Reviews of Infectious Diseases

Edward H. Kass, Editor
Neil R. Blacklow, Associate Editor
John R. David, Associate Editor
Sherwood L. Gorbach, Associate Editor
Alice S. Huang, Associate Editor
Dennis L. Kasper, Associate Editor
Jerome O. Klein, Associate Editor
Joan B. Daniels, Managing Editor
Nancy Kurz Voynow, Managing Editor
Julia M. Salas, Manuscript Editor
Steven Berman, Editorial Assistant
Sarah Acheson Stephens, Staff Assistant
Richard T. Johnson, Baltimore, Md.
Samuel L. Katz, Durham, N.C.
Thomas C. Merigan, Jr., Stanford, Calif.
Kenneth S. Warren, New York, N.Y.
Frank E. Young, Rochester, N.Y.

EDITORIAL BOARD
Michael M. Frank, Bethesda, Md.
Lawrence R. Freedman, Los Angeles, Calif.
D. Carleton Gajdusek, Bethesda, Md.
King K. Holmes, Seattle, Wash.
Harold J. Jennings, Ottawa, Canada

INTERNATIONAL BOARD OF DIRECTORS
Jacques F. Acar, Paris, France
Ralph van Furth, Leiden, The Netherlands
C. H. Huang, Beijing, China
Lars O. Kallings, Stockholm, Sweden
Jean Klastersky, Brussels, Belgium
P. Helena Mákelä, Helsinki, Finland
Francis O’Grady, Nottingham, England
Theodore G. Sacks, Jerusalem, Israel
Yuichi Yamamura, Osaka, Japan

In 1968, the Infectious Diseases Society of America undertook editorial responsibility for The Journal of Infectious Diseases. The growth of the Journal attests to the need that has been met by its publication. In 1979, a second journal, Reviews of Infectious Diseases, was added to the editorial responsibilities of the Society. Reviews of Infectious Diseases is intended to publish review articles in any of the fields that reflect the wide range of interests of the membership of the Infectious Diseases Society of America. While some reviews may be solicited, unsolicited reviews of any topic in infectious diseases are welcome, as are suggestions for central themes, symposia, teaching and training materials, hypotheses, and related seminars, conferences, and topics of current interest. Communications to the editor are welcome. The ultimate purpose of Reviews of Infectious Diseases is to supplement The Journal of Infectious Diseases in providing a means for improving communication among all of those interested in infectious diseases. Reviews of Infectious Diseases (ISSN 0162-0886) is published bimonthly at The University of Chicago Press, 5801 S. Ellis Avenue, Chicago, Illinois 60637.

Communications for the editors and manuscripts should be addressed to The Editor, Reviews of Infectious Diseases, Channing Laboratory, 180 Longwood Avenue, Boston, Massachusetts 02115. Business correspondence should be addressed to the University of Chicago Press, Journals Division, P.O. Box 37005, Chicago, Illinois 60637.

The copyright code on the first page of an article in this journal indicates the copyright owner's consent that copies of the article may be made only for personal or internal use, or for the personal or internal use of specific clients, and provided that the copy is not made or distributed for profit or for advertising or promotional purposes, or for creating new collective works, or for resale, kindly write to the publisher. If no code appears on the first page of an article, permission to reprint may be obtained only from the author.

Subscription rates to Reviews of Infectious Diseases and The Journal of Infectious Diseases.

<table>
<thead>
<tr>
<th>Subscriber</th>
<th>RID</th>
<th>RID/JID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institutions</td>
<td>$125.00</td>
<td>$225.00</td>
</tr>
<tr>
<td>Individuals</td>
<td>$ 57.00</td>
<td>$105.00</td>
</tr>
<tr>
<td>ASM &amp; IAMS*</td>
<td>$ 50.00</td>
<td>$ 90.00</td>
</tr>
<tr>
<td>Special†</td>
<td>$ 30.00</td>
<td>$ 50.00</td>
</tr>
</tbody>
</table>

NOTES. RID single copies: institutions, $15.00; individuals, $9.50. For subscribers from other countries, add for each year's subscription $10.00 for RID and $22.00 for both RID and JID to cover postage. Complete volumes are available in microfiche from Johnson Associates, P.O. Box 1017, Greenwich, Connecticut 06830.

