



# ERADICATION OF YAWS

## A guide for programme managers



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# Preface

In 2012, the Director-General of the World Health Organization (WHO) launched a roadmap for accelerating work to overcome neglected tropical diseases at a partners' meeting in London, United Kingdom, with a target set for the eradication of yaws by 2020. A publication in the *Lancet* that year on the efficacy of a single dose of azithromycin for the treatment of yaws was a major advance in the history of the disease and has renewed interest in its eradication. In 2013, the Sixty-sixth World Health Assembly adopted resolution WHA66.12 on neglected tropical diseases in support of WHO's roadmap. In this resolution, yaws is targeted for eradication by 2020.

In response to these developments, the WHO Department of Control of Neglected Tropical Diseases organized a consultation (Morges, Switzerland, 5–7 March 2012) to prepare a strategy for yaws eradication as the basis for national eradication plans. In light of the new development, the International Task Force for Disease Eradication at its 20th meeting (Atlanta, USA, 27 November 2012) reviewed the current global status of yaws and endorsed the new eradication strategy.

At a consultative meeting of experts (Geneva, 20–22 March 2013), two documents were developed to guide the yaws eradication process: a guide for programme managers on the eradication of yaws; and procedures for verification and certification of interruption of yaws transmission.

Some 43 participants from 17 countries deliberated in depth to finalize both documents. Participants included national yaws focal points in endemic countries, experts on yaws, and regional and selected WHO country staff responsible for yaws eradication within the portfolio of the neglected tropical diseases programme. Since then, these documents have undergone extensive review taking into consideration accumulated experiences gained during the pilot implementation of the Morges Strategy in a number of countries.

This document provides guidance for countries on how to implement activities to achieve the interruption of yaws transmission. It is intended for use by national yaws eradication programmes, partners involved in the implementation of yaws eradication activities and WHO technical staff who provide technical support to countries in the eradication of yaws.

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# Abbreviations

DPP	dual path platform (treponemal and non-treponemal) test
PCR	polymerase chain reaction
POC	point-of-care
RPR	rapid plasma reagin test
TCT	total community treatment
TPHA	<i>Treponema pallidum</i> haemagglutination assay
TPPA	<i>Treponema pallidum</i> particle agglutination assay
TT	total targeted treatment
WHO	World Health Organization



# 1. Introduction

## 1.1 Background

Yaws is a disfiguring non-venereal disease caused by infection with the spirochaete *Treponema pallidum* subspecies *pertenue* which is closely related to the causative agent of syphilis and those of the other endemic treponematoses, bejel and pinta. The disease is endemic in certain areas of the World Health Organization (WHO) African, South-East Asia and Western Pacific regions. Of the neglected tropical diseases identified for elimination and eradication, yaws is one of two diseases targeted for eradication (1). In 1949, the Second World Health Assembly adopted resolution WHA2.36, which addresses yaws, bejel and pinta as major public health problems that need attention (2).

About 50 million people were treated with a single dose of long-acting penicillin during the mass treatment campaigns conducted by WHO and the United Nations Children's Fund between 1952 and 1964, and the prevalence of yaws disease was reduced by more than 95% from 50 million to 2.5 million (3). The lack of sustained political commitment and resources slowed the campaign's progress to eradicate the disease. As a result, by the late 1970s the disease had begun to resurge, prompting the Thirty-first World Health Assembly in 1978 to adopt resolution WHA31.58 to renew efforts towards controlling endemic treponematoses in West Africa, but implementation of the resolution was not sustained. Subsequently, in 1995, WHO estimated 2.5 million cases of the endemic treponematoses (mostly yaws), with an incidence of 460 000 new cases per year (4).

## 1.2 Overview of the eradication strategy

### A new treatment strategy

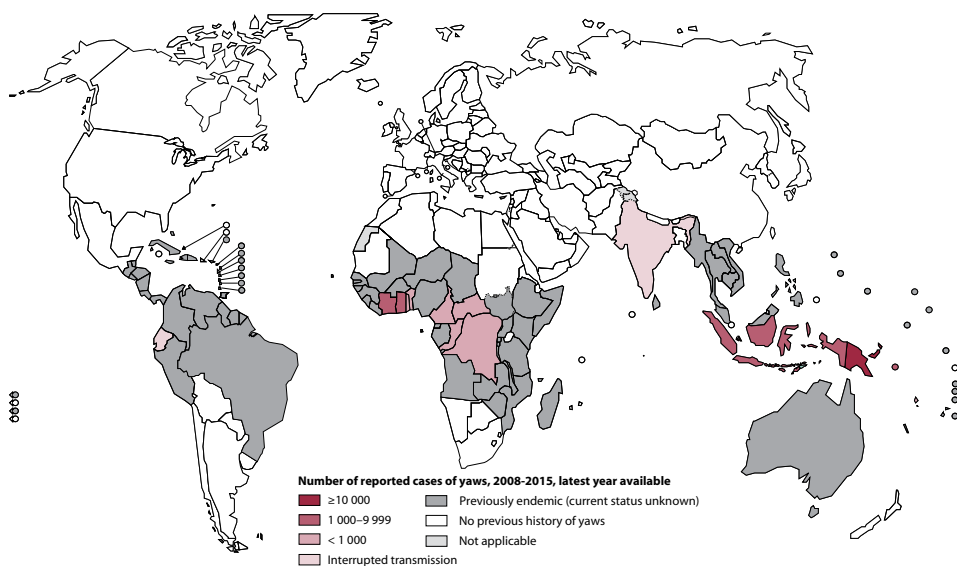
A single intramuscular dose of long-acting penicillin has long been used in mass treatment campaigns in areas where yaws is endemic. In 2012, the efficacy of a single oral dose of azithromycin (30 mg/kg body weight) in curing the disease was published (5,6). The same year, WHO held a consultation of yaws experts in Morges, Switzerland and recommended mass treatment using single-dose oral azithromycin to eradicate the disease by 2020. This new treatment strategy has been referred to as the Morges Strategy (3).

### **New treatment strategy for yaws eradication (3)**

WHO recommends a single dose of oral azithromycin (30 mg/kg body weight), which is to be used in the new treatment policies, during the initial campaign of total community treatment (TCT), followed by total targeted treatment (TTI) to achieve the complete interruption of transmission (absence of new cases of yaws) globally by 2020.

**Interruption of transmission** is verified by: (i) the absence of any report of an indigenous, infectious yaws case for 3 consecutive years; and (ii) the absence of new sero-reactors for 3 consecutive years among children in the community aged 1–5 years.

Accordingly, countries where yaws is endemic should reach zero new cases by 2020 followed by 3 years of clinical and serological surveillance to confirm the permanent absence of transmission.



**Figure 1.** Distribution of yaws, worldwide, 2008–2015 (Source: reference 7)

**Table 1.** Distribution of yaws endemic countries, by WHO region

WHO region	Group A.1 Interrupted transmission and certified	Group A.2 Interrupted transmission Pending verification	Group A.3 Currently endemic countries	Group B Previously endemic countries	Group C Countries with no history of yaws	Total number of countries and territories
African	0	0	8	28	11	<b>47</b>
Americas	0	1 <sup>b</sup>	0	32	14	<b>47</b>
South-East Asia	1 <sup>a</sup>	0	2	3	5	<b>11</b>
Western Pacific	0	0	4 <sup>c</sup>	19	14	<b>37</b>
Eastern Mediterranean	0	0	0	2	20	<b>22</b>
European	0	0	0	0	54	<b>54</b>
<b>Total</b>	<b>1</b>	<b>1</b>	<b>14</b>	<b>84</b>	<b>118</b>	<b>218</b>

Source: reference 8

<sup>a</sup> India was certified free of yaws by WHO in May 2016 (9).

<sup>b</sup> Ecuador reported interruption of yaws transmission in 1998 but has not been certified (10).

<sup>c</sup> The Philippines confirmed cases of yaws in 2017 (11) in addition to Papua New Guinea, the Solomon Islands and Vanuatu.

### 1.3 Geographical distribution

A review of the historical and current literature on yaws from 1950 to 2013 indicates those countries where the disease has been endemic (Table 1). Two principal reasons underpin this information:

1. In the 1950s, there was no formal procedure to verify the interruption of transmission and certify countries that might have previously achieved elimination of yaws. Hence, in many of these countries, the current status remains unknown.

2. Since the 1990s, formal reporting of yaws from a number of countries to WHO has ceased so it is unclear whether these countries no longer have yaws or have stopped reporting.

Based on the available information (8), countries have been classified into three groups for the purposes of verification and certification (Table 2). Figure 1 shows the global distribution of yaws for the period 2008–2015 and Table 3 the countries reporting yaws cases in 2008–2015 (7).

**Table 2.** Classification of countries for certification of interruption of yaws transmission

Group A	Countries whose status of yaws endemicity is currently known
A.1	Countries that have interrupted transmission and have been certified by WHO
A.2	Countries that have reported interruption of transmission in recent years but which need to be verified and certified by WHO
A.3	Countries with ongoing transmission for which activities to interrupt transmission are to be implemented as per the Morges Strategy
Group B	Countries with a previous history of yaws in the 1950s but no report since 2000 (current status unknown)
Group C	Countries with no history of yaws but that need to be certified for the purpose of global eradication.

