes other values possible and meaningful.

Contemporary African Situation

In Africa today, the situation is completely different, thanks to the combined effects and influences of colonisation, Christianisation, Westernisation, monetarisation of the economy, strict specialisation and ongoing globalisation; thanks to the rise and spread of medical charlatanism, especially in urbanised areas. For one thing, the African traditional worldview and outlook (Tangwa 1996) which were deeply communitarian, have slowly yielded, under the onslaught of these effects and influences, to an increasingly more individualistic worldview and outlook, whose chief motive force is commerce and the profit motive. One of the consequences of this state of affairs is that healthcare and treatment of illness in Africa today, unlike yesterday in the traditional past, have increasingly become individualised luxuries, beyond the reach and aspirations of the vast majority of the populations. In short, need is no longer a criterion for accessing healthcare or treatment; it no longer seems possible to combine poverty and health, as the latter is increasingly becoming a commodity available and affordable only for the rich.

To make things worse, this situation has coincided with the recent emergence of novel and extremely deadly epidemic diseases of which the acquired immune deficiency syndrome (AIDS) is, perhaps, the most terrifying. AIDS has the poise and posture of a global pandemic, but there is no doubt that it is particularly an African problem. According to recent statistics (WHO 2013, UNICEF 2015), about two-thirds of all global cases of HIV/AIDS occur in sub-Saharan Africa. In addition, of the approximately 6000 new HIV infections recorded each day, 68% are in sub-Saharan Africa. In 2013, nearly three times as many adolescent girls (15 to 19 years), (UNICEF 2015) in sub-Saharan Africa were newly infected with HIV than boys in the same age group. The HIV/AIDS epidemic is therefore taking a staggering toll in Sub-Saharan Africa and has overtaken every other disease as the top killer in Africa. HIV/AIDS is responsible for an estimated 1.5 million deaths in 2013 of which 1.1 million were in sub-Saharan Africa, In Cameroon, the prevalence of HIV amongst adults aged 15-49 is 4.2% (WHO 2013). The HIV (**human immunodeficiency virus**) probably found its way into Cameroon in the late seventies or early eighties (Parry 1986). By the late eighties, when the public health authorities first started timidly talking about it, most Cameroonians were still very sceptical about the existence of the virus, some claiming that it was a ploy to discourage sexual activities. Today, scarcely two

decades afterwards, there is scarcely a Cameroonian among the approximately 20 million inhabitants who can rightly claim not to have lost be it a close relative, neighbour, friend or colleague to the AIDS pandemic.

This Report:

The report of the on-going research that is presented here was initially inspired by the African adage that, when a child gets missing, it is justifiable to trespass even the sacred grove of the most fearsome of gods in searching for him/her; in the face of a deadly emergency, it is inevitable and justifiable to step over the procedural rules of normal times. This has been aptly demonstrated in the response to the recent Ebola outbreak in West Africa, whereby some Ebola Patients received experimental drugs/therapy (Butler 2014, Pollack 2014, Richardson 2014) that had not gone through the rigorous process of clinical trials, let alone having been proven effective in animal models. AIDS is such a terrifying and indomitable enemy, affecting and threatening so many people all over the globe that all efforts against it, no matter their origin or originators, deserve to be given a fair hearing and supported, if at all they hold any iota of credibility or ray of hope. Furthermore, it is a matter of simple rationality that the simpler and cheaper proposals available should be given a hearing first, before the more complex and more expensive ones. A complex problem need not necessarily have a complex solution. Examined in a simple manner, a complex problem may yield a very simple key to its own solution. The research reported here seems to have yielded precisely the key to such a simple solution to an otherwise complex problem, with very useful lessons for approaching and tackling similar problems. But, owing perhaps precisely to the apparent simplicity of the proposed solution, the research has, so far, failed to overcome the scepticism of those, both at home and abroad, who are best placed and in a position to help give it efficacious viability.

Some Ethical Considerations:

The contemporary world is one in which great wealth and affluence coexist with abject poverty, a world in which the assurance of robust health and longevity for some is standing face to face with deadly epidemic diseases and premature death for others. The contemporary world is a world, like all others before it, where power and wealth and influence determine the 'to be or not to be' of every other thing. A causal link has often been traced between the wealth of some and poverty of others in the world. Does a similar link exist between health for some and disease for others? If we consider the attention and resources devoted to research in the domain of luxury medicine, enhancement and cosmetic therapies, in the affluent parts of the globe, by contrast with primary health and epidemic diseases, it is hard to completely rule out the existence of a causal link. It cannot be gainsaid that the Western world or northern countries dictate the state, pace and tempo of things, including 'the good, the bad and the ugly', as they are in the world today, thanks to its science and technology, military might, power and influence, wealth and affluence. Western social and economic ideologies have played a role in the rapid development of medicine in our epoch, but it is apparent that medicine, on the one hand, and commerce, driven by the profit motive, on the other, are very bad companions and that the global community, in facing the health/healthcare challenges of the 21st century, should avoid being taken hostage by or capitulating to pure market forces. Business and commerce, no matter what can be said in their favour, pose a great danger to the ethics of health, healthcare, medicine and biomedical research in an era where poverty and disease have become bedfellows, an era in which it seems no longer possible to be poor and at the

same time dignified and respectable, because it seems no longer possible to be poor and healthy.