* Individual members. † Students, fellows, interns, and residents with written verification by a faculty member.

Claims for missing numbers should be made within the month following the regular month of publication. The publishers expect to supply missing numbers only when losses have been sustained in transit and when the reserve stock will permit. Postmaster: Send address changes to Reviews of Infectious Diseases, Journals Division, P.O. Box 37005, Chicago, Illinois 60637.

Second-class postage paid at Chicago, Illinois, and at additional mailing office. Notice to subscribers: if you change your address, please notify us promptly.

Cover design by Albert Alcalay.
Published by The University of Chicago Press, Chicago, Illinois 60637; The University of Chicago Press, London S. W. 1.
© 1985 by The University of Chicago.
INTERNATIONAL SYMPOSIUM ON YAWS AND OTHER ENDEMIC TREPONEMATOSES

Held at the Pan American Health Organization
Washington, D.C.
April 16–18, 1984

Guest Editors: JOHN P. BURKE, DONALD R. HOPKINS, JOHN C. HUME, PETER L. PERINE, and RONALD ST. JOHN
Sponsored by

Fogarty International Center
National Institute of Allergy and Infectious Diseases
National Institutes of Health

World Health Organization

Pan American Health Organization

Centers for Disease Control
Department of Health and Human Services

U.S. Agency for International Development

Wyeth International Limited

United Nations Children's Fund

International Union Against the Venereal Diseases
and the Treponematoses

Becton Dickinson and Company

Commission of the European Communities

Canadian International Development Agency
Reviews of Infectious Diseases

Volume 7 • Supplement 2 • May-June 1985

INTERNATIONAL SYMPOSIUM ON YAWS AND OTHER ENDEMIC TREPONEMATOSES

Participants
Welcoming Remarks
Preface
SESSION I: DEFINITION OF THE PROBLEM
OVERVIEW
The Control of Endemic Treponematoses
AFRICA
Surveillance and Control of Resurgent Yaws in Africa
Yaws in Ghana
Some Epidemiologic Aspects of Yaws in the Ivory Coast
Endemic Treponematoses in the Sudan
Endemic Treponematoses in Togo and Other West African States
ASIA AND THE MIDDLE EAST
Yaws in Southeast Asia: An Overview
Yaws in Malaysia
Yaws in Papua New Guinea: Extent of the Problem and Status of Control Programs
Endemic Nonvenereal Treponematosis (Bejel) in Saudi Arabia
THE AMERICAS
Yaws in the Americas
Yaws in Suriname
Yaws in Colombia
SESSION II: STRATEGIES AND TECHNOLOGIES FOR CONTROL
Mass Treatment Campaigns Against Endemic Treponematoses
Intervention of Yaws Control and Primary Health Care
Research: The Prerequisite for Innovative Strategies and Technologies
New Technologies for Use in the Surveillance and Control of Yaws

SESSION III: RESEARCH NEEDS

Prospects for Improved Laboratory Diagnoses of Treponemal Infections and Species Differentiation
Prospects for Development of a Treponemal Vaccine
Potential for Development of Antibiotic Resistance in Pathogenic Treponemes
Therapy for Nonvenereal Treponematoses: Review of the Efficacy of Penicillin and Consideration of Alternatives
Clinical Diagnosis and Changing Manifestations of Treponemal Infections
Impact of the Control of Endemic Treponemal Diseases in Ghana on Other Diseases

SESSION IV: WORLDWIDE CONTROL AND/OR ERADICATION OF YAWS

Feasibility of Eradicating Yaws
Control of Yaws and Other Endemic Treponematoses: Implementation of Vertical and/or Integrated Programs
Summary and Recommendations

