Severe fever with thrombocytopenia syndrome in China

In their Review of severe fever with thrombocytopenia syndrome (SFTS), Quan Liu and colleagues reported that almost 2500 cases of SFTS have been diagnosed with an average mortality of 7·3%.[1] However, they did not mention the frequent misdiagnosis of SFTS, especially surprising because it constituted a major problem before recognition of the disease in 2009. Several diseases, including leptospirosis, haemorrhagic fever with renal syndrome, and human granulocytic anaplasmosis, share many clinical features with SFTS.[2] SFTS is often misdiagnosed as these diseases (table), especially human granulocytic anaplasmosis, which is also a tick-borne disease, caused by the intracellular bacterium *Anaplasma phagocytophilum*. Serology-confirmed infections with *A phagocytophilum* were very rare in patients from endemic regions of China thought to have human granulocytic anaplasmosis. Furthermore, *A phagocytophilum* has not been isolated in China from patients with suspected human granulocytic anaplasmosis. Xu and colleagues assessed 285 samples from patients with suspected human granulocytic anaplasmosis, collected between 2007 and 2010 in Henan province. They found that 238 (83·5%) were positive for SFTS virus RNA, whereas only 24 (8·4%) were positive for *A phagocytophilum*.[3] Some patients with SFTS have been misdiagnosed with quite common diseases, including common fever, gastrointestinal disease, and respiratory disease (table). These data strongly suggest that most cases of human granulocytic anaplasmosis reported in China might actually be misdiagnosis cases of SFTS. Although this situation has been improving in hospitals where doctors have the knowledge and correct diagnostic tests to distinguish SFTS from other diseases, misdiagnosis is probably still common in endemic regions, even despite the discovery of the aetiological agent of SFTS.[4] We hope that this situation will benefit from the development of new diagnostic methods for the SFTS virus, the re-education of physicians, and effective guidelines from the central government.

We declare no competing interests. We have received grants from the National Science Foundation of China (31272305) and National Basic Research Program (973 project, 2010CB530000). We thank Prof Geoff Hide (University of Salford, UK) for the critical comments.

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	Confirmed cases	Misdiagnosed cases					
		HGA	HFRS	Common fever	Gastrointestinal disease	Respiratory disease	Unknown diseases
2006–11	489	266	0	11	6	3	13
2011–13	2047	24	9	0	0	0	17
Total	2536	290	9	11	6	3	30

See appendix for references. HGA=human granulocytic anaplasmosis. HFRS=haemorrhagic fever with renal syndrome.

Table: **Confirmed and misdiagnosed cases of severe fever with thrombocytopenia syndrome in China**

1 Liu Q, He B, Huang SY, et al. Severe fever with thrombocytopenia syndrome, an emerging tick-borne zoonosis. *Lancet Infect Dis* 2014; **14:** 763–72.
2 Yu XJ, Liang MF, Zhang SY, et al. Fever with thrombocytopenia associated with a novel bunyavirus in China. *New Engl J Med* 2011; **364:** 1523–32.
3 Xu BL, Liu LC, Huang XY, et al. Metagenomic analysis of fever thrombocytopenia and leukopenia syndrome (FTLS) in Henan Province, China: discovery of a new bunyavirus. *PLoS Pathog* 2011; **7:** 1–10.
4 Ding F, Zhang W, Wang L, et al. Epidemiologic features of severe fever with thrombocytopenia syndrome in China, 2011–2012. *Clin Infect Dis* 2013; **56:** 1682–83.

Brucellar aortitis and brucellar spondylitis

We agree with most of the interesting contents of the Grand Round by Jesica Herrick and colleagues,[1] although we find that the problem of brucellar aortitis and its potential coexistence with brucellar spondylitis was insufficiently addressed. The investigators found 34 cases of brucellar arteritis and only 23 cases of brucellar aortis described in the scientific literature, in patients with a mean age of 42·9 years.