**Table 3.** Number of yaws reported cases, worldwide, 2008–2015

Country	Number of cases reported								
	2008	2009	2010	2011	2012	2013	2014	2015	Total
<b>Africa</b>									
Benin	ND	ND	45	ND	11	ND	ND	ND	<b>56</b>
Côte d'Ivoire	ND	ND	3740	3343	3092	2256	2650	1940	<b>17021</b>
Cameroon	ND	ND	802	133	59	97	530	463	<b>2084</b>
Central African Republic	243	ND	ND	ND	230	ND	ND	ND	<b>473</b>
Congo	ND	646	ND	ND	197	ND	ND	ND	<b>843</b>
Democratic Republic of the Congo	383	ND	ND	ND	ND	ND	ND	ND	<b>383</b>
Ghana	20525	35248	18157	9674	8980	18702	1901	1620	<b>114807</b>
Togo	ND	ND	15	ND	ND	ND	15	27	<b>57</b>
<b>Asia and Pacific Islands</b>									
Indonesia	6083	7751	6178	6631	4360	2043	1521	3379	<b>37946</b>
Papua New Guinea	28989	25822	29061	28989	17560	19710	29886	28584	<b>208601</b>
Solomon Islands	ND	ND	20635	ND	12372	14909	13312	9736	<b>70964</b>
Timor-Leste	ND	ND	ND	ND	ND	ND	ND	ND	<b>0</b>
Vanuatu	ND	ND	1593	2331	2514	1198	615	317	8568
<b>Total</b>	<b>56223</b>	<b>69467</b>	<b>80226</b>	<b>51101</b>	<b>49375</b>	<b>58915</b>	<b>50430</b>	<b>46066</b>	<b>461803</b>

ND, no data available

Source: reference 7

## 2. The disease

### 2.1 Causative organism

Yaws is caused by infection with *Treponema pallidum* subspecies *pertenue*, a spiral bacterium (spirochete) closely related to the causative organism of syphilis. Related spirochetes are the cause of the other nonvenereal treponematoses bejel (*T. pallidum* subspecies *endemicum*) and pinta (*T. carateum*).

### 2.2 Transmission

Yaws is transmitted from person to person by direct skin contact with fluid from untreated early, infectious lesions (skin papillomas and ulcerations). Although the lesions may heal spontaneously, some lesions may recur. Without treatment, the disease may resolve spontaneously or become latent and re-emerge as late yaws. Late yaws lesions of 2 years or more (palmar and plantar hyperkeratotic lesions, bone lesions) are generally not infectious.

Cases of yaws are often seen in temporal clusters within neighbouring communities, as transmission occurs primarily among children at home, at school or at play (12). Poor hygienic conditions (limited access to water) and overcrowding are some of the factors that are believed to promote transmission of the disease.

About 75% of new yaws cases are seen among children aged less than 15 years (13). The incubation period is between 9 and 90 days, with an average period of 21 days (14).

### 2.3 Clinical features

The clinical manifestations of untreated disease present in the following stages (see also Annex 1, Table A1):

**Primary stage:** A papule (a raised lesion) forms at the organisms' site of entry (such as a micro abrasion) after an incubation period of 9–90 days. The papule may then develop into a small yellowish cauliflower-like lesion (papilloma), which grows gradually and develops a punched-out centre covered with a yellow crust (ulcer and ulceropapilloma). In 65–85% of cases, the primary lesions of yaws are seen on the legs and ankles (15,16). However, they may be found on the face, neck, armpits, arms, hands and buttocks.

The initial lesions, which are highly infectious, may take 3–6 months to heal, leaving a pitted scar with dark margins.

**Secondary stage:** The secondary stage of yaws is characterized by more generalized lesions, which may appear on the face, neck, armpits, arms, legs and buttocks. These lesions may also occur on the soles of the feet, forcing the patient to walk in an odd position; this condition has been termed “crab-yaws” (hyperkeratosis).

Secondary lesions occur following spread of the causative organism to the blood and lymph, and multiple lesions most commonly within the first 2 years following the

appearance of the primary yaws lesion. Joint pain (arthralgia) and malaise are probably the commonest, nonspecific symptoms of secondary yaws.

**Latent yaws:** If left untreated, the infectious lesions of primary and secondary yaws will heal spontaneously and the disease may enter a period of latency with no physical signs. Latent yaws can only be detected as a result of serological testing.

**Tertiary stage:** Although spontaneous healing may occur in many cases, a minority may progress from latency to the tertiary stage. This destructive, non-infectious stage of the disease is characterized by gumma formation and may appear after a variable period of latency. This stage affects the bones, joints and soft tissues, and frequently leads to deformities of the skin, cartilage and bone. Such cases may develop severe disfigurement of the face and legs, resulting in disabilities that prevent children from attending school and adults from working. Thus, the socioeconomic and humanitarian impact of yaws justifies intensification of yaws eradication activities (17).

## 2.4 Diagnosis and differential diagnosis

All individuals with suspected yaws lesions should be examined by trained health workers. A clinical diagnosis should be established based on the patient's history, endemicity of yaws in the area and characteristics of the lesions. Health workers should refer to the WHO yaws recognition booklet (18).

### 2.4.1 Clinical diagnosis

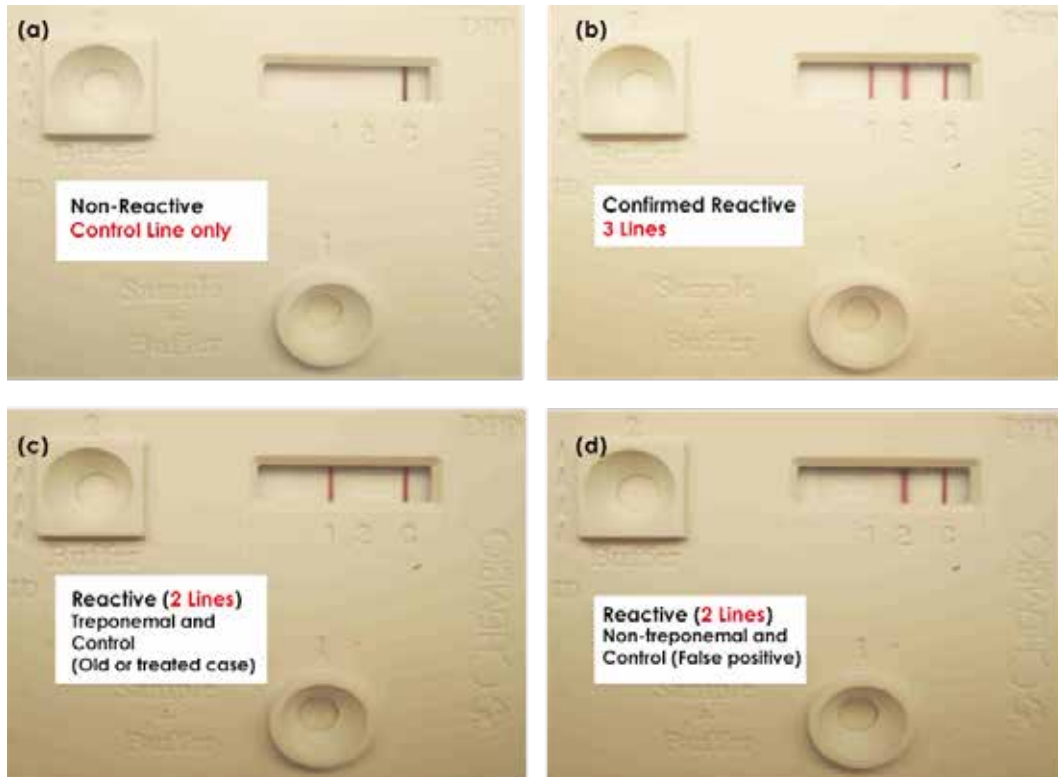
A clinical diagnosis is based on the following features:

- History of living in or having lived in a yaws endemic area;
- Age of an individual (more common among children aged < 15 years);
- Clinical appearance of skin/bone lesions suspicious of yaws (papilloma, ulceropapilloma, ulcer, papule, macule, see Annex 1 Table A1);
- Typical distribution being most common sites: lower limbs (70%); upper limbs (11%); trunk (6.2%); head and neck (8.2%); and multiple sites (4.0%).

Based on the clinical findings, the individual will be classified as:

- Suspected yaws case (pending serological confirmation); or
- Non-yaws case.

If health workers have difficulty confirming (or doubt) the diagnosis, the suspected yaws case remains on a list of suspects for subsequent examination by more experienced health staff (nurse or doctor). This step is critical after the initial total community treatment (TCT) campaign to ensure the reliability of any reported case. During a TCT campaign, everyone is treated.



**Figure 2.** Dual path platform (non-treponemal and treponemal) point-of-care test – Interpretation of results (Source: reference 19)

#### 2.4.2 Serological confirmation of clinically diagnosed yaws cases

Testing for treponemal and non-treponemal antibodies should be done to confirm a diagnosis of yaws so that reporting of cases by countries will shift from clinically suspected cases to laboratory-confirmed cases. Traditional laboratory methods such as rapid plasma reagin (RPR) and *Treponema pallidum* haemagglutination assay (TPHA) or *Treponema pallidum* particle agglutination assay (TPPA) testing can be used, but the delay in obtaining test results may negatively impact early treatment. Treponemal point-of-care (POC) tests can be used in the field for rapid screening and to exclude non-yaws cases, but subsequent confirmation of positive cases is necessary using a non-treponemal test. Treponemal and non-treponemal antibodies can also be simultaneously detected using a dual POC test such as the dual path platform (DPP) syphilis screen and confirm assay (19). Both tests can be performed by trained health workers in the field using a finger-prick blood sample and the results read within 20 minutes, thus facilitating immediate treatment. Typical results obtained when using the DPP indicating different patterns of reactivity and their interpretations are shown in Figure 2.