Reviews of Infectious Diseases publishes its Statement of Editorial Policy and Instructions to Authors in the first issue of each volume (January-February). Persons interested in submitting manuscripts to the Reviews are advised to consult both the Statement and the Instructions. Copies of both may be obtained by writing to the Editorial Office, Reviews of Infectious Diseases, Channing Laboratory, 180 Longwood Avenue, Boston, Massachusetts 02115.
Participants

VICTOR Kofi Agadzi
Ministry of Health
Accra, Republic of Ghana

YAW ABOAGYE-ATTA
Medical Services
Ministry of Health
Accra, Republic of Ghana

NILS AXELSON
Department of Treponematoses
Statens Seruminstitut
Copenhagen, Denmark

D. Barampitiye
DPC APRO
World Health Organization
Brazzaville, Republic of the Congo

PHILIP J. Bassford, Jr.
Department of Microbiology
University of North Carolina
School of Medicine
Chapel Hill, North Carolina, USA

MARK S. Beauchain
Fogarty International Center
National Institutes of Health
Bethesda, Maryland, USA

NEWTON Bowles
United Nations Children's Fund
United Nations, New York, USA

JOHN M. BOYCE
Department of Medicine
University of Mississippi Medical Center
Jackson, Mississippi, USA

STUART T. Brown
Division of Sexually Transmitted Diseases
Centers for Disease Control
Atlanta, Georgia, USA

ALFRED A. Buck
Office of Health
Bureau for Science and Technology
Agency for International Development
Washington, D.C., USA

JOHN P. Burkes
International Studies Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland, USA

R. DUNCAN Catterall
Warwick Gardens

GEORGES Y. CAUSE
Bacterial and Venereal Infections Unit
World Health Organization
Geneva, Switzerland

A. B. CHRISTIE
Liverpool School of Tropical Medicine
Liverpool, England, U.K.

CHARLES D. COX
Department of Microbiology
University of Massachusetts
Amherst, Massachusetts, USA

GEORGE W. Coxson
The John Hunter Clinic
St. Stephens Hospital

GEORGE CURLIN
Department of State
U.S. Agency for International Development
Bureau for Science and Technology
Washington, D.C., USA

JOHN C. CUTLER
Department of International Health
University of Pittsburgh
School of Public Health
Pittsburgh, Pennsylvania, USA

WILLIAM H. FORGE
Policy Development
Centers for Disease Control
Atlanta, Georgia, USA

CARLYLE GUERRA DE MACEDO
Pan American Health Organization
Washington, D.C., USA

NANCY GEBEIN
Health Population Section
Resources Branch
Canadian International Development Agency
Hull, Quebec, Canada

THORSTEIN GUTHE
Elken Clinic
Oslo, Norway

HAIDAR AUB AHMED MOHAMED
Epidemiology Department
Ministry of Health
Khartoum, Sudan

PAUL H. HARDY
Department of Molecular Biology and Genetics
The Johns Hopkins University
School of Medicine
Baltimore, Maryland, USA

DONALD R. HOPKINS
Office of the Center Director
International Health
Centers for Disease Control
Atlanta, Georgia, USA

JOHN C. HUME
The Johns Hopkins University
Schoo of Hygiene and Public Health
Baltimore, Maryland USA

PETER G. JANSSENS
Institute of Tropical Medicine "Prince Leopold"
Antwerp, Belgium

WILLIAM S. JORDAN, JR.
Microbiology and Infectious Diseases Program
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, Maryland, USA

FRANCOIS LAFOINTAINE
Science and Technology Commission of the European Communities
Washington, D.C., USA

SANDRA A. Larsen
Treponema Research Branch
Sexually Transmitted Diseases Laboratory Program
Center for Infectious Diseases
Centers for Disease Control
Atlanta, Georgia, USA

EDDIE K. E. Loo
Department of Health Sciences
Ministry of Health
Selangor, Malaysia

MICHAEL A. LOVET
Microbiology Institute
University of California at Los Angeles
Los Angeles, California, USA

ANTON LUGER
Krankenhaus der Stadt Wien Lainz
Dermatologische Abteilung
Wien, Austria

