LASSA FEVER UPDATE
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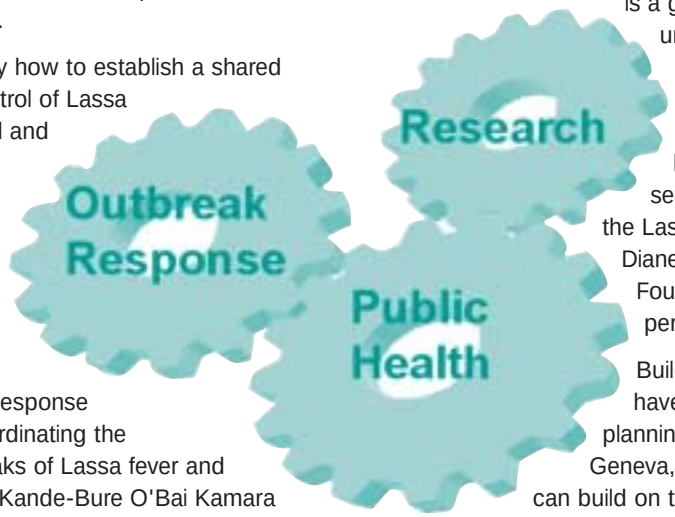
Health Care In Crises

Fighting back against Lassa Fever

There are a large number of different organisations involved in both public health and research into Lassa Fever or related diseases, but despite this there is a chronic shortage of resources for practical initiatives that can cost effectively and relatively quickly benefit those most affected by the disease. To do this greater integration is needed between public health, outbreak response and research.

Two challenges we face are firstly how to establish a shared vision of the priorities for the control of Lassa Fever, from both the international and local perspective, and secondly how to mobilise resources for improving the link between public health, health services and research recognising both the direct and the indirect benefits of those better linkages.



The Global Outbreak Alert and Response Network (GOARN), is key to coordinating the international response to outbreaks of Lassa fever and other diseases. Mark Salter and Kande-Bure O'Bai Kamara have written an article on GOARN, how it mobilizes resources from its network of partners, and the Lassa Fever outbreaks it has responded to.

An important example of research collaboration is illustrated in the programme led by Jan ter Meulen. He has built a research programme linking the University of Marburg with the Pasteur Institute in Lyon, with research institutes in Guinea and Cote d'Ivoire. In addition he has mobilized long term funding from the EU for this programme.

Ultimately control measures need to be effective on the ground. Here there are softer research issues to contend with, and there is a growing appreciation of the need to understand the local cultural perceptions of the disease and how that affects communities' involvement in control programme. Caspar Fithen looks at the link between knowledge and practice, set in the context of the experiences of the Lassa outreach team in Sierra Leone. Diane Kirkland reports on the Rockefeller Foundation supported work on the local perception of the disease.

Building on the networks of contacts that have grown during the project we are planning to convene an international meeting in Geneva, hosted by the WHO, to see how we can build on the current public health and research initiatives in this field. Your suggestions for the agenda would be much appreciated.

Thank you for your support.

Nicholas Mellor

Lassa Fever: The Role of the Global Outbreak Alert and Response Network (GOARN)

Mark Salter and Kande-Bure O'Bai Kamara

Epidemics and newly emerging infections are of increasing concern, threatening the health of people around the world and affecting travel and trade in the global village. Globalization, climate change, the growth of megacities, conflict and the explosive increase in international travel are increasing the potential for rapid spread of infections. Deforestation and urban sprawl bring humans and animals in closer contact and allow animal pathogens to "jump species" more easily and new epidemics to emerge. Many of these epidemics continually challenge health systems in countries with limited resources and have the potential to create new pandemics. Travel, trade and tourism are all affected by emerging and epidemic disease threats, which could cause intentional epidemics.

In recent years outbreaks of known infectious disease (e.g. Ebola, Lassa) and of unknown etiology, deliberate release of infectious agents, and the provision of appropriate responses are recognized as major Global Health Security issues. As a result of extensive discussions involving WHO and representatives of technical institutions, organizations and networks in global epidemic surveillance, "The Global Outbreak Alert and Response Network" was established in April 2000. In 2001, the World Health Assembly recognizing the threats to public health posed by epidemic prone and emerging infections, adopted the resolution "global health security - epidemic alert and response" urging WHO and its Member States to improve national and global efforts in communicable disease surveillance and control.