The dual DPP test has been found to be sensitive and specific for confirmation of both syphilis and yaws (20–23) and is easy to apply under field conditions.

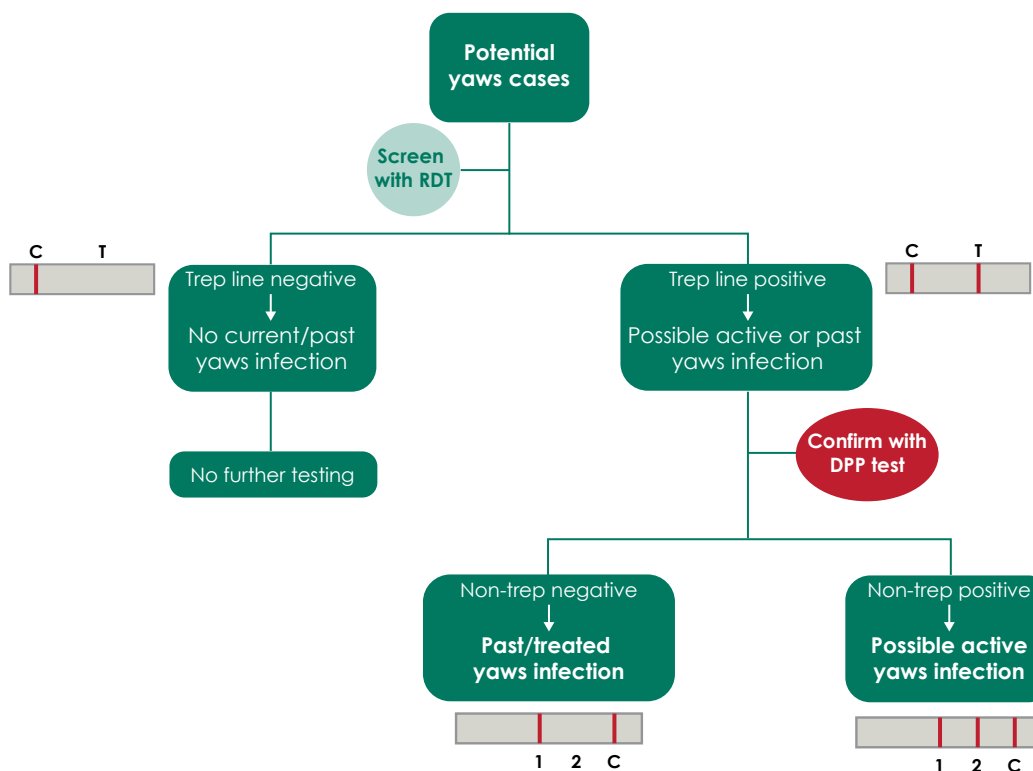


A specimen containing treponemal and non-treponemal antibodies exhibits three lines (treponemal, non-treponemal and control) in a developed test (Figure 2b), indicating a **confirmed reactive** sample, while a specimen containing neither treponemal nor non-treponemal antibody will exhibit only a control line (Figure 2a). Interpretations of other patterns of reactivity are also shown (Figure 2c and 2d). **Note: Reactive results do not necessarily mean that the lesion is active yaws, as it could be caused by other agents.**

By detecting both treponemal and non-treponemal antibodies, the use of this test should greatly reduce the rates of overtreatment inherent in current (treponemal only) rapid testing and permit a single point-of-care device to be used for yaws serosurveillance.

Where available, RDT and DPP tests may be used in combination (see Figure 3).

Although both treponemal and dual POC tests are easy to perform, strict adherence to the manufacturers' instructions is necessary to ensure accuracy. Adoption of POC tests at clinical sites requires ongoing supervision by a reference laboratory including provision of an external quality assurance programme.



**Figure 3.** Flowchart for the combined use of rapid treponemal and DPP tests

### 2.4.3 Differential diagnosis of yaws

A variety of skin diseases may be common among population groups living in areas where yaws is endemic. These may be mistaken for the lesions of primary and secondary stage yaws. The most common differential diagnoses are tropical ulcers and lesions caused by *Haemophilus ducreyi* (24). Health workers should consult WHO's *Yaws recognition booklet* (18) or *Handbook of endemic treponematoses* (25) for relevant information on alternative diagnoses.

## 2.5 Treatment

Yaws is amenable to treatment with either one of these two medicines: azithromycin or benzathine benzylpenicillin. Historically, mass treatment campaigns have relied on long-acting penicillin, which remains an effective treatment. Recently, however, oral azithromycin has been shown to be effective and is recommended by WHO for the eradication of yaws due to its ease of administration, the absence of a risk of anaphylaxis as is seen with penicillin and the fact that a cold chain is not required for storage.

### 2.5.1 Azithromycin

A single oral dose of azithromycin has been recommended for use in treatment of early yaws (primary and secondary) based on the results of clinical trials conducted in Papua New Guinea (5) and Ghana (6). In these studies, a single dose of azithromycin (30 mg/kg body weight; to a maximum dose of 2 g) has been found to be both effective and well tolerated with minimal adverse side-effects. The **cure rate** (> 98%) was found to be equivalent to that of a single intramuscular injection of long-acting penicillin, which was previously considered the treatment of choice for the disease. In 2017, the WHO Essential Medicines List has included azithromycin as an indication for the treatment of yaws (26).

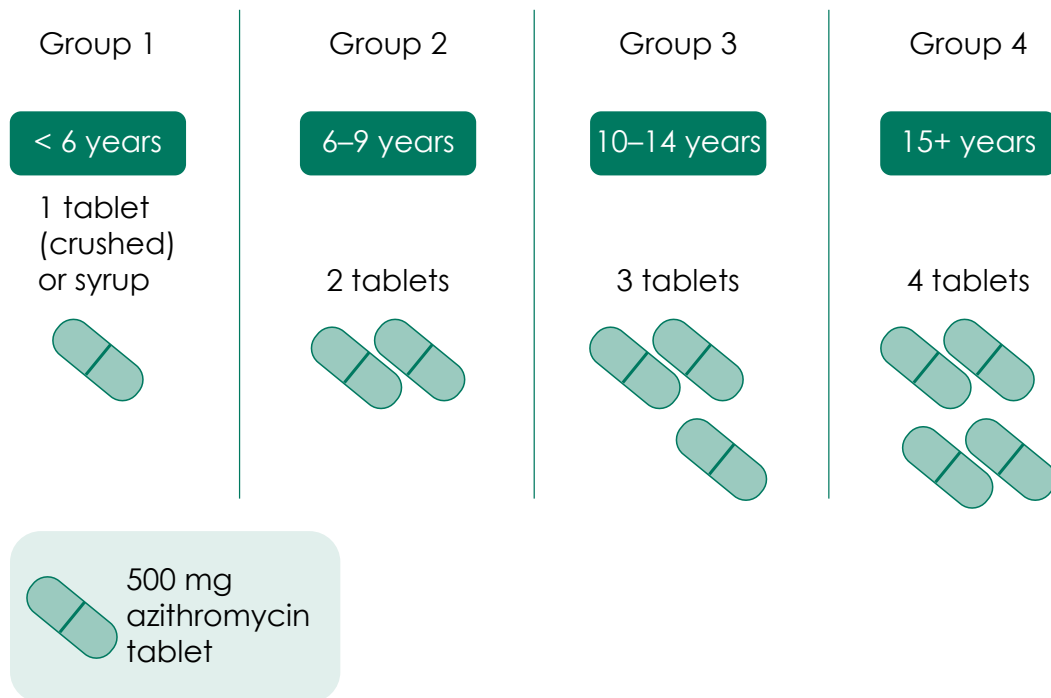
For the eradication of yaws, WHO recommends azithromycin (30 mg/kg body weight; maximum 2 g) as a single, oral dose given to the entire population of an endemic community in order to interrupt transmission of the disease (3).

While azithromycin is not recommended for children aged less than 6 months, it can be administered during pregnancy and breastfeeding.

The age-based recommendation for azithromycin dosages is shown in Figure 4. The use of 500 mg tablets is preferred to 250 mg tablets because this reduces the number of tablets that individuals are required to swallow, making treatment more convenient and less burdensome. For children aged under 6 years, the tablet should be crushed and mixed with water.

### Adverse events with azithromycin

Azithromycin may cause nausea, vomiting, abdominal pain and diarrhoea. Field experience from trachoma campaigns (27) and among patients with yaws (5,6) has indicated a rate of adverse events of less than 10% which could all be managed in the field or in nearby health facilities. Based on these observations, azithromycin has been found to be a safe drug for use in mass treatment campaigns with minimal severe adverse events and is well tolerated by both children and adults.