We have previously analysed[2] the epidemiological and clinical characteristics of 46 cases of brucellar aortic involvement. In 18 of these cases, the complication involved the ascending thoracic aorta; 16 of these cases were related to brucellar endocarditis. In the remaining 30 cases, the complication involved either the descending thoracic aorta or the abdominal aorta; in 13 of these cases, the complication was related to spondylitis of the lumbar spine. The mean age of the patients was 54·2 years, the median age of the patients 59·0 years (range 23–80 years), and 41 (89%) of the 46 cases were in male patients. The mean age of the patients with abdominal or descending thoracic involvement (65·5 years)

See Online for appendix

was significantly higher than that of patients with ascending aortic involvement (42·5 years, p=0·0006). This difference could be explained by the high prevalence of abdominal aortic comorbidity in elderly people.[2]

We recommend that patients older than 50 years, who have blood cultures positive for *Brucella* spp in addition to fever and back, abdominal, or chest pain, undergo an extensive diagnostic test for brucellar aortic involvement and aneurysm formation. Similarly, patients with aortic mycotic aneurysms or with pseudo-aneurysms should be assessed for brucellosis on the basis of medical history (in particular, epidemiological characteristics), clinical signs, and symptoms as well as by culture, serology, or molecular tests, if available. Patients with brucellar thoracic aortic involvement should undergo further screening to exclude concomitant endocarditis, and patients with brucellar abdominal aortic involvement should undergo further screening to exclude concomitant spondylitis or abdominal or pelvic abscesses. A converse procedure should be applied in patients with endocarditis or spondylitis. Anti-brucellar antibiotic therapy should be initiated as soon as possible, followed by an appropriate surgical approach.[2]

We declare no competing interests.

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1 Herrick JA, Lederman RJ, Sullivan B, Powers JH, Palmore TN. Brucella arteritis: clinical manifestations, treatment, and prognosis. *Lancet Infect Dis* 2014; **14:** 520–26.

2 Cascio A, De Caridi G, Lentini S, et al. Involvement of the aorta in brucellosis: the forgotten, life-threatening complication. A systematic review. *Vector Borne Zoonotic Dis* 2012; **12:** 827–40.

Ebola: lessons learned from HIV and tuberculosis epidemics

Amidst concerns of Ebola virus disease becoming a pandemic, the global medical community has mounted a crucial response. As the director of the US Centers for Disease Control and Prevention has said, "we have to work now so this is not the world's next AIDS."[1] Although different from HIV/AIDS, we could apply lessons learned from the HIV and tuberculosis epidemics to address the Ebola crisis. This experience suggests four near-term objectives.

First, as with HIV, a rapid, point-of-care test is imperative to quickly identify people who are infected with Ebola virus to reduce transmission. Whereas first-generation, laboratory-based HIV tests were essential to confirm disease, rapid HIV tests enabled the widespread screening of asymptomatic people in resource-limited settings.[2] As with first-generation HIV tests, present diagnostic Ebola tests are too expensive, time-consuming, and equipment-dependent. Two companies, Senova and Corgenix, are developing rapid, finger-prick, whole-blood tests, and their efforts should receive strong international support.[3]

Second, the stigma and fear of Ebola virus disease must be addressed. HIV taught us that stigma and fear drive people away from both testing and medical attention, which thereby perpetuates transmission. An accessible test does not automatically translate into people tested—54% of HIV-infected people worldwide are still unaware of their status.[4] If perceived fears outweigh perceived benefits, the erection of treatment centres might not benefit the people who need care. For HIV, stigma and fear have been addressed through information campaigns, peer education, and access to therapy—the same is likely to be necessary to eradicate the stigma and fear associated with Ebola virus disease.

Third, all exposed people should be screened for Ebola virus infection. Successful tuberculosis control programmes have included contact tracing of infected people and testing exposed people. Although 87% of west Africans with the disease had a fever according to a report,[5] 13% are missed in screening algorithms relying on the presence of fever, which is not acceptable. Anybody, including a health worker, who is exposed to patients infected with the virus, should be tested for infection irrespective of the presence of symptoms. The availability of a rapid Ebola test will help these efforts, and it could also be used to screen international travellers at airports.

Fourth, the protection of health-care workers must be paramount. Infection control practices, including use of personal protective equipment and isolation practices, were developed largely in tuberculosis control programmes. Poor infection-control practices lead to increased transmission to health workers and patients. As with successful tuberculosis control programmes in developed countries, health workers treating patients infected with Ebola virus need full training in the use of and access to personal protective equipment before encountering patients, and need the capacity to isolate infected patients.

Confronting the HIV and tuberculosis epidemics has needed a massive, coordinated response—the same will be needed for Ebola virus disease. However, our collective experience with HIV and tuberculosis has shown that such a response is possible.

I am supported by the Harvard Global Health Institute, the Fogarty International Clinical Research Scholars and Fellows Program at Vanderbilt University (R24 TW007988), the Infectious Disease Society of America Education and Research Foundation and National Foundation for Infectious Diseases, The Program in AIDS Clinical Research Training Grant (T32 AI007433), the National Institute of Allergy and Infectious Disease of the National Institutes of Health (K23 AI108293), the