The Global Outbreak Alert and Response Network (GOARN), coordinated from the operations centre based at the WHO Geneva, is a technical collaboration of some 110 international institutions and networks which pool human and technical

resources for the rapid identification, confirmation and response to outbreaks of international importance. The Network provides an operational framework to bring expertise and skill to affected populations, thereby improving epidemic response to keep the international community constantly alert to the threat of outbreaks and ready to respond. GOARN to date is primarily a response mechanism, identification and verification is done by WHO:

In delivering its mandate GOARN follows a clear set of guiding principles in carrying out its activities in relation to international Outbreak Alert and Response:

- WHO ensures outbreaks of potential international importance are rapidly verified and information is quickly shared within the Network.
- There is a rapid response coordinated by the Operational Support Team to requests for assistance from affected state(s).
- In case of an international field mission the most appropriate experts reach the field in the least possible time to carry out coordinated and effective outbreak control activities.
- There is a fair and equitable process for the participation of Network partners in international responses.
- There is strong technical leadership and coordination in the field.
- Partners make every effort to ensure the effective coordination of their participation and support of outbreak response.
- There is recognition of the unique role of national and international nongovernmental organizations (NGOs) in the area of health, including in the control of outbreaks. NGOs providing support that would not otherwise be available, particularly in reaching poor populations. While striving for effective collaboration and coordination, the Network will respect the independence and objectivity of all partners.
- Responses will be used as a mechanism to build global capacity by the involvement of field-based training programmes in applied epidemiology and public health practice.
- There is commitment to national and regional capacity building as a follow up to international outbreak responses to improve preparedness and reduce future vulnerability to epidemic prone diseases.

There are four crucial components to effective alert and response operations. There must be adequate epidemic intelligence with effective verification mechanisms in addition to a coordinated response with appropriate and timely logistic support.

Systematic gathering of global disease intelligence relies upon a wide range of formal and informal sources. One of the most important informal sources is a semi-automatic electronic system that continuously scans the worldwide web for reports and rumours of unusual disease events. This is the Global Public Health Intelligence Network (GPHIN), a computer application developed for WHO in partnership with Health Canada. The operations centre uses the global network of WHO and its partners to verify information about outbreaks derived from informal sources. Once the international public health importance of an event is established, information about the event is shared with key public health partners around the world via a weekly outbreak verification list.

At the same time WHO offers assistance to affected state(s) in the form of technical advice, supplies or by mounting coordinated international investigations/responses.

Lassa fever is one of a number of viral haemorrhagic fevers WHO monitors and for which GOARN is able to provide a timely response. Though restricted in its geographical distribution to West Africa, Lassa fever is a significant threat to tens of thousand of people and is responsible for causing many cases of life-threatening haemorrhagic fever, few of which come to the attention of the international health community.

The true disease burden of the Lassa fever is unknown as few facilities exist in the affected region to diagnose and treat Lassa fever cases. Recent conflicts in the affected area have compounded the difficulties, and general interest in Lassa fever at an international level has been restricted to high-profile media stories concerning Lassa fever contracted by international aid workers and UN peace keepers prior to returning to their countries of domicile.

In the last two years, the WHO operations centre was informed of nine incidents of Lassa fever and verified seven. GOARN responded to a number of incidences involving Lassa fever, including an outbreak in June 2000 in Freetown, Sierra Leone during which four cases of Lassa fever were confirmed. All cases died, and as a consequence of this outbreak panic spread throughout Freetown. GOARN responded by co-ordinating a Merlin and MOHS sponsored two-day workshop for healthcare workers and MOHS authorities. In addition Merlin collaborated with WHO conducting a mission to control an outbreak of Lassa fever Nigeria. Furthermore GOARN was involved in coordinating contact tracing following the arrival of four Lassa fever patients in Europe during 2000.

Within Sierra Leone, GOARN has assisted national authorities by sending a consultant from WHO to advise on Lassa fever response plans and infrastructure. Merlin and Public Health Laboratory Service (PHLS) have collaborated in strengthening diagnostic laboratory facilities in Kenema.

GOARN is only as good as its constituent organizations and surveillance mechanisms and depends on effective and active communications between these organizations. Lassa fever is a major health issue for peoples of endemic areas and compounds the problems of their struggling health delivery systems. The ability to focus the expertise contained in a wide variety of public health and technical institutions offers a new prospect of reducing the burden resulting from Lassa fever.