**Figure 4.** Recommended azithromycin dosage by age

### 2.5.2 Intramuscular benzathine benzylpenicillin

Intramuscular long-acting penicillin remains effective in the treatment of yaws (dosage for adults, 1.2 million units; children aged less than 10 years, 600 000 units). In some countries, the doses are doubled. Given the advantages of oral azithromycin, intramuscular benzathine benzylpenicillin should be considered as an alternative therapy only when cases or their contacts develop severe adverse events to azithromycin or for those who cannot tolerate or take azithromycin. Intramuscular benzathine benzylpenicillin is known to rarely cause severe hypersensitivity reactions, which can be fatal. Pain at the injection site and vasovagal reactions are the most common adverse events recorded.

### 2.5.3 Reporting adverse drug events

Health workers should report adverse drug events to their respective national programme manager through their district team. The national programme should send reports to WHO and relevant national authorities using the reporting format described in the WHO guidelines (28).

Adverse events arising as a result of treatment for yaws or as a result of mass drug administration should be managed promptly (Table 4).

- Provide rapid medical assistance to individuals and counsel the individual and family members to gain the confidence of the community.

- Clarify the rumour or misinformation (type of messages circulating, source, persons or organizations spreading the rumours) to village leaders, religious leaders, media persons (if any), nongovernmental organization and schoolteachers to alleviate any fear about the medication.

The community health workers (or volunteers) should remember the following points while managing individuals who refuse treatment:

- Explain the benefits of treatment (curing yaws and preventing its spread to individuals, their families and community members).
- Explain the benefits of treating other infectious and skin ulcers with azithromycin.
- Never force an individual to swallow azithromycin (or to receive a single injection of benzathine benzylpenicillin).
- Request community leaders or members who have taken azithromycin to encourage individuals who initially refuse treatment, citing their own experiences.

**Note: When an individual continues to refuse treatment after appropriate counselling, encourage the individual to accept treatment during subsequent follow-up rounds.**

**Table 4.** Managing adverse events

Medication	Azithromycin	Intramuscular benzathine benzylpenicillin
<b>Adverse events</b>	Abdominal pain, nausea, vomiting, diarrhoea	Hypersensitivity reaction (anaphylaxis or angioedema)
<b>Incidence</b>	4–14%	1 in 50 000
<b>Treatment</b>	Treatment by health worker on the spot in mild case with antacids, anti-diarrhoeal medicines or antiemetics depending upon signs and symptoms Move to nearest health facility or hospital if severe adverse events occur	Treatment by health worker on site with adrenaline and/or intravenous steroidal preparation and/or move to health facility immediately
<b>Counselling of individuals and family members</b>		
<b>Precautions</b>	Azithromycin should not be administered on an empty stomach to avoid gastric irritation Ensure that people have eaten	Question regarding possible allergies
	Community members should be informed about possible side-effects of azithromycin therapy, before administration	Community members should be informed about possible side-effects of penicillin therapy, before administration

#### 2.5.4 Managing treatment failure

Cases of treatment failure (that is, individuals who show no clinical improvement four weeks after ingesting a single dose of azithromycin) should be referred to a district or provincial hospital for further investigation and management. **Note: Clinical cure rate for confirmed yaws cases exceeds 98%.**

## 3. The eradication strategy

The current WHO yaws eradication strategy is based on the administration of a single dose of azithromycin during TCT of the entire population living in yaws-endemic communities. Pilot projects conducted in Papua New Guinea (29), Ghana (30) and the Solomon Islands (31) have resulted in a significant decrease in prevalence of active and latent yaws. TCT is followed by a phase of active clinical and serological surveillance and treatment of any residual cases and their contacts until there are no new infectious cases. Post-zero case surveillance consists of (i) continued active surveillance and treatment of incident cases, and (ii) yearly sero-surveys among children aged 1–5 years, until no sero-reactors have been found for a period of 3 consecutive years (Figure 5) (3).

**Total community treatment (TCT):** Entire endemic community receives treatment initially, irrespective of the number of active clinical cases or the prevalence of yaws disease. Experience from recent pilot studies has shown that one round of TCT is not enough to interrupt transmission. Therefore, two or three rounds of TCT at 6–12 monthly intervals may be required to interrupt transmission or significantly reduce prevalence of cases. However, a population coverage of > 90% is essential.

**Total targeted treatment (TTT):** All new yaws cases and their contacts (household, frequent family friends, schoolmates and playmates) are treated after the initial campaign.

**Health system approach:** Resurveys for case-finding, treatment and surveillance are continued by health system personnel. Where the health system is weak or nonexistent, initiate health system strengthening to sustain treatment services and surveillance using innovative approaches. The health system would be responsible for (i) confirming and treating suspected as well as missed cases including their contacts, and (ii) sustaining public awareness and interest through health promotion, case-finding and treatment activities.

**Essential supportive measures:** The central and district yaws eradication teams should provide technical and logistic support to health facilities throughout the yaws eradication process.

### 3.1 Technical definitions

The terms elimination and eradication were defined in 2012 by the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases (32) and referred to in the 2016 *Generic framework for control, elimination and eradication of neglected tropical diseases* (33). These definitions are:

**Elimination of transmission** (also referred to as interruption of transmission) is defined as *“reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographic area with a minimal risk of reintroduction, as a result of deliberate efforts; continued actions to prevent re-establishment of transmission may be required”*.

**Eradication** of a disease is defined as the *“permanent reduction to zero of the worldwide incidence of infection caused by a specific pathogen, as a result of deliberate efforts; with no more risk of reintroduction”*.

## 3.2 Operational definitions

Operational definitions to assist the programme in planning, implementation and monitoring activities are provided in Annex 1.

## 3.3 Criteria for interruption of yaws transmission

Two criteria for the eradication of diseases were established in 1960 by the WHO Expert Committee on Venereal Infections and Treponematoses (34); the same criteria were recommended by the Morges Strategy in 2012 (35). Molecular testing was added to the criteria in 2015.

**Clinical criteria:** The absence of any report of a **new, infectious, serologically-confirmed indigenous yaws case** for 3 consecutive years, supported by high coverage of active surveillance.

**Serological criteria:** The absence of transmission as measured by sero-surveys with evidence of continuous negative serological tests (rapid treponemal test) for at least 3 consecutive years in samples of asymptomatic children aged 1–5 years in the community.

**Molecular criteria:** The absence of molecular positivity (e.g. by polymerase chain reaction [PCR]) for *T. pallidum* spp. *pertenue* in the lesion of any serologically confirmed case during the post-zero surveillance period.<sup>1</sup>

In 1960, the WHO Expert Committee on Venereal Infections and Treponematoses recommended the following criteria for eradication of yaws (34):

**Epidemiological eradication** was considered as the intermediate stage to complete eradication, defined as the absence of **an indigenous infectious case** in the population for 3 consecutive years. The basis of findings includes information gathered from four sources: (i) all medical centres in the country where proper records of cases of the disease are kept; (ii) biannual medical examinations of all schoolchildren; (iii) annual surveys of randomly selected villages remote from medical facilities, schools, and towns; and (iv) cases reported from any reliable source of information such as publications from universities and private health sectors.

**Complete eradication** was considered as the final stage of achievement of eradication (interruption of transmission), defined as the absence of an indigenous case in the population for 3 consecutive years, with information from all the above sources having been considered and no sero-reactor in the age group 1–5 years having been found during sero-surveys.

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<sup>1</sup> In view of the recent findings of yaws-like lesions caused by other bacteria e.g. *Haemophilus ducreyi*.

## Experience of yaws eradication in Haiti in the 1950s

Haiti was one of the endemic countries that embarked on an aggressive effort to eradicate yaws in the 1950s. Although it is unclear whether the disease was completely eradicated, some important lessons should guide the conduct of the renewed efforts to eradicate yaws.

Extracts from the article detailing the experience of yaws eradication in Haiti as published in the *Bulletin of the World Health Organization* in 1956 are reproduced below (36).

### *Objective*

**There can be but one objective in a yaws programme—eradication. By eradication of yaws we mean a complete disappearance of all infectious cases from a country and the non-appearance of any primary autochthonous case after the intensive campaign efforts have been terminated; in other words, the complete interruption of transmission. This objective can be attained if suitable techniques are put into effect, as will be described below. Although the differences between an eradication programme and a control programme may seem to be only of degree, if we examine them carefully we will observe the tremendous public health and economic importance of an eradication programme. These differences may be tabulated as follows: <sup>a</sup>**

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<sup>a</sup> This tabulation has been adapted from document No. 1 of the Co-ordinating Office for Malaria Eradication Programme, Pan American Sanitary Bureau.

