Trans R Soc Trop Med Hyg 2016; **110**: 319–320
doi:10.1093/trstmh/trw032 Advance Access publication 6 June 2016

COMMENTARY

Yaws: towards the WHO eradication target

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Received 27 February 2016; revised 4 April 2016; accepted 19 April 2016

In 2012 WHO declared a target to eradicate yaws by 2020. The cornerstone of this strategy is community mass treatment with azithromycin. Initial studies suggest this is a very effective tool that may be capable of interrupting transmission. Alongside this there has been progress in the development and validation of diagnostic tests for yaws. Several new challenges have also emerged, in particular, evidence that *Haemophilus ducreyi* can cause phenotypically similar ulcers in yaws endemic communities, and evidence for a possible non-human primate reservoir. The 2020 eradication target remains ambitious and more challenges should be expected on the journey.

Keywords: Azithromycin, Eradication, Neglected Tropical Diseases, *Treponema pallidum*, World Health Organization, Yaws

In 2012 WHO launched a new strategy for the eradication of yaws[1] supported by World Health Assembly (WHA) resolution WHA 66.12, which called for global eradication of yaws by 2020. Yaws is predominantly a disease of children and, untreated, progresses to cause destructive lesions of the skin, soft tissues and bones. The disease is caused by *Treponema pallidum* susbsp. *pertenue*, a spirochaete closely related to syphilis,[2] and is considered a neglected tropical disease (NTD). The disease can be treated effectively with a single-dose of either benzathine-penicillin or azithromycin. Mass treatment with azithromycin is the mainstay of the new WHO yaws eradication strategy.

Yaws has been the target of previous eradication efforts.[3] Following WHA resolution 2.36, in 1949, a joint WHO/UNICEF eradication campaign treated more than 50 million individuals and is thought to have reduced the worldwide prevalence of yaws by 95%. Despite these successes, yaws eradication was not achieved. A number of factors contributed to this, including a failure to achieve adequate coverage of asymptomatic cases and inadequate surveillance following the completion of the initial phases of the eradication campaigns. The disease subsequently rebounded in a number of countries and despite a further WHA resolution in 1978 (WHA 31.58),[3] and accompanying control efforts, the disease has continued to be a significant public health problem in a number of countries.

Globally yaws is known to be currently endemic in 13 countries, predominantly in West Africa, South East Asia and the Pacific.[4] For a further 76 countries, which have previously reported cases of yaws, there are no recent epidemiological data to guide eradication efforts. Two countries, India and Ecuador, have reported local interruption of transmission of yaws following government led elimination efforts.

What are the prospects of achieving global yaws eradication? The feasibility of achieving eradication depends on biological, social and political factors.[5]

Biological factors

A fundamental requirement is the existence of a tool to interrupt transmission. A number of lines of evidence suggest that such a tool may exist for yaws. Previous eradication efforts using penicillin have shown that with extremely high coverage it is possible to interrupt transmission,[3] a finding that has been confirmed by the recent experience of the Indian yaws elimination programme.

Will mass treatment with azithromycin be as effective? Initial pilot data are encouraging and suggest mass treatment with azithromycin has a significant impact on prevalence and transmission of yaws.[6] A concern is the potential for emergence of resistance to azithromycin, now well documented in syphilis. Surveillance for resistance will be a vital component of yaws eradication efforts.

Adequate surveillance is needed at all stages of an eradication campaign. Where the clinical features of a disease are sensitive and specific, such as for guinea worm, clinical diagnosis alone may be sufficient. The clinical phenotype of early yaws is much less robust. In particular, *Haemophilus ducreyi* has recently been shown to be a major cause of similar skin lesions in yaws endemic communities,[7] in some cases accounting for more cases than yaws. A rapid serological test has been validated for yaws but, as *H. ducreyi* has been found both in seropositive and sero-negative individuals, serological diagnosis alone is unlikely to be sufficient. Access to serological diagnostics, and in the certification phase molecular diagnostics, will need to be scaled-up significantly if the eradication target is to be achieved.

A key requirement for disease eradication is the absence of an animal reservoir. An emerging body of evidence suggests there may be a non-human primate (NHP) reservoir for yaws. Serological and molecular evidence for a disease caused by *T. pallidum* has now been documented in NHPs across a range of countries in Africa, which are currently or formerly endemic for yaws.[8] Alongside this ecological data, there is evidence that experimental infection of humans with NHPs strains is possible, and vice versa. Whether zoonotic transmission occurs in the wild remains an open but vital question.

Social and political factors

Social and political support is of fundamental importance for the success of any eradication campaign. The WHA resolution is an important step towards galvanising international political support for yaws eradication. As a disease predominantly of morbidity not mortality, yaws may not be perceived as a public health priority even in the countries where it is endemic. Maintaining political support is likely to become an increasing challenge as WHO scales up eradication efforts, global case numbers fall but the costs of on going eradication efforts remain high.

Modelling work suggests that yaws eradication is cost-effective in the long term and it is hoped that this will help convince donors to support yaws eradication.[9] These findings are based on a number of assumptions, which may not hold true. Firstly, the model assumed that transmission would be interrupted everywhere by a limited number of rounds of high coverage treatment (90–99% coverage), although there are limited empirical data to support this. Secondly, data from NTD programmes shows that such high coverage is rarely achieved in the real world.[10] Finally, the model assumed that only surveillance would be required in all of the formerly endemic countries. If any of these countries were found to be currently endemic then the overall costs of yaws eradication may rise sharply.

Finally, many other NTD elimination/eradication programmes have benefitted from the creation of donation schemes to support drug and implementation costs. At present no such donation programme exists for yaws and this represents a significant barrier to the scaling up of yaws eradication efforts.

Conclusions

There are four years remaining until the 2020 target for yaws eradication. At this point it seems unlikely that this target will be met. The first phases of yaws eradication have already revealed a number of unexpected findings and it seems likely that further obstacles will emerge on the road to eradication. Despite these obstacles, progress has been made in the development of new diagnostic tools and pilot studies demonstrating the effectiveness of azithromycin mass treatment. A sustained commitment from the WHO, countries and the academic community will be required if the goal of yaws eradication is to be achieved.

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