Social Mobilisation against Lassa Fever in Sierra Leone

Caspar Fithen

During the brief improvement of security in Sierra Leone that followed the signing of the Abidjan Peace Accord in November of 1996, the social mobilisation programme against lassa Fever began at the end of that year with assistance from Merlin medical staff operating in Kenema.

With the prospect of a major resettlement programme to return internally displaced people and refugees to their villages of origin, some of which had been abandoned for over five years, concerns rose that the poor and overgrown state of the majority of dwellings throughout rural areas could provide the conditions for an epidemic of Lassa Fever. Moreover, initial, local studies indicated that in the face of widespread food insecurity, many people had eaten their cats in an attempt to supplement their diets with some form of additional protein. It was feared, therefore, that a resultant rise in the rodent population could occur with significant implications for public health.

In response to these concerns, it was decided that a social mobilisation campaign should be launched to prevent a major Lassa Fever epidemic overwhelming existing medical facilities which were already stretched to capacity. As a major part of this probramme, a Lassa Fever Outreach Team was created in late 1996 to undertake the grassroots activities required to increase awareness of the disease at town and village level, and to educate exposed populations in methods of avoidance as well as best practice in cases of suspected infection.

In order to maximise the impact of limited resources, the Outreach Team was charged with the primary tasks of incidence mapping to target villages most affected by the disease, as well as case referral to Kenema Government Hospital, and, following the confirmation of infection, contact tracing to warn relatives of the dangers of secondary infection, and brief those individuals on key issues regarding prevention.

These epidemiological activities went on to form the basis of the social mobilisation programme, which received some material support from Merlin and the Sierra Leone Ministry of Health. Initially, awareness was made the priority, and with some resourceful planning, local musicians were commissioned to write and perform songs about the dangers of Lassa Fever, routes of transmission and preventative measures that became a popular album. Cassettes of the music were distributed free in villages, where they were often played in public places, like the produce market or the barri, while the songs themselves were played on local radio stations.

To support this initiative, diagrammatic posters were printed to instruct villagers in techniques for protecting food from rodents, trapping, dealing safely with the carcasses of dead rats, symptom recognition, processes for referral and simple barrier nursing methods to prevent secondary infection. Since the budget was extremely limited, it was decided to print on cheap low quality newspaper-type paper in order to prevent the use of the posters for other purposes, such as wrapping or writing paper. Moreover, versions of each poster were printed in the major local languages, Krio and Mende. The posters were then freely distributed in villages for prominent display. While text can add significant value to such instructive instruments, literacy in rural West Africa is typically quite low, and pictorial representation is the optimum means of message broadcast. However, this can present its own unforeseen problems: a WHO poster showed a small boy rejoicing after impaling a rat on a sharp stick. While the image was meant to convey the importance of rodent control, it unwittingly presented a very dangerous way of handling dead, bleeding and potentially Lassa-infected Mastomys spp rodents.

The outreach workers would also hold informal focus sessions and discussions with available groups of villagers. In the evening, this might be with men drinking palm wine in the local pote , while in the morning, the interaction might be with women washing laundry. To reinforce this important process, the Outreach Team was provided with a small generator, a video and television, allowing it to show instructive public health films.

In areas where the population was less sedentary than in subsistence farming rural villages, like the extremely ethnically diverse mining centre of Tongo Field , the Outreach Team was presented with different sets of challenges. Not only did such sites experience major population fluctuations (which coincided directly with the troughs and peaks of Lassa Fever incidence), the inhabitants, typically male diamond diggers, often showed little interest in issues regarding health. In such circumstances, the Outreach Team had to enlist the support of relatively senior town and section chiefs to give momentum to the mobilisation process. In a number of situations, this assistance proved invaluable, and large, instructive billboards were erected at a number of key locations in mining centres and on the approach roads that served them. Some of the funding for these initiatives came in the form of donations from key diamond industry figures concerned not only at the general health of the communities in which they worked, but also at the implications of an epidemic for productivity! Moreover, the local chiefs were able to advertise by word of mouth educational seminars by Merlin personnel and the Outreach Team. These became very well attended, with 2-300 diggers and their dependants jammed into the local barri a not unusual occurrence.