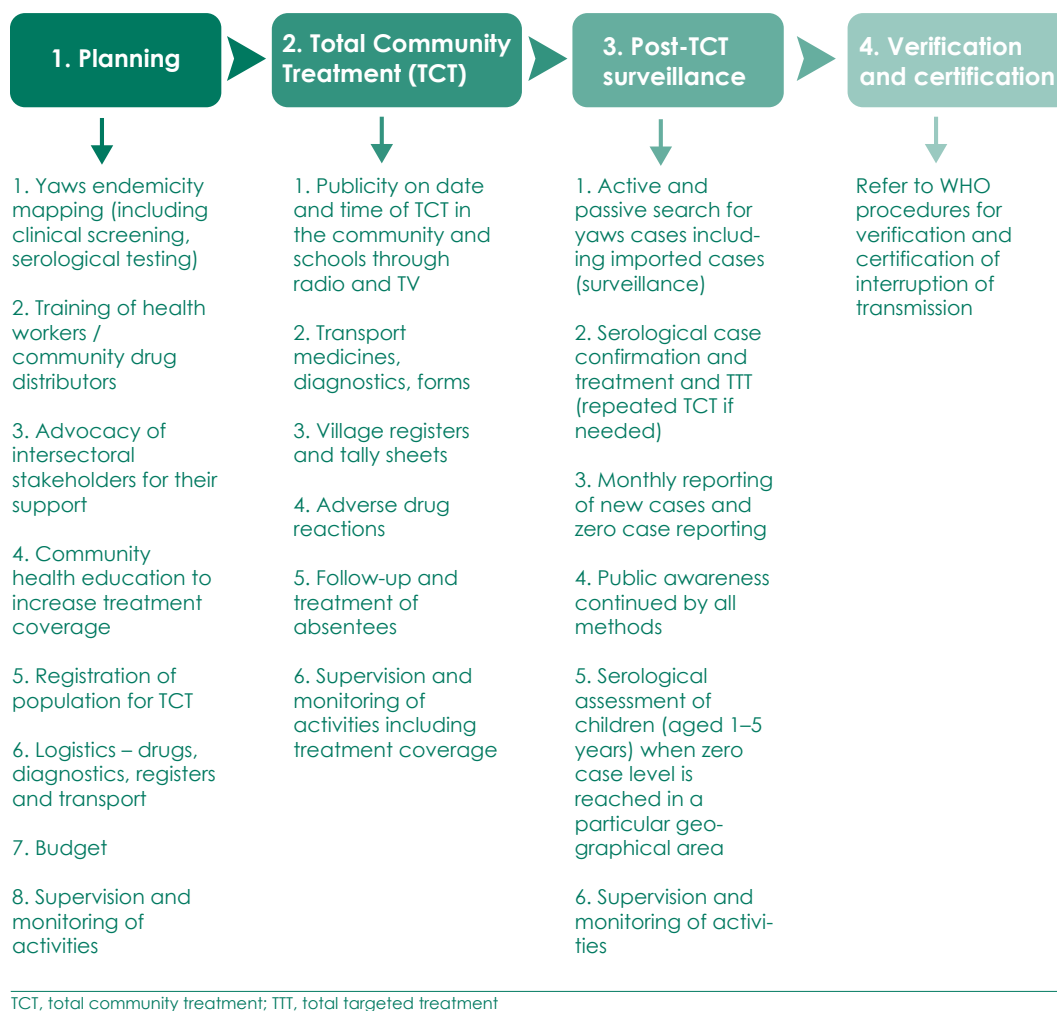
## Experience of yaws eradication in Haiti in the 1950s (continued)

<i>Elements</i>	<i>Control programme</i>	<i>Eradication programme</i>
1. Objective	To reduce morbidity.	To prevent the occurrence of any new cases of yaws.
2. Area of operations	Accessible zones, areas of yaws prevalence of high social, political and economic importance.	All the areas where cases occur.
3. Minimum quality of work	Good: reduction of number of cases.	Perfect: all infectious cases must be eliminated (which implies the treatment of contacts), and the chain of transmission must be stopped.
4. Duration of operations	Permanent.	Programme finishes when infectious yaws no longer exists. To be successful it must be an expanding programme to clean up all areas from which re-infection can occur.
5. Economic factors	Treatment measures applied in those areas where the cost is justified by the economic importance of the local area; expenditures must be continued indefinitely (recurrent service).	Treatment measures have to be applied in all areas and will rapidly reduce expenditures, representing a capital investment rather than a recurrent expense.
6. Case-finding	Important in all phases of the programme.	Important especially in the final stages of the programme.
7. Serological diagnosis	Important in all phases (and expensive).	Not important in mass phases.
8. Imported cases	Of relative interest.	Vital after mass treatment has stopped.
9. Epidemiological investigation of individual cases	Very expensive and seldom conducted.	Vital in spite of expense, especially in last phase of the programme; only measuring rod of eradication.
10. Administrative evaluation of the programme	Measurement of accomplishment (reduction in morbidity).	Measurement of what remains to be done.
11. Epidemiological evaluation	Reduction of serological rates.	Disappearance of primary autochthonous cases as proved by the yaws "intelligence service".



### 3.4 Implementation steps

The eradication strategy has four implementation steps that comprise various activities, as shown in Figure 5 and described below.



**Figure 5.** Implementation steps for yaws eradication strategy activities

## Mapping of yaws-endemic communities

Programmes may consider using various combinations of mapping methods to identify endemic communities/villages/hamlets/districts/islands/provinces according to the country situation. Mapping will also assist the programme with planning and implementation, including estimation of drug needs and budgetary requirements.

## Suggested steps for endemicity mapping

- Review historical records, reports and surveillance data with special reference to areas where the disease was known to be endemic.
- Perform clinical and sero-surveys of a sample of children aged < 15 years in areas (either in schools or communities) where the disease was known to be endemic.
- Once the data or information is gathered from various sources, baseline mapping should be plotted for planning purposes.

## Estimating the target population

- Obtain the last population census of each targeted community from the appropriate source.  
If the census is more than one year old then the population estimate should be adjusted using national growth rate data.
- Exclude children aged < 6 months (about 3%) from the population estimates for the purpose of estimating drug requirements.

## Estimating drug requirements

- Estimate the requirement of azithromycin tablets for the target population based on an average of 3 tablets of 500 mg per person.

## Developing a national strategic plan for yaws eradication

Countries should develop a strategic plan to implement the Morges Strategy, with annual plans of action for implementing activities. Yaws eradication activities should be linked to the United Nations Sustainable Development Goals for 2030.

## Mobilizing political and community support

Every effort should be made to mobilize political and community support for the implementation of the strategy at all levels using appropriate advocacy and health education materials. The success stories of other countries in interrupting transmission of yaws may be used to mobilize political support and investment.

## Advocacy with stakeholders and intersectoral collaboration

The programme should collaborate closely with health and non-health partners in implementing activities. Sectors such as education, water and sanitation, immunization, nutrition, school health programmes, health promotion and community development organizations (including poverty reduction programme organizations) should be involved in and contribute to national efforts to eradicate the disease.

## Formation of a national task force

The health ministries of yaws-endemic countries, in close collaboration with WHO, may consider establishing a national task force to guide the implementation, monitoring and evaluation of yaws eradication activities. Depending on the country, other mechanisms may be put in place to provide oversight and guidance.

## Training

A comprehensive training programme for health and community personnel with focus on essential tasks is needed for the successful implementation of eradication activities.

## Checking pre-campaign preparations

Before starting a TCT campaign, district and peripheral teams should prepare checklists in order to confirm that all preparations have been completed to ensure maximum treatment coverage (Annex 2). The checklists may be modified according to local requirements.

## Organizing yaws treatment campaigns

After completing the preparatory phase, the programme should implement an initial round of TCT. Comprehensive preparation will result in increased participation and treatment coverage. Experience from the pilot projects indicate that most communities will need at least two rounds of TCT at an interval of 6–12 months. Communities should be well informed about the TCT campaign using flyers or leaflets (Annex 3) in order to obtain high participation or coverage.

- All treatment with azithromycin should be administered under the direct supervision of team members.
- All adverse events should be recorded and reported.
- The administration of TCT in the implementation unit should be completed within a period of four weeks.
- Measurement of the immediate impact using clinical assessment should begin four weeks after completion of TCT or TTT.

## Approaches to achieve maximum treatment coverage and compliance

- Innovative approaches should be planned to achieve maximum (> 90%) treatment coverage during TCT. Those absent during the TCT should be followed up immediately within 7 days and azithromycin should be administered.
- Community members should know exactly when treatment teams will visit in order to minimize confusion and reduce the rate of absenteeism.
- The benefits (for treatment of yaws and other infections) of a single dose of azithromycin should be explained to the population to enhance high treatment coverage.
- Depending on the country, the following approaches or combinations thereof may be used to administer the treatment: house-to-house, central point and schools to achieve high (> 90%) coverage.

### 3.5 Provision of azithromycin and procurement of diagnostic tests

The quantities of azithromycin and diagnostic tests needed should be estimated based on the size of the population to be treated in endemic communities. If the census is >1 year old, the population size should be adjusted based on national growth rate data.

Uninterrupted, timely and adequate quantities of the supply of medicines and diagnostics are key components in ensuring the successful implementation of activities.

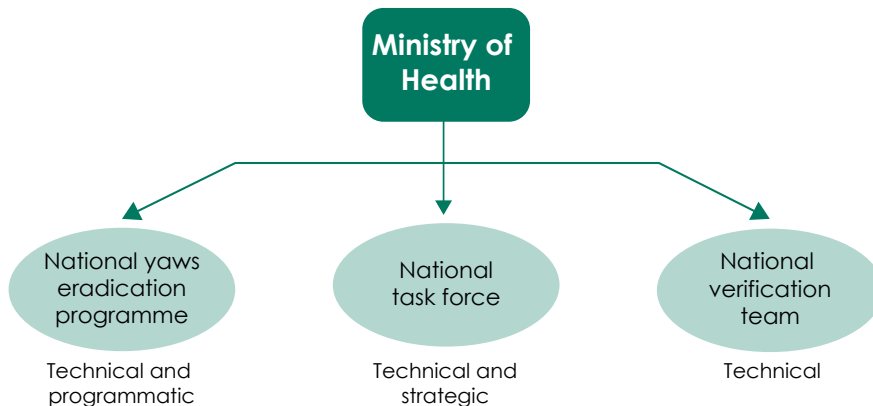
The programme should ensure that the azithromycin and diagnostic tests are stored according to the manufacturers' instructions. A stock register should be maintained to monitor drug receipts and distribution of drugs and diagnostics including expiration dates of all batches.

