The Case of the Libyan HIV-1 Outbreak

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El-Fateh Children's Hospital case has proven to be more enigmatic than most of us predicted when it first came to surface. The social and legal implications of this case have clouded the scientific thinking process of many. In our opinion, as scientists we should look for the truth no matter what its' outcome. Politicizing a scientific matter always leads to a dangerous abyss. The only way to do so is to try to comprehend what exactly happened based on scientific evidence regardless of who did it and why!

Currently, there are two opposing points of view. On one side stands some of the greatest Western AIDS experts, and on the other side is the Libyan National Experts Committee, composed of well-regarded authorities in the field of HIV-1/AIDS. There have been numerous reports published in well respected Scientific and non-scientific journals that appear to mostly represent the Western points of view. We attempted to rebut an article that appeared in the New England Journal of Medicine but were immediately turned down [1].

The Western scholars considered the tragedy the result of massive nosocomial infection due to poor infection control measures. Their conclusion was based on several facts, including the presence of HCV infection in some of the children infected with HIV-1, indicating the breakdown of the infection control system. The HIV-1 strain responsible for this nosocomial infection belongs to the subtype AIG, a recombinant form of virus frequent in Central and West Africa but nevertheless, a very unique HIV-1 strain. All samples sequenced from these children belong to a single and monophyletic HIV-1 strain never seen or reported previously in the HIV-1 database. Of note, the children were not infected by vertical transmission making the argument strongly in favor of nosocomial infection [2-4]. Western scholars are also puzzled by the unusual transmission rate of this outbreak.

Although all of the above arguments are based on facts, it can carry a different interpretation. There are three very important arguments that need to be addressed. First is the use of HCV to booster the scientific argument of nosocomial infection [1-4]. This logic would be successful in a normal situation, but in the Libyan outbreak this appears to be an unsound reasoning. HCV found in these children may have infected them by vertical transmission. HCV is a relatively common infection in Libya as well as in many parts of Africa. The four related genotypes of HCV reported in these children are also the same that are common in this part of North Africa [2-3]. In addition, vertical transmission of HCV is well established [5]. Second, it is already established that the mothers of these children were HIV-1 seronegative and the HIV-1 infection did not come to these children via vertical transmission [2-3]. Therefore, mixing these two viruses that have entirely different pathogeneses is scientifically unsound [5]. The third point relates to the uniqueness of the HIV-1 strain that was found in the infected children [2-4]. All three scientific data revealed that the Libyan outbreak was due to the monophyletic HIV-1 [2-4]. It is a unique sequence that did not exist previously [CRF02-AG: 2-4]. Some investigators have hypothesized the possibility of infection originating from the thousands of sub-Saharan immigrants to Benghazi [1-4]. If we take this hypothesis at its face value then it does not explain the monophyletic nature of the HIV-1. In sub-Sahara Africa, there are at least several hundred strains of HIV-1 [M, N, and O groups and subtypes: 6-7] and most likely several hundred thousand quasi-species of HIV-1 [8]. If a few infected individuals started the "outbreak" then it does not explain the monophyletic nature of this unique genetic virus. In the scientific literature the "monophyletic" lentivirus is found in experimental innoculation of "cloned" HIV-1 or SIVs utilized for vaccine trials in primates [9-10)]. Finding such a virus in human outbreak is unheard of and is very alarming. Furthermore, even in the experimental primates utilized for AIDS research, if more than one genetically closely related strain are used for vaccination, they develop a series of new recombinant quasi-strains, discrediting the argument of HIV-1 that initiated the outbreak originated from the immigrants [11].

The Libyan National Experts Committee refuted the Western reports, stating the assumption of a nosocomial infection lacked epidemiological evidence and scientific proof [12]. The incident was localized to a single hospital (El-Fateh Children's Hospital) and not observed in any of the other hospitals in the city of Benghazi.