Although the positive gains made by the Merlin-supported Outreach Team increased during the early part of 1997, the political situation in Sierra Leone deteriorated rapidly. Without a doubt, had it not been for a further five years of war, social mobilisation against Lassa Fever in Sierra Leone would now be at a fairly advanced and sophisticated level. Nevertheless, the dedication of the Outreach Team remains as strong as ever, and the ideas that were developed in 1996-7 have proved highly durable.

The Outreach Team, consisting of Willie Robert, Lansana Kanneh and Saffa Koroma (who contracted and survived the disease in 1997 in the course of his outreach work), and supported by Merlin Medical Co-ordinator Dr Valerie Bemo, is now planning a major relaunch of the social mobilisation programme. It is hoped that this initiative will be given considerable thrust by a ‘National Lassa Fever Day’, perhaps to be held annually, which will focus popular attention on the dangers of the disease. It is envisaged that radio stations will play Lassa-related music, broadcast interviews with members of the MOHS and Lassa clinicians, while youth groups and civil society organisations will support the campaign by arranging their own awareness activities. In Sierra

Leone, there is no shortage of enthusiasm for this kind of positive initiative, particularly as the country emerges from ten years of civil war.

It is expected that the National Lassa Fever Day will form a solid foundation for the building of a long-term social mobilisation strategy with the clear objective of significantly reducing disease incidence. With greater political and material support, the current team could be significantly expanded to cover not only the general Kenema/Tongo Field region, but also Kono, the country's largest diamond mining area to the north-east, which is now atypically experiencing a far higher rate of incidence of Lassa Fever than was usual in the past. Again, displacement, resettlement and bush encroachment may have a part to play in this development.

However, while such a broadening of the outreach process could be achieved in a very short space of time, funding, and consequently team mobility, remain major obstacles. More often than not, only one Land Rover will be available for the three members of the Outreach Team and will be used to transport the equipment necessary to show educational videos to villages. Once Kono is firmly within the sphere of operations , and the Outreach Team has grown to perhaps six individuals, this situation is likely to prove extremely problematic. Given the extremely poor quality of roads , and the high cost of four-wheel drive vehicles, relatively cheap, though very robust quad bikes may provide a solution .

Finally, while social mobilisation programmes exist in Sierra Leone for both HIV/AIDS and malaria, both processes have experienced problems for a variety of reasons . The Lassa Fever initiative could provide valuable 'lessons learned' which might in the future enhance other public health projects which have suffered either as a result of poor local education or 'issue fatigue'.

Knowledge + Practice = Prevention

Designing your own social mobilisation programme

Step one:

Establish which vital pieces of information need to be conveyed, then assess how to use the following:

1. Travelling campaign – megaphones and portable videos.
2. Poster campaign – not just posters, but t-shirts, caps, badges etc.
3. Radio campaign – announcements, interviews and themed music by local musicians.

Step two: ANALYSIS

A. Identify and organise local assistants.

These people must understand the disease they are battling against. They will need to earn the respect of local leaders and villagers if their activities are to make an impact.

B. Target the most vulnerable members of the community.

Targeting is very important because the available resources are likely to be limited. Targeting might be by geographical location, gender, employment or demographic grouping. Mapping the incidence and epidiology of a disease will be of great help to this process.

C. Identify the environmental factors that contribute to the spread of disease.

In the case of lassa fever, the war in sierra leone has created enormous population upheaval. This has led to a considerable deterioration in living conditions. For example, houses are damaged, villages have become overgrown and vermin levels have risen. Latrines have fallen into disrepair, there are less cats, and because of the insecurity, people have been wary of leaving villages to dispose of waste at long, safe distances from villages. These are all environmental factors which help to make lassa fever a problem.

D. Identify the social factors that contribute to the spread of the disease.

Social factors that contribute to the spread of disease might include literacy levels in a given area. For example, a previous public health campaign against lassa fever in sierra leone included the distribution of detailed disease prevention leaflets which were written in complex english. The programme failed because most of the target population were either mende or krio speakers, and the level of literacy in small, rural communities was often low.

Other social factors which may complicate a social mobilisation campaign might include a distrust of western medicine in more remote rural regions. If this the case, programme designers should consider how practitioners of traditional medicine could be asked to help effectively with a campaign in their own way.

Step three: TEST

Once steps one and two have been undertaken, and a basic design for the programme has been developed, a test should be mounted on a limited target population to gauge feedback, identify problems and develop solutions. This stage is particularly important as no programme design is likely to be perfect first time around.