### 3.6. Structures for yaws eradication at country and global levels

At the national level, each endemic country may consider establishing:

- a national yaws eradication programme as part of the national NTD programme;
- a national task force to give technical advice and strategic guidance for yaws eradication activities; and
- a national verification team to verify local interruption of transmission initially.

A possible structure for yaws eradication at country level is shown in Figure 6.



**Figure 6.** Possible structure for yaws eradication

Source: reference 3

At the global level, the WHO Yaws Eradication Programme will establish:

- an advisory group to provide technical advice and strategic guidance for yaws eradication activities; and
- an international verification team to certify that countries have met the criteria for interruption of transmission.

## 4. Supervision, monitoring and surveillance

### 4.1 Supervision and monitoring

Supervision and monitoring of yaws eradication activities are essential to assess progress and identify problems for rectification. Supervision and monitoring are undertaken by personnel at different levels. The frequency and duration of the visits depend on the circumstances of each country.

#### Activities to monitor during supervisory visits

Some of the following activities are monitored by the district/central teams:

- Progress in implementing treatment campaigns
- Treatment coverage (population and geographical)
- Confirmation of new suspected cases, zero case reporting
- Investigating possible treatment failures (no improvement)
- Records and management of adverse events to azithromycin
- Stocks of azithromycin and rapid tests
- Reviewing reported data, spot checks and consumer interviews
- Technical review meetings to identify and solve problems.

### 4.2 Indicators

Close monitoring of the following indicators is important to reach the set target of eradication of yaws by 2020.

- The number of new serologically-confirmed infectious cases reported monthly.
- Treatment coverage of the target population.

#### Calculating treatment coverage rates

Treatment coverage rates are calculated to monitor progress in effective implementation of TCT.

#### Geographical coverage

Geographical coverage assists the programme in monitoring expansion of treatment in the implementation units. It should be 100% in order to achieve yaws eradication.

The proportion of implementation units implementing azithromycin treatment is calculated as:

$$= \frac{\text{Total number of implementation units implementing treatment}}{\text{Total number of implementation units requiring treatment}} \times 100$$

## Treatment coverage of the target population

The treatment coverage of the target population is an important indicator in assessing how well the treatment campaign was planned and implemented. Ideally, the treatment coverage should exceed 90%.

It is calculated as:

$$= \frac{\text{Eligible population reported to have taken the medicine}}{\text{Eligible population requiring treatment with the medicine}} \times 100$$

## Preparation of summary data

At the end of TCT, the team will summarize the data from the tally sheet (Annex 4) into the daily summary sheet (Annex 5).

## 4.3 Follow-up activities after total community treatment campaigns

A post-treatment campaign follow-up should be planned 4 weeks after TCT to: 1) assess clinical cure or failure, and 2) identify and treat anyone missed during the mass treatment. Surveys at 6-months after TCT are to detect and treat any new cases. If geographical coverage is not complete (< 100% of known endemic communities) and treatment coverage is not very high (< 90%), TCT may be repeated (most communities will need more than one round of TCT to interrupt transmission or ensure significant reduction in prevalence). If the coverage requirements are fulfilled, TTT can be initiated. A community-based surveillance system using village volunteers and schoolteachers should continue to report the occurrence of any new clinically suspected cases to the local health workers. The health workers should investigate each of these cases and perform serological testing using a rapid treponemal test. Those cases found to be positive should be tested with a DPP test for clinical confirmation. The health workers should record all cases investigated and complete the case investigation form (Annex 6). All such suspected cases should be treated and all close contacts of the dually seropositive cases should also receive treatment (TTT) (Table 5). Treatment of individual cases should be registered using the form in Annex 7. There is no need to test contacts. Guidance for assessment of impacts is in Annex 8.

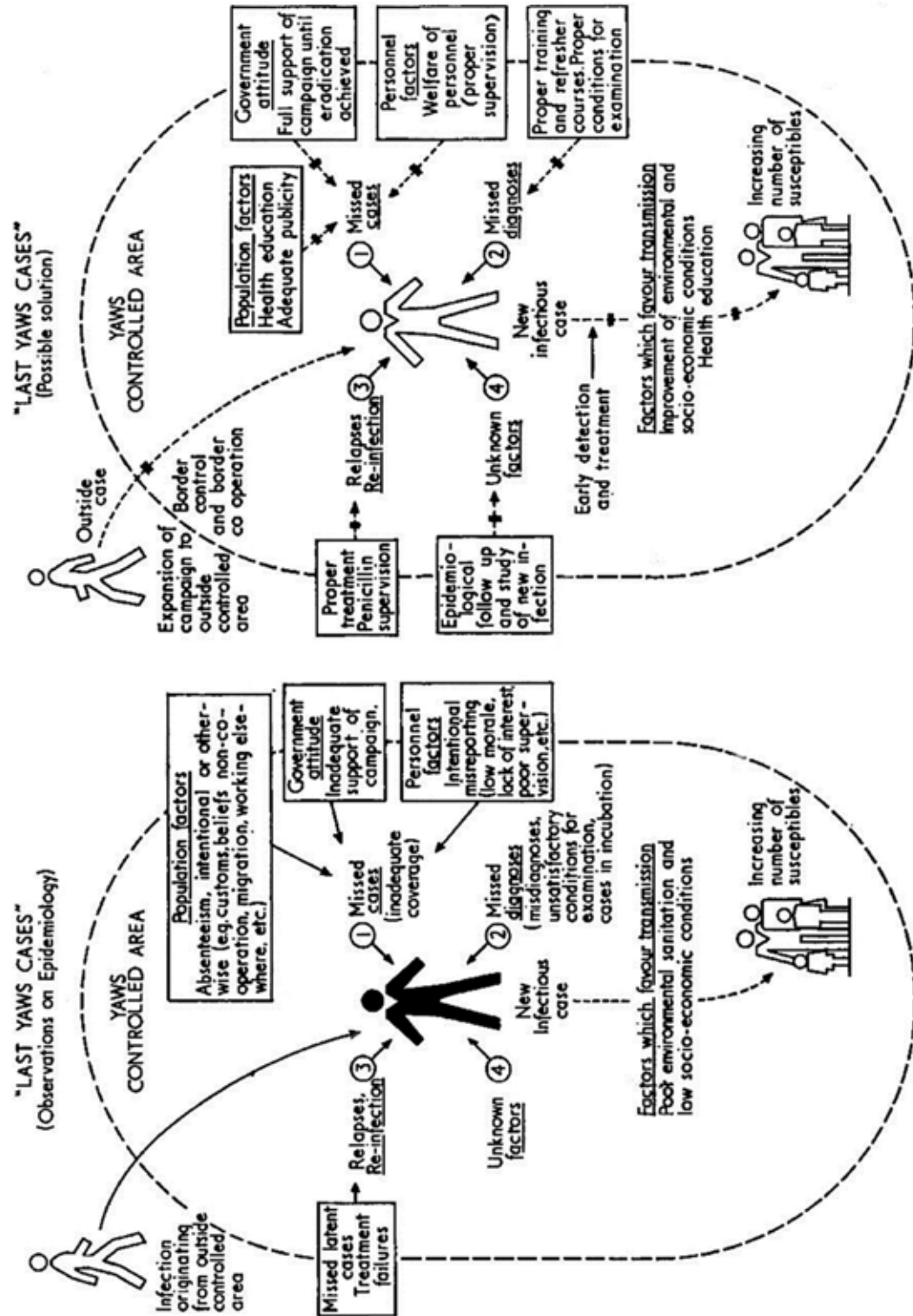
**Table 5.** Treatment of clinical yaws cases and their contacts by serology result

Serology result of the index case	Treatment of cases	Treatment of contacts
Negative treponemal point-of-care test	Yes	No
Positive treponemal point-of-care test but negative non-treponemal test	Yes	No
Dually positive treponemal and non-treponemal	Yes	Yes

In the 1950s, during the post mass treatment surveillance phase, some of the key problems that could be encountered were identified and possible solutions were also proposed. Figure 7 shows the steps taken then to address factors and problems that could undermine the eradication effort during this phase (37). The lessons learned may guide the current eradication efforts.

Figure 7. Yaws control: surveillance phase in the 1950s

Source: reference 37



## 5. The post-zero case phase

### 5.1 Clinical and serological surveillance

Once a zero-case level has been reached, the following essential activities should continue for at least 3 years before verification and certification can be conducted:

- Awareness to enhance voluntary reporting of cases
- Clinical surveillance at all levels
- Sero surveys conducted annually among children aged 1–5 years from previously endemic and non-endemic villages.

Surveillance should be of high quality and satisfy the following standards:

- At least 80% of expected routine surveillance reports (including ZERO cases) should be reported on a monthly basis.
- 100% of rumoured or reported cases should be investigated within 7 days of the initial report and the results of all investigations and actions taken recorded.
- Case investigation form (Annex 6) should be used to document new cases after TCT. A swab/scraping should be collected for *T. pallidum* spp. *pertenue* PCR test during the post-zero surveillance period.

