

Full Length Research Paper

Eradication of yaws

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Global Medline search have been done on yaws and its eradication since 1950 onwards through meshwork. In this research, reference journals and textbook materials were selectively chosen for detailed clinical characteristics. As the disease has not been common in Bangladesh, expert opinion was lacking. More precise concentration was done over eradication theme. Review target was to elicit questions on readers mind and how to achieve the target with many restrains of eradication of yaws.

Key words: Yaws, *Treponema pallidum*, eradication.

BACKGROUND

Yaws, caused by the spiral-shaped bacterium (spirochete) *Treponema pallidum* subspecies *pertenue* is a contagious, non-venereal infection in humans that presents mainly in children below 15 years which primarily affects the skin, bones and cartilage (Perine et al., 1984). The disease occurs primarily in poor, rural and marginalized populations in parts of Africa, Asia and South America, where conditions of overcrowding, poor water supply and lack of sanitation and hygiene prevail. Thus, it is a poverty-related disease. If left untreated, yaws leads to crippling and disfiguring consequences (Antal et al., 2002).

The major route of infection is through direct person-to-person contact. The treponemes associated with yaws are located primarily in the epidermis. The ulcerative skin lesions that develop early in the disease course teems up with spirochetes, which can be transmitted via direct skin-to-skin contact and via breaks in the skin due to trauma, bites or excoriations. Yaws, like syphilis, has been classified into the following 4 stages: (1) Primary stage: The initial yaws lesion develops at the inoculation site (Backhouse and Hudson, 1995); (2) Secondary stage: Widespread dissemination of treponemes results in multiple skin lesions similar to the primary yaws lesion (Backhouse and Hudson, 1995; Bora et al., 2005); (3) Latent stage: Symptoms are usually absent, but skin lesions can relapse (Chulay, 2000); (4) Tertiary stage:

Bone, joint, and soft tissue deformities may occur (Chulay, 2000; Engelkens et al., 1991).

Another classification distinguishes early yaws from late yaws. Early yaws includes primary and secondary stages and is characterized by the presence of contagious skin lesions. Late yaws includes the tertiary stage, when lesions are not contagious.

(1) Primary lesions, also called mother yaw, develop at the site of inoculation after an incubation period of 3 weeks (range, 9 - 90 day) (Figures 1 and 2). The primary lesion often appears at a site of prior skin injury or an insect bite. During the incubation period, *T. pertenue* invades the subcutaneous lymphatics and disseminates hematogenously. The initial yaws lesion is a papule that enlarges to become a papilloma or frambesioma which resolves spontaneously after 3 - 6 months (Engelkens et al., 1999; Farnsworth and Rosen, 2006; Fuchs et al., 1993).

(2) Secondary yaws lesions may occur near primary lesions or elsewhere on the body which may last for more than 6 months. Macules, papules, nodules and hyperkeratotic lesions may appear (Figure 3). Hyperkeratosis, referred to as crab yaws, may appear on palms and soles. Lesions may ulcerate. Bone and joint involvement may occur in early disease and may cause pain and swelling. In the dry season, lesions are fewer and macular in appearance. Papillomas are found in moist areas of axilla, skin folds and mucosal surfaces (Hook, 1999; Lupi et al., 2006). Secondary lesions heal spontaneously.

(3) During latent periods, skin lesions may relapse for as

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Figure 1. Initial papilloma, also called mother yaw or primary frambesioma (from Perine et al. Handbook of Endemic *Treponematoses: Yaws, Endemic Syphilis and Pinta.* Geneva, Switzerland: World Health Organization, 1984).



Figure 3. Plantar papillomata with hyperkeratotic macular plantar early yaws (that is crab yaws) (from Perine et al. Handbook of Endemic *Treponematoses: Yaws, Endemic Syphilis and Pinta.* Geneva, Switzerland: World Health Organization, 1984).



Figure 2. Yaws causes ulcerative skin lesions, and is found in areas where poor sanitation exists. Yaws was prevalent in some of the relief camps set up during the Nigerian-Biafran war (1967 - 1970). Credit: US Centers for Disease Control and Prevention/Dr. Lyle Conrad. doi:10.1371/ journal.pntd.0000275.g002].



Figure 4. A saber shin deformity is an abnormality of the tibia characterized by marked anterior bowing of the lower leg. This defect may be seen in some children with congenital syphilis and in patients with yaws. Credit: US Centers for Disease Control and Prevention/Dr. Peter Perine. doi:10.1371/ journal.pntd.0000275.g001(20).

long as 5 years after infection. Most patients remain in a noninfectious latent stage for their lifetime.

(4) Late yaws develops in 10% of cases, usually 5 - 10 years after disease onset.