SHEILA A. LUKNHART
Department of Medicine
Division of Infectious Diseases
University of Washington
School of Medicine
Seattle, Washington, USA

EDGAR J. MARTIN
Chevy Chase, Maryland, USA

RAPHAEL MEDINA
Instituto Nacional de Venerologia
Ministerio de Sanidad y Asistencia Social
Caracas, Venezuela
ANDRÉ Z. MEHEUS
Department of Epidemiology and Social Medicine
University of Antwerpen
Antwerpen, Belgium

ARNOLD S. MONTO
Department of Epidemiology
School of Public Health
University of Michigan
Ann Arbor, Michigan, USA

KONAN N'DA
Ministère de la Santé Publique
Abidjan, Ivory Coast

JOHN W. NELSON
International Health Program Office
Centers for Disease Control
Atlanta, Georgia, USA

PAUL A. NIELME
Dijkzigt Ziekenhuis
Department of Venerology
University of Rotterdam
Rotterdam, The Netherlands

MICHAEL Y. NORGAARD
Department of Microbiology
University of Texas Health Science Center
Dallas, Texas, USA

A. OLU OSIBA
Department of Medical Microbiology
University College Hospital
Ibadan, Nigeria

PETER L. PERINE
Department of Preventive Medicine and Biometrics
Uniformed Services University of the Health Sciences
Bethesda, Maryland, USA

MILTON PUJIAS
Bacteriology and Virology Branch
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, Maryland, USA

M. SOPHIE REID
The Gap
Queensland, Australia

RONALD K. ST. JOHN
Epidemiology Unit
Pan American Health Organization
Washington, D.C., USA

IBRAHIM M. SAMBA
Onchocerciasis Programme
World Health Organization
Ouagadougou, Burkina Faso

NANCY E. SHAPIRO
International Studies Branch
Fertility International Center
National Institutes of Health
Bethesda, Maryland, USA

RICHARD S. SCHWEIZER
American Council of Life Insurance
Washington, D.C., USA

CHECK SOW
Organization of Coordination for the Control of Endemic Diseases
Bobo Dioulasso, Burkina Faso

SOEDEARTOSOBADJIIOO
Control of Diseases with Direct Transmission
Communicable Disease Control
Ministry of Health
Jakarta, Indonesia

HAE MAMBY TOURE
Centre Médico/OCGGE
Babo Dioulasso, Burkina Faso

J. TOWPIE
Instytut Wenerologii
Akademia Medyczna
w Warszawie
Warszawa, Poland

WILLIAM RODRIGUEZ URIBE
Section 51AM
Pan American Health Organization
Bogota D.E., Colombia

FERDINAND A. VORST
Department of Public Health
University of Limburg
Maastricht, The Netherlands

KARL A. WESTERN
International Research
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, Maryland, USA

RCSS WIDY-WIRSKY
Inter-Country Epidemiological Surveillance and Disease Control
World Health Organization
Nairobi, Kenya

R. R. WILLCOX
St. Mary’s Hospital

A. ZAHRA
World Health Organization
Geneva, Switzerland

Organizing Committee

JOHN C. HUMI (Chairman)

ALFRED A. BUCK

GEORGES Y. CAUSSE

DONALD R. HOPKINS

WILLIAM S. JORDAN, JR.

EDGAR J. MARTIN

RONALD K. ST. JOHN

KARL A. WESTERN

JOHN F. BURKE (Executive Secretary)

Editorial Committee

JOHN C. HUMI (Chairman)

JOHN F. BURKE

DONALD R. HOPKINS

PETER L. PERINE

RONALD K. ST. JOHN

Session Chairmen

A. OLU OSIBA (Session I)

GEORGES Y. CAUSSE (Session II)

KARL A. WESTERN (Session III)

WILLIAM S. JORDAN (Session IV)

Rapporteurs

R. DUNCAN CATTERALL (Chief)

JOHN C. CUTLER (Session I)

JOHN W. NELSON (Session II)

JOHN M. BOYCE (Session III)