### 5.2 Verification and certification of interruption of transmission

The details of the procedures to be followed for the verification and certification of interruption of transmission of yaws are available in a separate WHO guideline (38).



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# ANNEXES

## Annex 1. Operational definitions

The following definitions are recommended for use by the programme in order to maintain uniformity in case reporting and data management, and to facilitate the verification and certification process. A meeting on yaws eradication held at WHO headquarters (Geneva, 2013) suggested minor revision of the definitions described in the Morges Strategy 2012 for operational reasons.

- **Suspected case of yaws:** A person of any age who is or was living in a previously or currently endemic area, presenting with clinical signs consistent with yaws (Table A1).
- **Confirmed case of yaws:** A clinically suspected infectious case who is confirmed with dual positive serology (either DPP-dually positive or TPHA/TPPA+RPR positive). PCR may be used during the implementation phase to monitor azithromycin resistance but is not an essential part of the case definition.<sup>1</sup>
- **Endemic village:** A village containing at least one indigenous confirmed infectious case.
- **Previously endemic village:** A village which formerly reported a yaws case but not currently reporting an indigenous confirmed case.
- **Non-endemic village:** A village from where no indigenous case of yaws has ever been reported.
- **Endemic country:** A country with at least one indigenous confirmed infectious case.
- **Formerly endemic country:** A country which formerly reported yaws but which has either eliminated the disease or for which there is no current data.
- **Implementation unit:** The implementation unit will be flexible covering a population of 100 000–250 000 living in a region where there are known endemic villages.
- **Evaluation unit:** A defined administrative unit that may include one or more implementation units.
- **Imported case:** A case from a current or previously yaws endemic area who presents with infectious lesions, which may be confirmed by dual non-treponemal or treponemal sero-positivity.
- **Index case:** A first case of a confirmed yaws that is detected in a community.
- A **contact** is a person who lives with or comes into close and frequent contact with an infectious yaws case. Contacts, for the purpose of yaws eradication, are household members, schoolmates, or close playmates.
- **Treatment success (cure):** An infectious yaws case who received a single oral dose of azithromycin (or injection of benzathine benzylpenicillin) leading to complete healing of the active lesion(s) within 4 weeks after treatment may be labelled as “**cured**”.

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<sup>1</sup> During the post-zero surveillance phase, a suspected case with both dual positive serology and positive PCR of lesion material for *T. pallidum* subsp. *pertenue* is considered a confirmed case.

- **Treatment success rate (cure rate):** The total number of patients who display complete healing of lesion(s) out of those who received treatment for suspected or confirmed infectious yaws lesions.
- **Treatment failure:** A serologically confirmed infectious yaws case who received a single oral dose of azithromycin (or injection of benzathine benzylpenicillin) and who did not show any clinical improvement (persistent skin lesions) 4 weeks after treatment.
- **Treatment failure rate:** The total number of cases with persistent lesions out of those who received treatment.
- **Total community treatment (TCT):** The treatment of all eligible people in an endemic community with a single dose of azithromycin (30 mg/kg body weight; maximum 2 g).
- **Total targeted treatment (TTT):** The treatment of all new cases (including imported cases) and their contacts (household, frequent family friends, school, and playmates, etc.) with a single dose of azithromycin.

**Table A1.** Clinical classification of yaws<sup>1</sup>

Type of lesion	Example	Infectiousness
<b>Early yaws lesions</b>		
Initial lesion	Papilloma	+++
Papillomata	Papillomata	+++
Ulceropapilloma		+++
Ulcer		+++
Macules	Squamous macules	+
Maculopapules	Maculopapules	++
Papules	Squamous micropapules	++
Micropapules	Polymorphous	++
Nodules		+
Plaques		+
Hyperkeratosis	Plantar and palmar	–
Bone and joint lesion	Polydactylitis Osteoperiostitis	–
<b>Late yaws lesions</b>		
Hyper-keratosis	These lesions may be same both in early and late stage	–
Nodular	Scars	–
Ulcerated nodular	Gangosa	–
Plaques	Osteoperiosteitis	–
Bone and joint	Sabre tibia, gondou	–
Juxta-articular nodules		–

– not infectious; + infectious; ++ very infectious; +++, highly infectious

<sup>1</sup> Adapted from: Perine PL, Hopkins DR, Niemel PLA, St John RK, Causse G, Antal GM. Handbook of endemic treponematoses: yaws, endemic syphilis and pinta. Geneva: World Health Organization; 1984.

## Annex 2. Pre-treatment campaign checklist

- Adequate budget is available to implement yaws eradication activities.
- The communities have been involved in planning the treatment campaign.
- The communities have been well informed to ensure their maximum cooperation and to achieve the highest possible treatment coverage.
- Necessary written or oral permissions have been obtained from communities and schools.
- The target population has been defined and information fliers have been distributed.
- Villages/schools are aware of the TCT schedule and follow-up (dates and times).
- Azithromycin stock has been delivered and stored in local health facilities, including common emergency medicines, to deal with azithromycin-related adverse events (antidiarrheal drugs, oral rehydration solution, antiemetics, antacids).
- A small stock of benzathine penicillin and adrenalin/steroids for penicillin anaphylaxis reaction etc. is available for those who cannot tolerate azithromycin.
- Point-of-care diagnostic tests are available (treponemal and dual DPP).
- Safe waste disposal containers are available.
- Data collection forms (clinical case records, survey records, laboratory test request forms, tally sheets, registers, etc.) are ready.
- Potable water and drinking cups for swallowing tablets are available.
- Vehicles are available and in good condition, and adequate fuel is available.
- Required numbers of health personnel/laboratory technicians/volunteers are available for the campaigns.
- Others (e.g. dressing materials, etc): \_\_\_\_\_

## Annex 3. Community information on total community treatment

This information is intended as **guidance for health workers** in conducting health education ahead of the mass treatment campaign.

Below is a suggested commentary to be used when describing yaws to your local community:

Yaws is a common skin and bone disease, which predominantly affects children aged under 15 years. It spreads through direct skin-to-skin contact with an infected person with active yaws. The treatment of yaws has long been a single injection of benzathine penicillin.

Today, tablets of azithromycin are administered in a single-dose treatment by mouth and cures yaws disease like a benzathine benzylpenicillin injection.

A single dose of azithromycin protects your family and neighbors.

Azithromycin is safe for all age groups (except those aged less than 6 months) including pregnant women and during breastfeeding.

Very rarely, someone may develop mild side-effects such as nausea, vomiting, abdominal pain and diarrhea. Do not panic. Inform your local health worker about the side-effect to get medical assistance.

- Azithromycin should not be taken on an empty stomach in order to minimize side-effects.
- If you are already experiencing diarrhea, nausea and vomiting for other reasons, inform health workers before taking azithromycin tablets on the day of the campaign. The tablet can be taken later on.

Some people may be infected (that is, have the germ which causes yaws in their blood) **without any skin lesions**. Such people can only be identified through a simple blood test. **If they are not treated**, they will develop skin lesions in a few weeks or months and can infect others.

Today, we are in your village because yaws occurs here. Our aim is to give everyone living in this village the new treatment, which can completely cure everyone. If we are able to successfully treat every person living in the village, your village will be free from yaws disease within a very short time.

**If you have a skin disease**, we will examine you for yaws and also collect a very small amount of blood and a small swab or scrapings from your skin lesion to confirm or disprove the diagnosis in the laboratory.

To those who will be or who were absent during the first round of treatment, please contact your village health worker (Name: \_\_\_\_\_) to receive treatment.

Four weeks after the treatment, health workers will come back to check whether yaws skin lesions are completely healed. If skin lesions persist even after a single dose of azithromycin, you will be further examined to see if the lesion is truly yaws. With your consent, blood and swabs/scrapings may be collected to find out why the skin lesions have not healed.

**Yaws disease will spread if you do not bathe and wash clothes daily.  
Good hygienic habits within your family keep yaws disease away.**

Feel free to ask any questions regarding this exercise. You may contact the following people if you want more information:

1. Name and contact information of the district responsible person (e.g. district health official or district focal person for yaws eradication)
2. Name and contact information of the regional focal person
3. Name and contact information of the national focal person (e.g. Programme manager, yaws eradication or nodal officer for yaws eradication).

Your cooperation and participation is much needed in taking the azithromycin treatment in order to make your village free of yaws.

Thank you for your support to the Yaws Eradication Programme.