PART TWO: SCIENTIFIC REPORT

1. Introduction.

An ideal vaccine for the HIV should:

• Provoke immune responses in a vaccinated person that actually eliminates the Virus;

• Contain all the critical viral antigens, so that the provoked immune responses can act on the whole virus without ignoring any of its parts or components;

• Be simple and cheap to produce.

2. Conceptual Starting Point:

The search for such vaccine started with the puzzle as to why the natural HIV infection provokes immune responses that fail to kill the virus and eliminate it from the body. If this puzzle could be unravelled, then the factor responsible for the failure could be identified and, if possible, removed. The immune system could then be induced to produce immune responses that kill the virus. Understanding the virus was thus for us the key to understanding the required credentials of an effective vaccine.

3. The structure of the HIV:

It has been known ever since the discovery (Barré-Sinoussi, Chermann et al. 1983)) and study of the fine structure of the HIV(McKeating and Willey 1989)) that it is an enveloped virus. The viral envelope is derived from the host cell CD4 wall, as the virus emerges from the infected cell The presence of the host cell wall elements as the viral envelope has very important immunological implications that have, apparently, been ignored by the scientific community.

4. The immune response to the HIV:

The ability of the immune system to destroy any given virus depends on how the immune system perceives the virus in question: whether as completely alien or foreign to the body, i.e. **non-self** or as kindred, i.e. **partly-self,** because the virus shares some of its structures with those of the body. The HIV is perceived by the host immune system as **partly-self** because its envelope is derived from CD4 cells. All things being equal, immune responses to a **non-self** virus will be considerably stronger and more effective in killing such a completely alien virus than that to a virus, like the HIV, which is perceived as somehow kindred or **partly-self**.

Now, if the immune system were somehow to ignore the presence of its own cellular elements in the virus, and to consider the HIV as a completely alien intruder or **non-self** (instead of as **partly-self**), the corresponding immune responses would destroy not only the virus with its envelope but also all CD4 cells from which the viral envelope was derived. This would constitute a serious autoimmune disease. To avoid such a fatal outcome, the immune system is "obliged", that is, "black-mailed", so to speak, to produce immune responses that do not destroy the virus in order not to destroy itself with the virus. The instinct of self-preservation is at work here. The viral envelope of the HIV is unquestionably it's most powerful secret weapon, which it uses to great effect. Blackmail is its *modus operandi*!

5. Ideal Solution for the Body:

The ideal solution for the body is one where the immune responses kill only the virus without any damage to its envelope and therefore the CD4 cells. To provoke such ideal immune responses in an uninfected person, i.e. by vaccination, one must start with HIV antigens from which the viral envelope has been destroyed before hand, transforming it into **non-self** antigens. Such

immune responses will kill an **invading virus,** sparing its envelope and CD4 because the envelope was absent from the viral antigens used to vaccinate the uninfected person. The procedure is effective because, from the start, it is directed against the virus only.

All HIV antigens, minus its envelope, would thus be an effective vaccine for the HIV! Since there is no established hierarchy for HIV antigens, all its critical antigens should be present in the vaccine. (It is significant to note that in HIV infected persons, there are no immune responses to the viral envelope, because of its host origin; it has been taken as a hostage, so to speak, by the virus).

To prepare an effective vaccine for the HIV, therefore, one destroys the viral envelope with lipid solvents, by using, for example chloroform which acts on the phospho-lipo-proteins of the envelope. The chloroform destroys only the HIV envelope and the supernatant, VANHIVAX, was injected either as a simple vaccine subcutaneously or after culture in vitro with the washed peripheral leucocytes of the patients (Ngu, Ambe et al. 2006). The solvent is removed and the residue constitutes the vaccine. It is a safe vaccine because, without its envelope, the HIV cannot infect other cells and the vaccine would thus consist of non-self, non-life and non-enveloped HIV viral antigens only.

6. Pre-testing the vaccine as an autologous vaccine:

Ideally, a prospective HIV vaccine should be subjected to a three phase trial involving: 1) test for antigenicity in animals; 2) test for safety in humans; 3) test for effectiveness in preventing infection. But, given the extreme urgency of our situation, the lack of financial resources, the scepticism of possible funding agencies, the general incredulity of the public, such a *parcours* could not be followed in this case. This might have led to the wide spread rejection of VANHIVAX by the scientific community, despite the scientific logic behind the proposed vaccine and the conditions (epidemic) under which it was being studied. The important thing at this stage, moreover, was quickly to show that the vaccine provoked immune responses that actually do kill the virus. What was done then, after obtaining the approval of the ethical committee and the informed consent of those concerned, was to prepare the vaccine from the viruses of sero-positives who had not yet developed clinical AIDS and whose immune systems were judged to be still more or less competent. The vaccines were then pre-tested, in each case as *autologous* vaccines in the very persons providing the virus. This is a new idea which will, no doubt, be contested by some orthodox immunologists.