Step four: IMPLEMENTATION

The adjusted and improved programme is now ready for broad implementation. However, adjustments will continue to be required in response to occasional changes in the environmental and social factors which determined the original programme design.

Preliminary findings on the socio-economic impact of Lassa Fever in Sierra Leone

Dr Diane Kirkland

Introduction

There is a growing need to provide accessible, culturally appropriate health care for individuals with Lassa Fever (LF) in Sierra Leone. As suggested by B.D. Paul[1] 'if you wish to help a community improve its health, you must learn to think like the people of that community'. It is important to ascertain existing behaviours within the community and understand their underlying meanings and the functions they serve. With these issues in mind, the views of local people on the socio-economic impact of LF were sought. Data were collected by means of focus groups and semi-structured interviews, which were facilitated by trained local health workers. Two groups consisting of chiefs, elders, female and male adults and male youths have been conducted thus far, one in an affected and the other a non-affected region of Sierra Leone. Two interviews with relatives of patients on the LF ward and one with a District Nurse sister were also conducted. Data were collected in or translated into English, tape-recorded, transcribed and analysed thematically. Participants were asked about the socio-economic impact of issues relating to risk factors, early diagnosis, medical treatment and the sequelae of LF.

Issues relating to risk factors

Clearly, prevention is better than cure. Of the risk factors for LF, the major concerns voiced by participants related to rodent control. Without exception, it was suggested that rodent control and a clean environment would reduce the risk of LF and other similar diseases. However, it was reported that not everybody in the community shared this knowledge and that further education relating to this is required. On a practical note, participants described infested homes, where rats not only ate food, but also clothing, books and bank notes. There were no suggestions of how to reduce the rat population and only one comment about the disposal of killed rats:

Remember, in Africa, we have a rat which happens to be the sweetest meat and you tell that person not to eat that meat because it creates LF and before this time, long before this time, there has never been a sickness called LF .You have to involve the community people, let them see the effects of eating rat…

There appeared to be a clear understanding that LF can be contracted through contact with an affected person. In fact, fear of contracting the disease through human contact leads to victims and their families, being isolated and stigmatised, even after recovery. Several participants discussed the necessity to containing LF by means of isolating affected people.

If people think you have had LF, which causes more problems within the community, thinking that you should not talk to people, anybody will not touch you…so it is a great social embarrassment in the community.

When my wife was admitted to Lassa ward, well, it was not only an economic depression, it also created social embarrassment, because my children no longer go to other houses, to their relatives…so that is why it is a complete social embarrassment.

However, comments indicate a limited understanding of the specific modes of transmission between humans. The exception to this was a woman who expressed concern about being at risk when helping women who miscarry. Without gloves to protect her from blood born diseases, she felt she could be infected with LF. Throughout the data, repeated references are made to the social embarrassment caused by LF. The issue of social exclusion appears to be linked with reluctance to seek a diagnosis of, or medical treatment for, the symptoms of LF. Further education, specifically in relation to the safe disposal of rat carcasses and the mode of human transmission may be necessary in order that people are absolutely clear about specific risk factors, but do not fear and isolate people unnecessarily.

Issues relating to diagnosis

There was a consensus that early diagnosis of LF is good for two reasons:

If we detect people early in our community, then we are preventing people from dying…and once well, they can come back and work in the community.

Yes, it is beneficial to the community, if you discovered that somebody has been affected by Lassa, he or she is quickly taken to the appropriate quarters, where the disease should be controlled, instead of allowing the disease to spread.

However, it was reported that in reality, early diagnosis is impeded by lack of knowledge and the absence of a test that may be carried out in the community.

Many people don't know about LF, they don't recognise it, it resembles Malaria, which is common. Lassa is really difficult, because these sicknesses are really alike, typhoid, Lassa… so to the native people in our community, it is very difficult to diagnose.

Both groups discussed the need to educate the population about the signs and symptoms of LF. In addition, the group from the affected area discussed the necessity for a local laboratory in their area.

We are begging for a Lab, so we can go there for a proper check up…so we can be serious and fast to know which is the sickness, instead of giving blind treatment to people.

