We need a vaccine for Lassa fever

Shima Gyoh laments that while the Lassa fever is powerful its commercial clout is disappointingly low. How might a vaccine emerge?

An epidemic of Lassa fever swept over 10 States of Nigeria from December 2015 to January 2016. A World Health Organization (WHO) report said there were 140 suspected cases with 53 deaths giving a case fatality rate of 37.9% This is shocking, but we must remember that Lassa is the cause of viral haemorrhagic fever in West Africa, and its cousin, Ebola, used to live exclusively in the rain forest of the Congo basin until it came calling two years ago. The virus is a commensal of the common rat that the people consider a delicacy, and I was nearly heckled out of a lecture by the audience during what was supposed to a solemn formal, academic ritual for daring to suggest that their delicious field rat was the carrier of a deadly disease. Epidemiologists have suggested that the disease could be minimised if not eradicated by intensive environmental measures that would reduce or eradicate rats from the environment. It is not a joke that, throughout West Africa, the majority of the population, is in denial, insisting that the rat they regard as a delicacy could not possibly be the carrier of the nasty Lassa virus. They emotionally insist that *Mastomys natalensis* is altogether a vastly different animal from their delicious rat. 'You want to exterminate our main source of protein? You'd have to do us in first!' Fortunately, it wouldn't come to that since the financial, political and logistic obstacles are presently pretty insurmountable.

The WHO report of that epidemic spoke of containment without mentioning vaccination. The situation, however, makes vaccination an obligatory weapon. It is estimated that over 200 000 Lassa infections occur every year, with some 3000 deaths. Despite the denial of the indigenes, the reservoir rats live both in the fields and within our houses.

Lassa fever has been known for the last 47 years. If people from the developed world can avoid catching a tropical disease, research into its cure and prevention move at snail speed, and the viral haemorrhagic fevers came into this bracket. Two factors have altered the equation. First, because they are so lethal, viral haemorrhagic fevers could be developed into biological weapons. Second, modern air travel means patients incubating these diseases can fly to and become infective in the developed world. These factors drew smouldering attention of the developed world until the tragic West African Ebola epidemic shocked everyone, emphasising the need for their vaccine development, but it is no easy task.

First, it is commercially unattractive to develop vaccines that would be used only when epidemics threaten, and in poor countries that can hardly afford it. Second, vaccines made from killed Lassa virus have been found to give good humoral response, but little protection, even after several booster doses. Effective vaccines need to contain live but attenuated virus that are still replication-competent. This combination stimulates robust cellular response and gives adequate protection even from one dose. However, the virus in such vaccines can undergo reassortment, recombination and once again become pathogenic, especially in the immunocompromised, like HIV-infected individuals.

Genetic strategies can avoid these complications. Geisbert et al of Canada took the outer protective glycoprotein envelop of the Lassa virus and inserted it on Recombinant Vesicular Stomatitis Virus (VSV). Used as a vaccine, it has been shown to protect Lassa-susceptible monkeys from infection against even the highly pathogenic Josiah strain. The unanswered questions are, how long would this protection last? Would it cover all other strains of the Lassa virus? How safe is the VSV carrier itself?

The vaccine has not yet been tried on humans. First, the sporadic occurrence of Lassa does not easily lend itself to vaccine trials. Second, the precaution for avoiding infection are well known and it would be unethical, too dangerous to relax them for vaccine trials. It is also unlikely that any ethical committee would approve inoculating vaccinated volunteers with the pathogenic Lassa virus. Nevertheless, if it passes comprehensive animal tests, careful trials for safety in human volunteers is feasible.

Outbreaks of Lassa fever occur practically every dry season, coinciding with the period when young people go burning the jungle and digging underground rodent channels to catch rats. They get infected by bites or contamination of skin abrasions with rat biological fluids. While 80% of the infected show little symptoms, few develop serious illness and seek medical attention, exposing health workers to the more aggressive strains.

Once the vaccine has been shown to be safe in humans, it could be rushed to areas of infection and used to vaccinate health workers and other susceptible individuals, thus creating a ring of immunity around the nidus of the potential epidemic. The Giesbert vaccine should urgently undergo human safety tests so that it could play a role in limiting the annual carnage from Lassa fever outbreaks, which are now becoming perennial in Nigeria.