The scientific and immunological basis for pre-testing is given in a previous paper (Ngu 1997)). Briefly, it is as follows: circulating in the peripheral blood leucocytes of normal persons, are various groups of immunocytes - macrophages, monocytes and lymphocytes including T_4 T_8 lymphocytes - assigned, as it were, to the various pathogens in the body including the HIV, bacteria, parasites and fungi etc. If the immune system of the person is indeed still competent, there would be other immunocytes, fresh from the bone marrow, that are on "standby", as it were, not yet committed to any specific pathogen but ready to deal with any new pathogen that invades the body. That uncommitted immunocytes exist in HIV infected persons can be deduced from the fact that at the beginning of the HIV infection, most other pathogens are held in check adequately. The progressive destruction of the immune system by the HIV, however, reduces the stock of uncommitted immunocytes available to deal with new infections, which as opportunistic infections, overwhelm the patient eventually.

When an autologous vaccine, prepared from the blood of a sero-positive with adequate uncommitted immunocytes UI is cultured *in vitro*

with his/her washed peripheral leucocytes in a medium free of host serum, the UI in the peripheral leucocytes perceive the vaccine as **non-self** antigens of the HIV and start to process them as such. When the cultured UI are later re-injected into the person concerned, they will constitute in him a sub-set of immunocytes sensitised only to the **non-self** antigens of the HIV. The immune responses provoked by this sub-set and its descendants will progressively kill the HIV, leaving its envelope intact. Repeating the procedure at suitable intervals can reinforce this action.

The progress of viral elimination can be monitored by estimating the virus load (RNA/PCR), where possible, and the $CD_{4,}$ CD_{8} counts and by other immunological and haematological parameters. The improvement in the clinical status of those with symptoms can also be considered as indirect evidence of viral destruction. It is sufficient to show that there is significant viral destruction in an infected person for the effectiveness of the vaccine to be demonstrated. If, however, total viral killing were achieved in an infected person as shown by RNA/PCR, this would, in addition, provide a new form of immunotherapy for the HIV. Vaccines prepared on this basis can be expected to be effective in a general population of uninfected persons.

7. Preliminary Results:

Twenty (20) patients were seen since 1996 when CD4 could be counted. These included 10 males and 10 females, with ages ranging from 29-55, the active sexual age. There were only 2 patients with CD4 counts considered normal, 9 showed moderate immune depression, 6 with severe and 3 with very severe immune deficiencies.

Following immunotherapy, all patients showed a rise of CD4 which was slight in the 2 with no immune deficiency at the start, moderate in most cases and was quite high in the patient-6, for reasons that we are as yet unable to explain. All patients showed an improvement in their clinical status – diarrhoea stopped, weight was gained and haematological parameters improved.

Follow up studies have since been documented as peer reviewed journal articles (Ngu and Ambe 2001, Ngu, Ambe et al. 2002, Ngu, Besong-Egbe et al. 2007) and conference presentations (Ngu, Ambe et al. 2006)

8. Discussion.

Most of the patients had clinical AIDS whereas early sero-positives would have been preferred. Follow-up was difficult for logistic reasons. Routine laboratory tests including CD4 counts were frequently beyond the financial means of most patients; poverty is high and some families abandon some of these patients. Viral load estimates by RNA/PCR was not available.

Despite these and other limitations of the study, and in particular the variations in the methods used for preparing the auto-vaccines and the time intervals for evaluating the CD4, the clinical recovery of the patients and the rise of their CD4 suggest that the vaccine *provoked* immune responses that killed the virus in the patients. The viral killing was probably incomplete in most of them but it did occur, which is the important point. (No other candidate vaccine, so far, has been able to do this). The activity of this vaccine deserves the attention of those engaged in the field of vaccines. For persons infected with the HIV already, the proposed immunotherapy, when perfected, should offer, especially for the early sero-positives, a relatively simple and cheap form of treatment.

8. Conclusion:

The promises of this preliminary report will be fully realised only after its confirmation in a study involving a better and bigger selection of

patients, in a collaborative effort, with adequate logistic support. After such confirmation, effective and cheap vaccines could be confidently proposed for trial to the public with a very high probability of acceptance, because these vaccines have shown their effectiveness in patients. The WHO and other interested partners could then lead the production of vaccines on a regional or sub-regional basis, using the type or sub-type of the virus prevalent in the region. The time frame for this will depend on the speed and seriousness with which these suggestions are pursued.

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Conflict of Interest: None

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