Characteristic deformities, called saber shins (Figure 4), result from chronic untreated osteoperiostitis of the tibia (Engelkens et al., 1991, 1999). Other lesions observed in patients with late yaws include monodactylitis, juxta-articular nodules, and gangosa (also called *Rhinopharyngitis*

Table 1. Suggested target for treatment of the community.

High endemic	Total population
Moderate endemic	Active cases, their contacts and all children below 15 years
Low endemic	Active cases and their contacts in households, schools and workplaces

Table 2. Alternative drugs for treatment among patients with penicillin hypersensitivity.

Tetracycline	500 mg twice daily to adults and 250 mg to children over 8 years for 15 days
Erythromycin	500 mg twice daily to adults and 8 mg/kg/body weight to children of over 8 years and smaller dose for children below 8 years for 15 days
Doxycycline	100 mg twice a day for 15 days to adults and 2.5 mg/kg/body weight in two divided doses to children over 8 years

mutilans), in which nasal cartilage is destroyed (Macgregor, 2004; Nnoruka, 2005; Parish, 2000; Perine et al., 1984).

Physical lesions

Early yaws lesions: (1) Papilloma; (2) Serpiginous papilloma; (3) Ulceropapillomata; (4) Squamous macules; (5) Maculopapules; (6) Nodules; (7) Plaques; (8) Hyperkeratosis of palms and soles; (9) Bone and joint lesions; (10) Generalized lymphadenopathy (may occur)

Late yaws lesions: (1) Hyperkeratosis; (2) Nodular scar; (3) Gangosa; (4) Saber tibia; (5) Goundou; (6) Monodactylitis; (7) Juxta-articular nodules.

DIAGNOSIS

Yaws is usually diagnosed based on clinical findings. Serodiagnostic tests for venereal [RPR] (Venereal Disease Research Laboratory [VDRL] test) results are positive in all stages, except for very early lesions (Backhouse and Hudson, 1995; Hook, 1999). Confirmatory treponemal tests (eg, *Treponema pallidum* hemagglutination [TPHA], microhemagglutination *T. pallidum* [MHA-TP], fluorescent *Treponema* antibody absorption [FTA-ABS]) are not practical in remote areas (Nnoruka, 2005). Results of dark-field examination of early lesions are positive. Biopsy of late lesions may be needed to show characteristic histopathology. Typical histopathology of early yaws shows papillomatous epidermal hyperplasia, focal spongiosis, and intraepidermal microabscesses (Backhouse and Hudson, 1995; Parish, 2000; Rothschild, 2005). *Treponemes* are found in the epidermidis.

THE TREATMENT

Long-acting Penicillin is the drug of choice for treatment of yaws cases and their contacts. 1.2 million units of

Injection Penicillin G Aluminium Monostearate (PAM) to adults as single intra-muscular injection and 0.6 million units to children below 10 years cures the disease and make the patient non-infectious within 24 h (Rothschild, 2005; Sarangapani and Benjamin, 2001; Sehgal, 1994). Penicillin is contraindicated in patients/contacts with history of drug hyper-sensitivity. No penicillin resistant strains have been reported so far (Walker and Hay 2000; Young and Murphy, 2006). Based on the level of seropositivity among children, suggested targets for treatment of the community are shown in Table 1.

Tetracycline, erythromycin or doxycycline are the alternative drugs for treatment among patients with penicillin hypersensitivity as shown in Table 2.

ERADICATION: EARLY ATTEMPTS, FAILURE, LESSONS AND NEW HOPES

An estimated 50 - 100 million persons were infected before mass treatment campaigns in the 1950s. In the 1970s, yaws cases declined to fewer than 2 million. In the 1980s, fewer than 500 cases per year were reported in the Western Hemisphere. A resurgence of yaws has occurred in West and Central Africa, Southeast Asia and the Pacific Islands, with recent outbreaks in Thailand, India, Indonesia, Papua New Guinea and the Solomon Islands. Sporadic cases are reported in South America. Between 1952 and 1964, WHO and the United Nations Children's Fund (UNICEF) led a worldwide campaign to control and eventually eradicate yaws and other endemic *Treponematoses* (Guthe and Willcox, 1954). This was a major disease control effort undertaken by WHO just after its establishment in 1948 (WHO, 1988). Control programme were established in 46 countries and by the end of 1964, the number of cases had been reduced from 50 million to 2.5 million (a 95% reduction) (Antal and Causse, 1985). The yaws control efforts paved the way for the development of the primary health care system in affected areas (Troupin et al., 1953). In the late 1960s, there was a shift in strategy from the vertical programme to integration of yaws surveillance and control into primary

primary health care to tackle the remaining 5% of cases. However, this approach did not succeed.

