**Previous symptoms of yaws only infrequently relate to present positive syphilis serology.**

**Francis Sarkodie1, 2, Ellis Owusu-Dabo3, 4, Oliver Hassall2,Imelda Bates2, Ib C. Bygbjerg 5 , Henrik Ullum6.**

*1Komfo Anokye Teaching Hospital, Kumasi, Ghana, 2Liverpool School of Tropical Medicine, UK, 3 School of Public Health, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, 4Kumasi Centre for Collaborative Research, KNUST, Ghana,  5Department of Public Health, University of Copenhagen, Denmark.,* *6Department of Clinical Immunology, Copenhagen, University Hospital Denmark.*

***Abstract***

**Objective:** The objective is to describe the reported medical history and clinical manifestations of yaws and syphilis among syphilis sero-reactive blood donors in Kumasi, Ghana

**Methods**: 471 syphilis sero-reactive blood donors from Komfo Anokye Teaching Hospital, Kumasi, Ghana, who were additionally tested with rapid plasma reagin (RPR), were interviewed to determine past or present clinical manifestations of yaws and syphilis.

**Results**: 28 (5.9%) donors gave a history of skin lesions and sores. Four of the 28 donors (14.3%) who were all males and RPR positive, recalled a diagnosis of syphilis. All four reported having lesions/bumps on the skin and slow healing sores but only one of them had these before the age of 15.

**Conclusions**: Only a minority of confirmed sero-reactive donors had any recall of symptoms or treatment of yaws or syphilis. Our data suggest that clinical questioning adds little further information to this screening algorithm. Thus the relative contribution of yaws and syphilis to frequent positive tests in endemic areas remains speculative.

**Background**

Yaws is a neglected non-venereal endemic treponematosis caused by the bacterium *Treponema pallidum*, subspecies *pertenue* [1](#_ENREF_1). It is spread by direct skin-to-skin contact predominantly affecting children < 15 years of age living in poor socioeconomic conditions in certain rural, wet, tropical areas [2](#_ENREF_2). In Ghana, a total of 28,000 cases were reported in 2008 and 25, 000 in 2010. In 2012, WHO launched a new initiative to eradicate yaws, (defined as the complete interruption of transmission) globally by 2020 [3](#_ENREF_3) using the Morges strategy. The clinical manifestations of yaws include multiple papillomas, non-tender ulcers, sores, plantar hyperkeratosis and pigmentation of the palms and soles, followed by gummata in the last stage [1](#_ENREF_1).

 Syphilis is a sexually transmitted disease (STD) caused by *Treponema pallidum* subspecies *pallidum*. It can also be transmitted via blood transfusion although the actual risk is low [4](#_ENREF_4). Syphilis starts with primary lesion (chancre) followed by polymorphic rash and lymphadenopathy. This is followed by occurrence of generalized condition with parenchymal, systemic, and mucocutaneous manifestations [5](#_ENREF_5). The end result may include insanity, gummata, blindness, paralysis, or death.

Usually yaws and syphilis can only be distinguished by epidemiological characteristics and clinical manifestations as the commonly used antibody tests cannot discriminate one disease from the other [6](#_ENREF_6).

The paper describes the reported history of clinical manifestations of yaws/syphilis among syphilis sero-reactive blood donors in Kumasi, Ghana.

**Methods**

A total 526 blood donors who were syphilis sero-reactive tested with Fortress rapid test (Fortress Diagnostics Limited, Antrim – UK) to antibodies (IgG and IgM) to *T. pallidum* in serum or plasma, were further tested with rapid plasma reagin (RPR, BD Macro-VueTM Card test - USA). Out of these, 479 were confirmed with Ortho-Vitros® Syphilis TP test as gold standard. These confirmed consenting donors were interviewed to determine past or present clinical manifestations of yaws and syphilis. Subjects were interviewed on the presence or absence of sores or skin ulcers, lesions/bumps on skin, face, hand, feet, and/or genitals. They were additionally interviewed on slow healing sores and at what age for these symptoms. They were also asked on treatment given if any.

Data were recorded into a spreadsheet and exported into STATA (STATACORP, Texas, version 12.0) for analysis. We obtained approval for this study from the ethics committees of Kwame Nkrumah University of Science and Technology (KNUST) Kumasi, Ghana, and Liverpool School of Tropical Medicine, UK.