Shima Gyoh has held many posts ranging from village doctor to DG of Nigeria's Federal Ministry of Health and Chair of the Medical and Dental Council of Nigeria.

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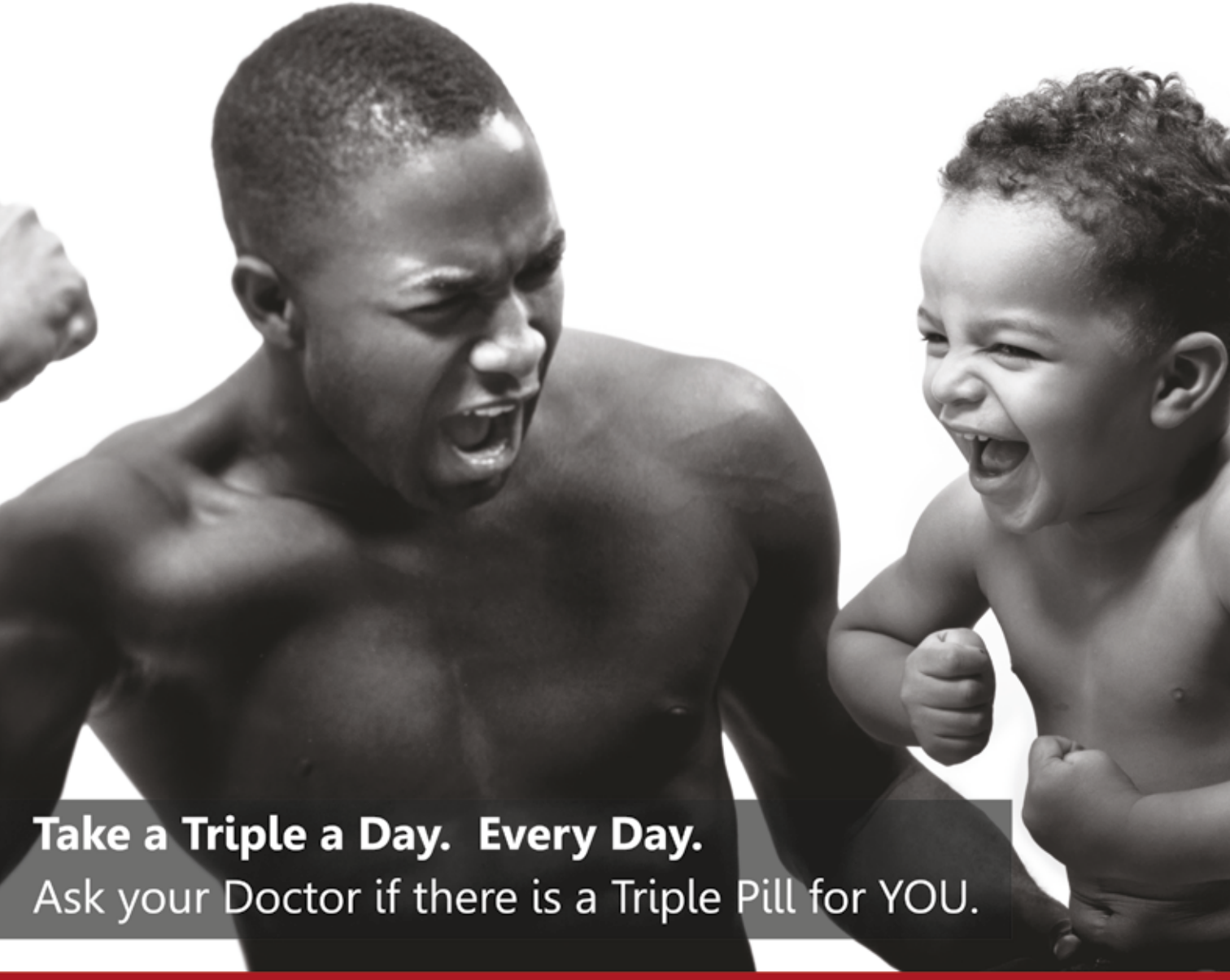

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The 2014 Namibian Guidelines for Antiretroviral Therapy and The World Health Organization recommend Fixed-Dose Combination Therapy
Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, Geneva, World Health Organization, 2013, (http://www.who.int/hiv/pub/guidelines/arv2013/en)

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