By the end of the 1970s, reemergence of yaws in many countries prompted a World Health Assembly Resolution requesting the implementation of integrated *Treponematoses* control programmes (WHO, 1978). Renewed control efforts were implemented in several countries, e.g. Benin, Burkina Faso, Côte d'Ivoire, Ghana, Mali, the Niger and Togo, but these efforts were not sustained. In 1984, a global meeting was organized in Washington, DC (Burke et al., 1985) followed by regional meetings with the aim of reviving eradication activities. These attempts were half-hearted and the goal of eradication remained elusive (Meheus and Antal, 1992). At this time, most of the yaws programmes had been integrated into primary health care which were generally too weak to implement the activities of a vertical programme (Meheus, 1985). Since then, yaws has remained as a public health problem in a few pockets, including three countries in the SEA Region - India, Indonesia and Timor-Leste (Figure 4).

In 1995, WHO estimated the number of infectious cases to be 460 000 worldwide of which, 400 000 were in west and central Africa, 50000 in South-East Asia and the rest in other tropical regions (WHO/EMC/95.3). The South-East Asia Region of WHO kept yaws high on its agenda and set the goal of regional eradication by 2012 in its two remaining endemic countries - Indonesia and Timor-Leste after India achieved elimination.

Since 2004, India has reported no new cases (Elimination of yaws in India, 2008). In the Western Pacific Region, three countries remain endemic - Papua New Guinea, the Solomon Islands and Vanuatu. The main lessons learned from the past are that yaws can be eliminated with sustained efforts as shown in many countries and recently in India.

Factors favorable for yaws eradication

(1) Man is the principal reservoir; (2) Patients with early lesions are the main sources of infection; (3) Progressive decline in the number of reported cases over the years; (4) Direct contact with secretions of skin lesions is the main mode of transmission; no insect vector involved; (5) Intimate and prolonged contact needed for person to person spread; (6) Effective treatment for cure available; (7) Treatment is safe, effective and operationally feasible; (8) Disease restricted to a few backward tribal communities; (9) Few neglected foci do not cause epidemics and do not spread to other areas; (10) Mass campaigns aimed at total population examination to detect cases and treat them along with contacts have greatly reduced the prevalence and transmission; (11) Improvement in personal hygiene, sanitation, community awareness of the disease, especially free availability of effective treatment and improved socio economic conditions facilitate reduc-

tion of transmission.

REGIONAL STRATEGY

The Regional Strategic Plan for Yaws Eradication 2006 - 2010, lists the plan aims at the goal of eradication of Yaws in the Region by 2012. Eradication is defined as absence of new cases and certification, three years after achieving nil cases. The objectives are: (a) To detect and treat all Yaws cases and their contacts; (b) To interrupt transmission and (c) To prevent disability and minimize the suffering and economic impact on the affected populations. The key elements of the strategy include active case-finding and treatment of cases/contacts, mobilization of community support through IEC campaigns, capacity building of health staff, surveillance, operational research and monitoring/evaluation.

BARRIERS FOR ERADICATION

“Unfortunately, yaws remains among the most neglected diseases and there is little global attention or focus on this disease, although, it primarily affects the most poor and vulnerable sections of the society; the tribal or indigenous people living far away from mainstream. The World Health Organization should publicize the currently known and unknown status of surveillance for this disease in each of the remaining suspected endemic countries and encourage mapping and more detailed reporting of surveillance data” (International Task Force for Disease Eradication, 2007), thus playing a steering role in addressing this curable and preventable disease. WHO, it must be stressed, is responding to the appeal. In a consultation round-up held recently at the organization's headquarters in Geneva, experts and officers from the health ministries of those countries where yaws is still a menace agreed on a basic agenda for future action (World Health Organization, 2007). The agenda includes a rapid assessment of the burden of disease and infection in selected countries; revival of activities to control yaws; and establishment of an elimination program for yaws, directed by WHO in the context of its larger Neglected Tropical Diseases initiative. Elimination of clinical cases (zero cases) supported by active case-finding and serological surveys has been declared as the goal, but no timeline has been set. Although, it is generally agreed that political and financial inertia are the biggest obstacles to interrupting transmission of yaws, some eradication experts point out that biological and medical barriers also exist. For example, although, it is usually claimed that humans are the only reservoir of infection, 17% of the members of a wild gorilla population in the Republic of Congo presented typical yaws skin lesions (Levrero et al., 2007). Yaws may also affect African baboons and widespread serological testing of wild popu-

lations has been performed; genetic analyses of a strain collected from a Guinean baboon shows that it is closely related to human yaws strains (Levrero et al., 2007).