Country:





# Annex 5. Total community treatment daily summary sheet

## Yaws Total Community Treatment Daily summary sheet

District: \_\_\_\_\_ Community/Village: \_\_\_\_\_

Team Supervisor: \_\_\_\_\_ Team Coordinator: \_\_\_\_\_

A	B List of communities	C Round of treatment	D TARGET  Target (community population)	E 6mths-5yrs						F 6-9yrs				G 10-14yrs				H 15yrs+		I Total no. of persons treated with azithro (E+F+G+H)	J % coverage of persons treated with azithro (I/I*100)
				Male		Female		Male		Female		Male		Female		Male	Female				
1																					
2																					
3																					
4																					
5																					
6																					
7																					
8																					
9																					
10																					
11																					
12																					
13																					
14																					
15																					
TOTAL																					

Compiled by: \_\_\_\_\_ Sign: \_\_\_\_\_

# Annex 6. Case investigation form

Country: \_\_\_\_\_ Province/Region: \_\_\_\_\_ District: \_\_\_\_\_

Name of Father:		Name of Mother:	
<b>Section A: Demographic data</b>			
1	Name of case:	Phone n°:	
2	Case ID number:		
3	Date of birth (dd/mm/yyyy): _____	Age (years): _____	
4	Sex: <input type="checkbox"/> Male <input type="checkbox"/> Female	Community/village	
<b>Section B: History and clinical examination</b>			
5	Duration of illness (in weeks):		
6	Previous treatment (if any):		
7	Travel history:		
8	Clinical forms of yaws ( <i>Refer to WHO pictorial guide</i> ) <sup>1</sup>		
	<input type="checkbox"/> Papilloma/papules <input type="checkbox"/> Ulcers <input type="checkbox"/> Macules	<input type="checkbox"/> Swellings of bones and joints <input type="checkbox"/> Hyper-keratosis of palm/sole <input type="checkbox"/> None of above	
9	Photograph of lesion: <input type="checkbox"/> Yes <input type="checkbox"/> No		
<b>Section C: Diagnosis</b>			
10	Sampling method: <input type="checkbox"/> Finger prick blood for Trep POC	<input type="checkbox"/> Finger prick blood for DPP POC <input type="checkbox"/> Swab/scraping from lesions for PCR	
11	<i>Enter laboratory results once available:</i>		
	<b>Treponemal POC test</b> <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	<b>PCR results</b> <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	
	<b>DPP dual POC treponemal line/TPHA</b> <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	<b>DPP dual POC non-treponemal line/RPR</b> <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	
<b>Section D: Treatment</b>			
12	Treatment given: Date (dd/mm/yyyy): _____ <input type="checkbox"/> Azithromycin (number of 500 mg tablets): _____ <input type="checkbox"/> Benzathine benzylpenicillin (check): _____ 0.6 MU or _____ 1.2 MU <input type="checkbox"/> Others (please specify): _____		
<b>Section E: Conclusions of clinical assessment</b>			
13	<input type="checkbox"/> Suspected case <input type="checkbox"/> Confirmed case <input type="checkbox"/> Not a yaws case		
Notes or comments (including adverse events, diagnosis and management of serologically negative cases):			
Date (dd/mm/yyyy): _____		Signature (health worker)	

<sup>1</sup> Yaws: recognition booklet for communities. Geneva: World Health Organization; 2012 (WHO/HIM/NTD/IDM/2012.3; [http://apps.who.int/iris/bitstream/10665/75340/1/9789241504096\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/75340/1/9789241504096_eng.pdf)) DPP, dual path platform (treponemal and non-treponemal) test; PCR, polymerase chain reaction; POC, point-of-care test; RPR, rapid plasma reagin test; TPHA Treponema pallidum haemagglutination assay



# Annex 8. Assessment of impact of TCT using azithromycin: guidance for yaws eradication programmes

## 1. Prior to azithromycin administration in the community

All children aged  $\leq 15$  years should be examined for skin lesions. Those with active lesions (papillomas, ulceropapillomas, ulcers) consistent with a clinical diagnosis of yaws and dually-positive using a dual path platform (DPP) treponemal and nontreponemal test (or positive using a rapid syphilis test) should have swabs taken directly from the bases of ulcerations or scrapings taken with a curette from papillomata. The specimens should be put into 1.2 ml of Assay Assure® nucleic acid transport medium (Thermo Fisher Scientific, Waltham, MA, USA) in vials that can withstand freezing at  $-70$  °C. All specimens should be kept in cold boxes at  $+4$  °C in the field and subsequently stored frozen at  $-20$  °C prior to shipping, on dry ice if possible, to a reference laboratory for storage at  $-70$  °C.

In the reference laboratory, the specimens will be tested for *Treponema pallidum* spp. *pertenue* and for specific mutations that are known to be associated with azithromycin resistance, as well as *Haemophilus ducreyi*-specific DNA sequences and other local causes of skin ulcers (e.g. pyogenic and Buruli ulcers). This will give a measure of the proportion of skin lesions in these children that could be definitively diagnosed as yaws, and those which harbour *H. ducreyi* and other local causes of skin ulceration.

## 2. Four weeks follow-up

Four weeks after treatment, all children with initial active lesions should be examined to assess cure. Those with persistent ulcers despite the initial treatment should have swabs taken from their ulcers to determine the cause of their lesions and be treated with benzathine benzylpenicillin. If some children have developed new lesions, they should also follow the same procedure of sample collection as mentioned above and be given a single dose of azithromycin (30 mg/kg).

## 3. Six months follow-up

Once again, all children with active skin lesions should be examined and tested as previously mentioned. Those found to be dually seropositive should have either swabs or scrapings taken from lesions for polymerase chain reaction (PCR) testing to determine the impact of the mass treatment on concomitant skin lesions caused by *T. pallidum* spp. *pertenue*, *H. ducreyi* and other causes of ulcers.

## 4. One year or more follow-up

If there are follow-up clinical and serological surveys planned at one year after the TCT, or later, children with active skin lesions should be tested using a DPP test (or rapid treponemal syphilis test). Those found to be positive should have either swabs or scrapings taken from lesions for PCR testing.

## Procedures for collection, storage and transport of swab samples

### • Ulcers

- If the ulcer is dry, put a little saline or distilled water to soften it before taking the swabs
- Gently press and roll a sterile cotton-tipped swab over the lesion to collect the pus
- Insert the swab into a pre-labelled cryotube containing assay assure and spin
- Press and roll along the side of the tube to express the exudate and discard the swab. **Tightly close the tube.**

### • Papillomas

- If the papilloma is dry, put a little saline or distilled water to soften the scab before taking the scrapings
- Use a plastic blunt curette (Sklar ear curette, [www.orsupply.com](http://www.orsupply.com)) to gently remove the outer covering of the papilloma (scab) and place it in a pre-labelled cryotube containing assay assure
- Gently press and roll a sterile cotton-tipped swab over the expose surface of the papilloma
- Insert the swab into the same pre-labelled cryotube containing assay assure and spin
- Press and roll along the side of the tube to express the exudate and discard the swab. **Tightly close the tube.**

### Storage and transport

All specimens should be placed into 1.2 ml vials of Assay Assure® nucleic acid transport medium (Thermo Fisher Scientific, Waltham, MA, USA) and kept in cold boxes at +4 °C in the field. They should subsequently be stored frozen at –20 °C at the district laboratory prior to shipping, on dry ice if available, to a reference laboratory for storage at –70 °C.

Alternatively, the swabs can be expressed onto an Whatman Indicating FTA Elute Micro Card (GE Healthcare Life Sciences, Pittsburgh, PA, USA) and allowed to dry before sealing in an envelope together with a desiccator pouch (both supplied with the FTA cards). Envelopes can be sent at room temperature to a reference laboratory. When the biological sample is applied onto the card, proteins are inactivated and the released nucleic acids are entrapped in the fibres of the card matrix. The sample may remain stable for up to a year at room temperature.

### **NB: DRESS WOUNDS AFTER TAKING SWABS**

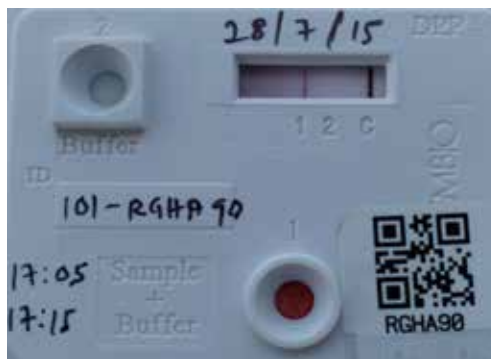
# Examples of DPP tests and PCR results used to confirm clinical cases of yaws



A dually-positive DPP test showing treponemal line (1), non-treponemal line (2) and control line C. This confirms an active infection of yaws and **lesion confirmed positive by PCR.**



A dually-positive DPP test showing treponemal line (1), non-treponemal line (2) and control line C. This confirms an active infection of yaws **but lesion confirmed negative by PCR.**



DPP test showing only the treponemal line (1) and control line (C). This is an old treated infection of yaws and **lesion confirmed negative by PCR.**



DPP test showing only the control line (C). This is a negative infection of yaws and **lesion confirmed negative by PCR.**

# Yaws is curable with a single dose of oral azithromycin

Before treatment



Four weeks after treatment













A young boy from Congo with typical lesions of papilloma on the face, macules on the hand and bone swelling of the fingers. This child was cured with a single dose of oral azithromycin. (Credit: MSF/Epicentre, Paris, France)

Yaws mainly affects children living in poor communities in 14 countries of the World Health Organization (WHO) African, South-East Asia and Western Pacific regions. The disease is targeted for eradication by 2020.

This document provides guidance for countries on how to implement activities to achieve the interruption of yaws transmission. It is intended for use by national yaws eradication programmes, partners involved in the implementation of yaws eradication activities and WHO technical staff who provide technical support to countries in the eradication of yaws.

***Eradication of yaws: a guide for programme managers*** should be used together with ***Eradication of yaws: procedures for verification and certification of interruption of transmission*** and ***Summary report of a consultation on the eradication of yaws, 5–7 March 2012, Morges, Switzerland.***

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