Epidemiology and control of Marburg haemorrhagic fever epidemics in Central Africa

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The Marburg haemorrhagic fever (HF) outbreak in Watsa, Democratic Republic of Congo 1998-2000, was the first of its kind documented to occur in the virus' natural environment. Participating in the international response efforts and conducting follow-up studies permitted me to gain epidemiological insights in a hitherto largely unknown disease. Participating in the response effort to the second major Marburg HF outbreak in Uige, Angola 2005, enabled me to culminate the experience by exploring opportunities on how to optimise the outbreak response in the hospital and in the community.

In the context of the Watsa outbreak 154 cases were identified, of whom 83% were fatal. The epicentre was located in Durba, a mining village near Watsa town. Primary transmission from the unknown reservoir appeared to have occurred predominantly, if not exclusively, in men illegally exploiting the Gorumbwa gold mine in Durba. These miners occasionally transmitted the virus to care giving family members or health workers. The Marburg viruses isolated during the outbreak corresponded to at least nine distinct genetic lineages. This is evidence of repeated primary introduction of the virus into the human population and hints at a reservoir species residing in Gorumbwa mine in large numbers, e.g. small mammals, so that several virus lineages could be sustained.

It is likely that unrecognized Marburg HF cases occurred in Durba and Watsa prior to the outbreak in 1998-2000. We found evidence for outbreaks compatible with Marburg HF in hospital records from earlier years, and Marburg antibodies in a survivor of a putative outbreak in 1994.

We identified a large cluster of Marburg HF cases during the Watsa outbreak. It was exceptional in that it included an infant and cases of very mild disease. During the Watsa outbreak, initial symptoms typically included fever, headache, general pain, nausea, vomiting and anorexia, followed by hemorrhagic manifestations and, terminally, confusion, agitation, coma, anuria, and shock. However, clinical documentation was found to be poor, even taking the local circumstances into account, and we successfully lobbied for a substantial and co-ordinated effort to collect clinical data of better quality in future outbreaks.

A serosurvey in the population of Durba and Watsa confirmed that working in Gorumbwa gold mine and attending health care facilities were risk factors for Marburg infection. We refuted the hypothesis that pygmy hunters are another population at risk, given their frequent exposure to wildlife. Furthermore, our post-outbreak serosurveys

among household and health worker contacts of Marburg patients confirmed the rarity of mild disease. The – post-intervention – reproductive number was calculated to be 0.9, which is in line with the hypothesis that the long lasting Watsa outbreak was sustained by prolonged and repeated primary transmission from the reservoir to man.

Concomitantly, we demonstrated that the hospital barrier nursing approach previously established for Ebola HF worked well for Marburg HF. However, cases of Marburg HF continued to occur outside the isolation wards. We found that infection control measures had been too narrowly focussed on the isolation wards, and provided evidence of shortcomings in the provision of protective gear to health workers in other wards. Furthermore, we also found that health workers took avoidable risks. Qualitative research amongst health workers shed light onto the complex psychological and sociological determinants of their risk-taking behaviour – especially when taking care of ill colleagues. These insights should be taken into account when training health workers in future outbreaks.

We systematically analysed and documented the lessons we learned during the subsequent Marburg HF outbreak in Uige Angola, regarding interventions in the hospital and in the community. We demonstrated the importance of hospital wide infection control, pro-active supportive treatment, involvement of local authorities in Uige, transparency in the workings of the isolation ward, and the provision to families of opportunities to grieve in case of a fatal outcome. Sharing the experience of making mistakes initially and then successfully adapting the intervention will help future teams to take advantage of the learning process the response team went through in Uige.

In the final section of this thesis general conclusions and perspectives are presented. Ongoing and future research activities and their implications for public health are discussed, including the search for the reservoir species and the development of antifiloviral vaccines, drugs and innovative supportive treatments. While success in these fields would undoubtedly be most welcome, it is important to remember that the threat filoviruses pose for Central African populations would decrease significantly if standard public health interventions were in place and functional: epidemiological surveillance, swift outbreak investigation and response, and basic hospital hygiene. We end by making the case for maintaining the international dimension in filovirus research.