If complete eradication is to be enforced, nonhuman reservoirs need to be cleared as well. Successful treatment campaigns have already been carried out on primates against various infectious diseases; in the case of yaws, affected baboons were darted and treated with penicillin and an additional antibiotic (Wallis and Rick, 1999). In parallel, more information is needed on the way pathogens cross transmit between humans and primate populations, so that suitable strategies to prevent disease spreading and/or resurgence may be developed. As for humans, untreated victims may remain infective for months, favoring the spread of *Treponemes* within populations. A vaccine is still lacking and so is a reliable test able to distinguish yaws from the various other *Treponematoses* and monitor its impact on populations, as discussed earlier. Furthermore, some researchers noted, the recurrent shortage of benzathine penicillin G in North America due to production problems which could make mass treatment difficult (Scolnik et al., 2003).

HOPE FOR THE FUTURE

Yaws can be effectively controlled, at least at the national level and even swept out if sufficient energy is applied (Bora et al., 2005; Lahariya and Pradhan, 2007). "Yaws had been declared to be eliminated from India on 19 September, 2006 as no case of the disease was reported since 2003. The new target set for yaws eradication from India is year 2008. The elimination has been achieved based on a two-pronged strategy which primarily consisted of: first, active case finding and treatment of cases and prophylaxis of the household contacts using a single injection of long acting penicillin; second, community mobilisation. The programme used a campaign approach; health workers went from village to village every six months looking for yaws cases and offering treatment/prophylaxis to those needing it (Aylward and Birmingham, 2005). The serosurveillance activities in the selected districts in the children aged less than five years are also being done to ensure that the *T. pallidum pertenuis* is not present in the community.

RESEARCH AND OPERATIONAL CHALLENGES

- a) Primate status: The impact of yaws in primates needs to be further documented and stronger evidence should be published from large-scale studies.
- b) Development of Pre School Age Children (PSAC) needs to be confirmed and properly tested in different epidemiological settings.
- c) Outreach/cost/feasibility Innovative ways of out-reaching and delivering penicillin alone or with other

medications should be documented, with particular attention to feasibility and cost-effectiveness. It is essential that such approaches are properly monitored and evaluated at country level and their successes documented in order to enhance advocacy and guide international agencies and policy makers to promote appropriate tools for the control of yaws infections and other diseases in children.

d) Adverse Event Reporting Forms (AERS) need to be included in any campaign delivering penicillin drugs so as to routinely capture data on the number of children having problems with injection. In the meantime, WHO and UNICEF should continue advocating for the development of novel paediatric formulations (rapid dissolving tablets or alternating drug like macrolides).

e) Pharmacovigilance: Safety of giving penicillin with other drugs in population-based interventions needs to be evaluated in large-scale control programmes by a review of observational evidence.

f) Monitoring drug efficacy: Drug efficacy of penicillin delivered in large-scale interventions and the early occurrence of treatment failures needs to be monitored; any suspect episode of drug resistance should be properly reported.

g) Monitoring coverage an integrated monitoring system to collect and manage data related to the number of children treated needs to be developed to report on coverage of different age and high risk groups.

h) Evaluating interactions vaccine interactions: Possible synergies and interactions related to delivering injection penicillin with different vaccines (measles, BCG, polio) in large-scale vaccination campaigns needs to be further evaluated and properly followed up in the mid and long term.

i) Malaria/TB/HIV: Interactions of yaws with the management of the three big killers-malaria, TB and HIV-needs further study and science-based evidence to advocate and suggest novel means of combating malaria, TB and HIV infections in yaws endemic areas.

Conclusion

Besides the general criteria of biological and technical feasibility, costs and benefits and societal and political considerations, each disease eradication attempt has its own peculiarities, which should be carefully considered in order to achieve success. Yaws, in this regard, is a one-of-a kind opportunity, because a lot can be learnt from past practical efforts, with less need for speculation. We need to build the network and develop the necessary partnership for tackling yaws in a sustainable manner. Indeed, collaboration with existing programs could allow resources to be shared and facilitate elimination and surveillance activities. There is also a clear need for increased advocacy and generation of interest, both in the disease itself and in engaging countries. What seems

most interesting about the renewed effort in South-East Asia is that it is aggressively targeting both cases and their contacts, for which there seems to be evidence that this could overcome the earlier challenges. The disease is extremely amenable to eradication epidemiologically, technologically, historically and from political commitment point of view. We believe also that efforts on yaws eradication could be an entry point for primary health care for the most marginalized populations, the fortunate thing for yaws is that we do not need whopping amount to realize our efforts. The total amount of money required to achieve yaws eradication would be only a small fraction of what is being spent for polio eradication annually. Ultimately, eradication of another disease—take for example that of smallpox in 1978 would by itself be an achievement for public health! The other side of the coin is that a second failure against this vincible enemy could cast discredit and mistrust on other ongoing and future eradication efforts, directed against more pernicious and less vulnerable pathogens. Let's just hope this is not the case.

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