Published in final edited form as:
Lancet Infect Dis. 2017 May ; 17(5): 470–471. doi:10.1016/S1473-3099(17)30027-0.

Ebola virus disease sequelae: a challenge that is not going away

Janet T Scott[*] and **Malcolm G Semple**
Institute of Translational Medicine and NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool L69 3GE, UK

The Ebola virus disease (EVD) epidemic of 2013–16 resulted in 28 616 cases and left more than 17 000 survivors.1 Researchers—pulled globally from other projects—benefited hugely from previous research on EVD, albeit carried out by teams working in difficult funding environments. However, the sheer number of patients meant that much of what was encountered about EVD was new: the extent, longevity, and complexity of post-EVD sequelae,2,3 mild or asymptomatic disease, persistent viraemia,4 sexual transmission,5 and recrudescence.6 This outbreak has shown that research can and must be integrated into the harshest of circumstances to benefit patients in real time. Now the immediate emergency has passed, full exploitation of information gained is necessary to fully delineate and act on the lessons learnt.7

The Postebogui study,3 reported in this issue of *The Lancet Infectious Diseases*, is a good example of full exploitation of available data. It is a comprehensive multidisciplinary longitudinal study of 804 EVD survivors in Guinea after discharge from Ebola treatment centres. The Article reports an interim analysis of the data and the study will be completed when further data at follow-up up to 24 months after enrolment will be available. This cohort included 158 children aged 1–18 years (median 11 years). 76% of patients presented with post-EVD symptoms a median of 1 year after discharge. The most frequent symptoms were those classed as general (fatigue, fever, and anorexia; 40%), musculoskeletal pain (38%), headache (35%), depression (17%), abdominal pain (22%), and ocular disorders (18%). Positive Ebola virus RT-PCR was found in 5% of adult men at a maximum of 548 days after disease onset, measured using both the standard RealStarFilovirus Screen RT-PCR kit 1.0 and an in-house technique targeting the viral nucleoprotein.

A picture is now emerging of post-EVD sequelae. Pain—musculoskeletal, abdominal, or headache—appears to be a dominant symptom, as are psychosocial issues and ocular problems. Although pain is subjective and a common complaint in the general population, our impression is that the combination of these problems in EVD survivors is related to their acute EVD. Further controlled studies are likely to clarify this connection. The Postebogui cohort3 and similar studies underline that for many patients with post-EVD sequelae, problems continue long after the acute illness. Can we learn from other conditions to improve existing management strategies?8

jscott@liverpool.ac.uk.

Europe PMC Funders Author Manuscripts

EVD is not unique in predicating post-viral consequences. Chikungunya is a notable example: 20% of patients with chikungunya are left with post-viral chronic inflammatory joint disease.9 Chronic synovitis from virus-infected joints or the virus acting as a pro-inflammatory stimulus have been postulated for post-chikungunya rheumatic disease. Such patients with inflammatory joint disease have responded well to methotrexate or anti-tumour necrosis factor therapies.10 These drugs might prove problematic in fledgling health-care settings; however, sulfasalazine—an oral therapy that requires minimal monitoring—could be an option for post-EVD sequelae.

Some aspects of post-EVD sequelae are similar to those of chronic fatigue syndrome or myalgic encephalomyelitis, a debilitating and complex disease characterised by prolonged and disabling fatigue. The range of symptoms for this condition includes headache, muscle and joint pain, and post-exertional malaise.11 The aetiology and pathophysiology of chronic fatigue syndrome is not yet determined, with investigations done into infection and inflammation as well as altered immunity. Evidence-based treatment programmes include graded exercise and cognitive behavioural therapy, and tricyclic antidepressants such as amitriptyline can be used for symptomatic pain relief. Could inspiration be taken from this approach for post-EVD sequelae?