Issues relating to medical treatment

Having identified the benefits of early diagnosis, participants suggested, for a variety of reasons, that many people were unlikely to seek medical care if they suspected they had LF. In the first instance, medical treatment is expensive and may be accessed at the direct expense of other necessities such as food for the family and school fees. Participants repeatedly explained that when one member of the family required medical treatment, the other members suffered financial hardship, even hunger. Cultural issues such as a belief in traditional remedies and mistrust of the medical treatment offered at the hospital were also described as important, for example:

For medical attention they have to pay so much, that is why most people fear to go to the medical centre, to prove whether they are affected by Lassa or not.

There are certain people in the community we live in, they believe in herbs, in going to the bush to get some tea herbs. So

whatever disease they have, they think herbs can mend them, so that is why they don't come to hospital.

Some people say the appropriate dosage is not yet available, therefore, they rarely go for the treatment of LF.

'People don't go to medical facilities, because sometimes they fear when they go to the hospitals, especially when they say they have LF, they will be given injections to kill them'.

Participants in each group and interview reported this apparently common belief that people are killed after being admitted to the LF ward. Clearly, this issue needs to be addressed, since there is little point developing health facilities, which people are too afraid to use.

In addition to financial and cultural factors, participants discussed the practical problems that arise when parents are hospitalised, in particular, childcare and 'maintaining agricultural commitment'. It was suggested that such commitments prevent people using medical facilities. Participants acknowledged that they would try to look after and feed children in their extended family if necessary, but that this might be problematic, given the shortage of food and limited money available. It was reported that in this circumstance, it would be impossible to pay school fees and thus the child would not be educated.

It is important to identify and address the issues that prevent people from seeking medical attention when they suspect they have LF. Of equal concern however, is the difficulty reported in accessing medical facilities when required, because of the expense incurred, geographic inaccessibility of medical facilities and poor transport availability. Participants from the affected area reported that although they were just 27 miles from the hospital, the journey was expensive and took them at least five hours over rugged terrain.

So because people are just coming out of war, there is no money, so for people to take this sick person to hospital is very difficult.

In the rainy seasons, the river runs, there is no means of transportation…there is no ambulance service to transport the sick

This would suggest it is important to educate people locally to recognise the signs and symptom of LF and about what course of action they should take to give the best opportunity for recovery.

The Sequelae of LF

The impact of three factors, which commonly occur as a result of LF, namely death, miscarriage and deafness were discussed. There was little reference made to the emotional impact the death of a family member due to LF would cause. However, there was much concern about the immense burden exerted on the extended family when responsibility for children or women is transferred, following a man's death.

More specific to LF, the social calamities of miscarriage and deafness were discussed at length. In relation to miscarriage, the blame appears to lie directly with the woman. Participants suggested miscarriage is often attributed to witchcraft and commonly leads to the breakdown of a marriage, for example:

If there is somebody who cannot bear children, whether this is due to LF, that person will be isolated in the community and that person will be false treated. People class you as a witch because you have aborted. They say witchcraft is responsible for abortion.

In fact, that (miscarriage) also helps to split marriages, because certain people, they don't believe it is because of the LF that has made you miscarry, they think you are barren, and that marriage is spoilt, it is broken down.

Deafness was described as a social embarrassment and recognised as having a catastrophic effect on family relationships. Several references were made to the person affected being 'as though they were mad', crazy or stupid due to their inability to communicate effectively.

Deafness creates social embarrassment in a community. Deafness can make the person not even responsible within the family

In fact, if you are female, and you have LF and you are deaf, and you are not married before you are discharged from the Lassa ward, no man will marry you/

My last wife that I married, lost her hearing during the attack of LF and that lady, I can hardly deal with now at all…she behaves like a crazy somebody because she can not hear, and she used to be important within the community.

Even the children cannot communicate with her. She is now like someone who is crazy, stupid, because she has lost her hearing sense.

The psychological impact of miscarriage or deafness on the individual concerned or what support could be offered to them were not discussed. These sequelae were described from the perspective of frustrated family members and in terms of the lost ability to fulfil their roles within the family and the community.

Conclusions

These preliminary findings illustrate some of the problematic issues, which face agencies working towards controlling LF in Sierra Leone. The challenges are not only practical and financial, but also cultural in nature. These data suggest that there are key areas in which the education of local communities is vital and welcomed, namely, in identifying risk factors, the disposal of rat carcasses and modes of human transmission of LF. Education about the signs and symptoms of LF and the importance of seeking medical treatment quickly would also seem to be vital. In addition, it is important to identify and address misconceptions such as the belief that people are deliberately killed on the Lassa ward. Other information about the causes of miscarriage and 'signing' skills might facilitate the return to previous social roles for the people affected. However, education is a two way process. It is equally important to continue to explore behaviours and beliefs within the community, to gain insight into the barriers that prevent the effective utilisation of health facilities for LF. Similarly, to ensure future health developments regarding LF, in whatever form they take, are acceptable to, understood by and ultimately accessible to the local communities.