The final report by the Libyan National Experts Committee raised several valid questions, considered by the Western media and some scholars as generalities. However these generalities represent the core of the problem. Lack of basic hygiene and infection control measures in hospitals is still a major problem in most of the developing countries. Libya is just one country in a long list of developing countries with

infection control problems. El-Fateh hospital is one of several government hospitals in Benghazi. Keeping this in mind compels us to question why similar incidents never happened before. The theory that a single patient started this epidemic somewhere in 1994-97 suggests a very unrealistic and unreported rate of HIV-1 transmission [2-4]. If such a rate was achievable by any strain of HIV-1, then that strain would have been widely spread all over the region. Moreover, similar incidents would have occurred in several developing countries in the region with poor infection control measures. What makes El-Fateh hospital such an unusual place to have this alleged high transmission rate of a unique and monophyletic HIV-1 strain, in contrast to all the other hospitals in the same city? In addition, the high rate of transmission blamed on nosocomial infection has serious flaws. For example, if one takes the CDC guidelines that are accepted worldwide that there is a 0.3% infection rate by so-called unhygienic conditions then one must have injected several thousand children with the contaminated needles [5]. One needs to realize that if one injects an uninfected child with a needle that was used recently for a infected child and then dipped it in hot water (that is a common practice in many developing nations), the infection rate from that particular needle would be between 0.3%-0.009%, (3 in 1000 to 9 in 100,000) according to the CDC guidelines [5] (of note, 0.3% risk is for health care workers who were accidentally stabbed with a contaminated needle that was just used for an HIV-1-infected patient, and these individuals have to incur a deep subcutaneous wound with that particular needle without dipping in hot water; [5]. However, in the case of Libyan children the dirty needles were not reused at all [12]. Supposing we consider the Western scientists' argument and take these rates at face value, then one has to infect between 200,000 to several hundred million children with contaminated needles. Obviously, the numbers do not add up! These numbers exceed the number of children, not only in Benghazi, but in the whole country of Libya.

Finally, we would like to point out a major scientific flaw in the calculation of the timeline for this particular strain of HIV-1 [2-4]. All three studies have utilized some version of the Bayesian method to determine when this particular strain of HIV-1 came about in these infected children. The genetic phylogenic method which they have utilized is based on relatively sound mathematical analysis tools [2-4], and had been used to calculate the timeline of genetically stable proteins and nucleic acids. Unfortunately, in the case of HIV-1 such analytical tools are less reliable and in certain cases become useless. For example, all these authors assumed that in the case of HIV-1 molecular change is a linear function of time and that base substitutions accumulate according to a Poisson distribution. [13]. However, the genetic analyses completed by both of these groups are based on false assumptions. These investigators appeared to have ignored the most basic characteristics of retroviruses [8,11]. As compared to other viruses or genes, retroviruses have an amazing ability to rapidly form new recombinant viruses and the Libyan HIV-1 strain is a recombinant virus itself [2-4]. Utilization of Bayesian algorithm in the case of retroviruses has been challenged on mathematical grounds by Schierup and Hein [14]. Therefore, we argue that recombination is the simplest explanation for the lack of a molecular timeline in many data sets of viruses. For example, the recombination rate for HIV-1 is likely to be higher than even the largest value used in the published studies on the Libyan HIV case [2-4], making the timeline estimates invalid or at least inaccurate [13-14]. Thus, dating the origin of the HIV-1 in this outbreak from early sequences may yield misleading results [14].

It is important to note also that the Libyan committee failed to give any proof that the outbreak was the result of an act of bioterrorism, and instead concluded that data available did not contradict the possibility of a deliberate transmission of HIV-1 to the infected children. Scientifically, one can state that in light of the glaring evidence of a monophyletic HIV-1 strain that has never been reported previously, and an unlikely scenario that such a high transmission rate was the result of the incompetence of the infection control unit at El-Fateh hospital, one suspect that some sort of malpractice has taken place. However, we as the outsiders cannot make this judgment. Like in any sovereign nation, this has to be decided by the judiciary arm of the Libyan government.

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