The paediatric cohort in the Postebogui study3 might provide insight into the development of post-EVD sequelae. Although their cycle threshold values (a proxy measure for viral load) were similar on diagnosis of their acute illness compared with adults, children had fewer symptoms during the acute phase of their disease and subsequently reported fewer clinical events or specific post-EVD symptoms. However, general signs and psychological distress were more common in the paediatric cohort than in adults. This pattern was also seen when younger and older children were compared. Are children who survived EVD more resilient than are adult survivors? Or did children only survive if they had milder symptoms in the acute phase? Unfortunately, we cannot discriminate with these data.

After all that EVD survivors have been through, the final insult appears to be that they might not be in the clear. Recrudescence can occur,6 and although transmission events have been extremely rare, in a few adult men semen has remained RT-PCR positive up to 18 months post-infection, which implies that sexual transmission remains a risk. 40% of patients in the Postebogui cohort reported general symptoms including fever:3 should this be concerning? Fever is a common symptom in west Africa with many causes, including malaria. These fevers are often treated empirically. An agreed protocol for screening for potential recrudescence (which could be mild) would be prudent. We applaud efforts to instigate access for EVD survivors to quality health care, including adequate diagnostic tests. Such efforts are not only a humanitarian act, but needed for public health surveillance.

The Postebogui study covers a wide variety of disciplines from psychosocial assessment to virological analysis of body fluids, reflecting the wide range of challenges that remain in the fight against EVD. The research effort is not over.

Acknowledgments

JTS and MGS report grants from the Wellcome Trust, outside of the submitted work.

Europe PMC Funders Author Manuscripts

References

1. WHO. Situation report: Ebola virus disease. Geneva: World Press Organization; 2016 Jun 10. 2016
2. Scott JT, Sesay FR, Massaquoi TA, Idriss BR, Sahr F, Semple MG. Post-Ebola syndrome, Sierra Leone. Emerg Infect Dis. 2016; 22:641–46. [PubMed: 26983037]
3. Etard JF, Sow MS, Leroy S, et al. Multidisciplinary assessment of post-Ebola sequelae in Guinea (Postebogui): an observational cohort study. Lancet Infect Dis. 2016; published online Jan 13. doi: 10.1016/S1473-30w99(16)30516-3
4. Brainard J, Pond K, Hooper L, Hunter P. Presence and persistence of Ebola or Marburg virus in patients and survivors: a rapid systematic review. PLoS Negl Trop Dis. 2016; 10 e0004475.
5. Diallo B, Sissiko D, Loman NJ, et al. Resurgence of Ebola virus disease in Guinea linked to a survivor with virus persistence in seminal fluid for more than 500 days. Clin Infect Dis. 2016; 63:1353–56. [PubMed: 27585800]
6. Jacobs M, Rodger A, Bell DJ, et al. Late Ebola virus relapse causing meningoencephalitis: a case report. Lancet. 2016; 388:498–503. [PubMed: 27209148]
7. Gates B. The next epidemic—lessons from Ebola. N Engl J Med. 2015; 372:1381–84. [PubMed: 25853741]
8. WHO. Clinical care for survivors of Ebola virus disease: interim guidance. Geneva: World Health Organization; 2016 Apr 11. 2016
9. Win MK, Chow A, Dimatatac F, Go CJ, Leo YS. Chikungunya fever in Singapore: acute clinical and laboratory features, and factors associated with persistent arthralgia. J Clin Virol. 2010; 49:111–14. [PubMed: 20674479]
10. Blettery M, Brunier L, Polomat K, et al. Brief report: management of chronic post-Chikungunya rheumatic disease: the Martinican experience. Arthritis Rheumatol. 2016; 68:2817–24. [PubMed: 27273928]
11. Baker R, Shaw EJ. Diagnosis and management of chronic fatigue syndrome or myalgic encephalomyelitis (or encephalopathy): summary of NICE guidance. BMJ. 2007; 335:446–48. [PubMed: 17762037]

Europe PMC Funders Author Manuscripts

Kristin Palitza/DPA/PA Images