[1] Paul BD. Health, Culture and Community. 1995, page 1; Russell Sage Foundation.

10 years of viral hemorrhagic fever research in the Republic of Guinea: linking research with public health and capacity building.

Jan ter Meulen

Background.

In 1992, the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany, started collaboration with IRBAG, a Guinean research institution, to study the epidemiology of Lassa fever in the southern part of the Republic of Guinea (Guinée forestière). These population-based studies revealed 14% Lassa-antibody prevalence in the general population and proved that the local custom of hunting rodents for consumption is a major risk factor for the transmission of Lassa fever. With the help of the GTZ (German Technical Cooperation) a small serological laboratory equipped with a glove box for safe handling of infectious material was established in the regional hospital of Gueckedou. It could be shown that approx. 3% of all hospitalised patients with the diagnosis "fever of unknown origin" were actually suffering from Lassa fever. During the epidemiological and clinical studies in this remote part of the country it was soon realized, that a much better developed infrastructure would be needed in order to conduct sustainable viral hemorrhagic fever (VHF) research in the Republic of Guinea. It was also noted that despite the presence of Lassa fever virus throughout the country and the circulation of Yellow fever virus along the borders with Liberia and Sierra Leone, no laboratory or public health infrastructure capable of responding to an outbreak of these diseases existed in Guinea at that time.

Dr. Lamine Koivogui, national coordinator of the PFHG (standing, left) with Dr. J. ter Meulen, scientific adviser, and members of the PFHG-team outside the project laboratory in Conakry

Photo © Jan ter Meulen.

Establishing the “Projet de Recherche sur les Fièvres Hémorragiques en Guinée (PFHG)”

The Institute of Microbiology at the University of Conakry was therefore chosen as the academic partner for broader based research collaboration. Contracts with both the Ministry of Education and the Ministry of Health formed the basis for developing a national viral hemorrhagic fever research project. The integration of this new project into both the academic and medical structures of Guinea proved a very successful way of conducting scientific research and satisfying public health needs at the same time. In 1999, the first virological laboratory of the Republic of Guinea could be established in the University teaching hospital Donka, Conakry, with the help of major grants from the Volkswagen Foundation, Germany, and from the European Community (INCO program for the collaboration with developing countries). Through the INCO-grant, coordinated by EPICENTRE (Groupe Europeen d’Expertise en Epidemiologie Pratique, Paris, France), the project was linked with other research centres working on VHFs, like the Pasteur Institutes in Paris, Lyon, Dakar and Abidjan, and the University of Marburg, Germany. Large serosurveys carried out in the framework of the INCO-project confirmed the presence of Lassa virus and Yellow fever virus (approx. 30% antibody prevalence) in Guinée forestière and the border region of Côte d’Ivoire. Physicians in many small hospitals and health posts were trained in "barrier nursing" techniques and standardized clinical questionnaires for suspected VHF cases were developed.

Dr. Lamine Koivogui, chairman of the Institute of Microbiology, was appointed as national coordinator of the PFHG and head of the new virological laboratory. Dr. Koivogui earned his PhD in Warsaw, Poland.

VHF- diagnostics in the PFHG laboratory at the University Hospital Donka.

The laboratory is housed in five rooms on the hospital campus, adjacent to the infectious disease ward. It is fully climatised and equipped with a Class 3 biological safety cabinet (glove-box with negative pressure and HEPA-filters), an autoclav for highly infectious waste, a Class 2 safety cabinets and technical equipment for performing ELISA-tests, the polymerase chain reaction (PCR) and the indirect immunofluorescence technique (IIF) for detection of Lassa antibodies. A back-up generator guarantees constant power supply. Sera from suspected VHF cases are routinely tested for Yellow fever antibodies by IgM- and IgG-ELISA and Lassa fever antibodies by IgM- and IgG – IIF. Lassa virus is detected by PCR. Serum samples can be stored in liquid nitrogen or in a -80°C freezer for further analysis in reference laboratories. This laboratory is apart from the Pasteur Institutes in Paris and Abidjan the best-equipped lab for VHF-diagnostics in this part of West Africa. The staff of the laboratory comprises one biologist (PhD), one pharmacist and three technicians. The project scientists have received training in various foreign institutions to increase their proficiency in VHF-diagnostics (Pasteur Institutes in Paris, Lyon and Dakar; Bernhard Nocht Institute; Institute of Virology, University of Marburg). Apart form VHF-diagnostics, the laboratory routinely performs serological assays for HIV, hepatitis B and measles, both for the hospital and for national programs.