**Results**

Out of the 479 sero-reactive blood donors confirmed, 471 responded to the interview (a response rate of 98.3%). The confirmed syphilis sero-reactive donors showed a range of 17 to 53 years with a mean age of 31 years (SD=8.6) of which females were 6.2% (p=0.019). A total of 28 (5.9%) gave a history of skin lesions and sores (Figure 1). Four individuals out of the 28 donors (14.3%) with history of skin lesions and sores - all males and RPR positive – recalled a diagnosis of syphilis. These four donors had previously received penicillin treatment during their exposure to syphilis. Additionally, the four donors with a recall of syphilis exposure reported appearance of lesions/bumps on skin and slow healing sores but only one of them had these symptoms before the age of 15.

As a study limitation, the syphilis sero-reactive blood donors were not asked to distinguish the location of the sores and ulcers on the skin and genitals, thus making it difficult for exact diagnosis. We also recognized the potential of recall bias in influencing the study outcomes.

**Discussion**

The present data suggests that a clinical history of yaws is not frequent among syphilis positive blood donors. However, syphilis symptoms were also not reported frequently. Children aged below 15 years are the most vulnerable to yaws infection [7](#_ENREF_7). In effect, only a minority of confirmed sero-reactive donors had any recall of symptoms or treatment of yaws or syphilis. There was a poor correlation between clinical history indicating spirochaete infection and positive screening test. Thus the relative contribution of yaws and syphilis to frequent positive tests in endemic areas remains speculative. We have previously suggested combined specific and nonspecific syphilis testing to identify potential infectious donors [8](#_ENREF_8). The present data suggest that clinical questioning adds little further information to this screening algorithm.

**Acknowledgements**

Special thanks go to Dr. (Mrs.) Shirley Owusu-Ofori and Dr. Alex Owusu-Ofori for their contributions. We also thank Dr. Daniel Ansong , Research and Development Unit, Messrs. Derek Agyeman Prempeh and Eliot Eli Dogbe and the entire staff of Transfusion Medicine all of Komfo Anokye Teaching Hospital, Kumasi for their support.

***Statement of Conflict of Interest***

None of the authors declare any conflict of interest regarding this manuscript.

***Funding Source***

The study was funded by the European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement No. 266194 through T-REC, a transfusion research capacity for building research in Africa, and part of PhD requirements at the Liverpool School of Tropical Medicine, UK.

**Reference**

**1.** Mitja O, Asiedu K, Mabey D. Yaws. *Lancet.* Mar 2 2013;381(9868):763-773.

**2.** Rinaldi A. Yaws eradication: facing old problems, raising new hopes. *PLoS Negl Trop Dis.* 2012;6:e21837.

**3.** WHO. Eradication of yaws—the Morges strategy. *Wkly Epidemiol Rec.* 2012;87:189–194.

**4.** Van Dyck E, Musonda R, Zekeng L. Study Group on Heterogeneity of HIV Epidemics in Zeltser R, Kurban AK. Syphilis. *Clinics in Dermatology.* 2004;22: 461–468.

**5.** Tramont E. Spirochetes. Treponema pallidum syphilis. *Mandell, Douglas and Bennett's Principals and Practice of Infectious Disease (ed 4) New York, Churchill Livingstone.* 1995:2117-2132.

**6.** Gerstl S, Kiwila G, Dhorda M, et al. Prevalence study of yaws in the Democratic Republic of Congo using the lot quality assurance sampling method. *PloS one.* 2009;4(7):e6338.

**7.** Meheus AZ, Narain JP, Asiedu KB. Endemic treponematoses. In: Cohen J, Powderly N, eds. St Louis, Mosby Incorporated. *Infectious diseases textbook.* 2008.

**8.** Sarkodie F, Ullum H, Owusu-Dabo E, Owusu-Ofori S, Owusu-Ofori A, Hassall O. A novel strategy for screening blood donors for syphilis at Komfo Anokye Teaching Hospital, Ghana. *Transfusion medicine.* Feb 2 2016.

Figure 1. A flowchart of syphilis sero-reactive blood donors interviewed for clinical manifestations of yaws

526 syphilis sero-reactive blood donors tested with RDT

47 not confirmed

479 confirmed with Ortho Vitros®

**471 Interviewed (98.3%)**

Four had a recall of syphilis exposure

24 had no recall of syphilis exposure

Three donors had slow healing sores after 15 years of age

One donor had slow healing sores below 15 years of age

443 had no history of skin lesions and sores

28 had history of skin lesions and sores