PFHG’s responses to public health emergencies.

In 2000, a cluster of Lassa fever cases in Kenema, Sierra Leone, raised concerns of posing a threat to the UN peacekeeping forces (UNAMSIL) stationed in Sierra Leone. The local bureau of WHO in Sierra Leone sent sera from 22 suspected Lassa cases and 33 contacts (including 21 UN staff members and 2 NGO members) to Conakry by helicopter. Within a couple of days,

Lassa fever was confirmed in nine suspected cases by PCR and the virus could later be isolated from six specimens.

Later in the year 2000 the first large epidemic of Yellow fever occurred in the savannah region of Guinea, spreading quickly north towards Senegal. More than 800 cases including 250 deaths were reported and containment of the epidemic required mass-vaccination of approx. 1.9 million people. On demand of the Ministry of Health and WHO Guinea, the PFHG sampled blood from suspected VHF cases throughout the country, performed Yellow fever serology in Conakry and shipped a large number of sera for confirmation of the diagnosis to reference laboratories.

BSL3 glove box: Inside the PFHG-laboratory: Biosafety level 3 glove box for handling of highly infectious material

Photo © Jan ter Meulen.

Current research program of the PFHG.

Understanding the humoral and cellular immunity against Lassa virus in order to develop a recombinant vaccine is the main research interest of the project. Dr. J. ter Meulen from the University of Marburg is the scientific adviser of these studies. He was recently appointed as an International Research Scholar of the Howard Hughes Medical Institute (Infectious Disease and Parasitology Program), which includes administration of a five-year grant given to the University of Conakry for performing T-cell studies on Lassa fever survivors. Because the immunity against Lassa virus is mainly T-cell based, the identification of dominant and conserved CD4 and CD8 T-cell epiotpes of the virus is very important for vaccine design. Dr. ter Meulen is also the coordinator of a new INCO-grant, aimed at understanding the mechanism of Lassa virus neutralizing antibodies. To this end, recombinant human antibody-libraries are generated by phage-display from the lymphocytes of Lassa-immune donors and screened for binding to Lassa virus antigens. It is hoped that thus the epitopes of naturally occurring neutralising antibodies can be identified and added to the recombinant vaccine.

Another major area of interest is a better understanding of the phylogeny of the principal reservoir of Lassa virus, the multimammate rat Mastomys. In collaboration with the Muséum National d'Histoire Naturelle, Paris, several thousand rodents will be caught in Guinea and Côte d'Ivoire and animals classified morphologically as Mastomys spp. will be further typed using sophisticated molecular techniques. The detection of Lassa virus in the animals will allow the identification of certain species and sub-species of Mastomys with a high vector-capacity for the virus. This could help explain the obvious contradiction of the widespread occurrence of Mastomys in West Africa contrasting with the very focal occurrence of Lassa fever even in endemic areas.

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Looking into the future.

The "Projet de Recherche sur les Fièvres Hémorragiques" has established itself as an important centre for the study of Lassa fever and other viral hemorhagic fevers in West Africa. Its scientific excellence was acknowledged by a prestigious grant from the Howard Hughes Medical Institute and continuing support by the European Community. It has been possible in the past years to create a scientific environment and a technological platform, which attracted numerous international collaborators and hopefully will continue to attract them. Because VHFs constitute public health emergencies, the project has made significant contributions to the management of Lassa fever and Yellow fever in the region and will continue to offer both technical and personnel assistance to neighboring countries.

It is hoped that the results of the immunological research will soon lead to the development of recombinant anti-Lassa virus antibodies and a Lassa fever vaccine, which should be evaluated not only in the Republic of Guinea but also in all countries affected by Lassa fever.

Mastoyms dissection: Dr. Elisabeth Fichet-Calvet from the National Museum of National History, Paris, dissects a wild-caught Mastomys in the field

Photo © Jan ter Meulen.

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