A. B. CHRISTIE (Session IV)

Conference Coordinator

NANCY E. SHAPIRO
Welcoming Remarks

It gives me special satisfaction to inaugurate this meeting and welcome the participants to the headquarters of the Pan American Health Organization. I want particularly to acknowledge the presence of Mr. Richard S. Schweiker, former Secretary of the Department of Health and Human Services, and to give a special welcome to Dr. Mark Beaubien; to our Chairman, Dr. John Hume; and to our Chief Rapporteur, Dr. Duncan Catterall. The Pan American Health Organization welcomes the opportunity to again host an activity in cooperation with the Fogarty International Center of the U.S. National Institutes of Health.

In quantitative terms, yaws itself is no longer a serious health problem. However, its fundamental importance is that, if we consider the available knowledge and existing epidemiologic conditions, there is a real possibility that we can eradicate the disease and that this task can be carried out in the short term, at least, I am sure, with regard to the region of the Americas. The discussion here will be of great practical value in making it possible to reach this goal more readily. We of the Pan American Health Organization foresee and wish for you a fully successful meeting.

Carlyle Guerra de Macedo

It is a pleasure to welcome you to this symposium on behalf of the Fogarty International Center of the U.S. National Institutes of Health. This symposium had its origins in 1980, when the Fogarty International Center brought experts in infectious diseases from around the world to the National Institutes of Health to consider the amenability of diseases to improved control and potential eradication. Many possible candidates were evaluated, but three diseases were selected. The report of the meeting (the International Conference on Eradication of Infectious Diseases) [1] advised that “measles, poliomyelitis, and yaws are ... clearly suitable for at least regional eradication.” The report also indicated that the “study of the desirability and feasibility of regional and global eradication of these diseases is recommended to the Fogarty International Center ...” That study of yaws is our task today.

Mark S. Beaubien

Reference

Preface

The endemic treponematoses, which include yaws, endemic syphilis, and pinta, are a group of non-vaccineable infections that primarily afflict children in tropical and subtropical areas. It was estimated that before 1950 some 160 million persons were infected with yaws; about 1 million, with endemic syphilis; and 0.7 million with pinta. More than 40 million victims of yaws and endemic syphilis in particular suffered symptoms varying from skin lesions to — in severe cases — gross destruction of tissue, joints, and bone, and facial disfigurement. Mass campaigns sponsored by the World Health Organization (WHO) and the United Nations Children’s Fund (UNICEF) from 1952 to 1969 resulted in a drastic reduction in the number of cases of endemic treponematoses worldwide. However, lack of surveillance and control measures, persistence of poor sanitary conditions, and increasing mobility and growth of populations have led to the resurgence of yaws and endemic syphilis in some areas over the past 15 years. Foci where prevalence rates approach those experienced before the mass campaigns of the 1950s and 1960s have reappeared in some African and Asian countries.

Since 30 years have elapsed since the last international conference on yaws was held in Enugu, Nigeria, in 1955 (the first such conference was held in Bangkok, Thailand, in 1952), it is an appropriate time to reappraise the global situation regarding these infections.

This International Symposium on Yaws and Other Endemic Treponematoses is the third in a series of infectious disease conferences in which the Fogarty International Center, following the example of the successful effort by WHO in eradicating smallpox, is sponsoring an examination of potential disease candidates for improved control and possible eradication. Of the diseases considered at an International Conference on the Eradication of Infectious Diseases held at the Fogarty International Center in May 1980, yaws was judged to be the disease most amenable to eradication.

The purpose of today’s symposium was to assess the current extent of the endemic treponematoses and of the control programs directed against them; to consider strategies, technologies, and research needed for the control of these diseases; and to consider the feasibility of their global eradication and/or control.

My own interest in yaws began in 1978, when a member of my staff in the U.S. Senate suggested that here was an easily preventable cause of illness that had previously been brought under control in many countries by mass campaigns during the 1950s and 1960s but that was resurgent among some African children. That same spring, the 31st World Health Assembly also noted the lapse in the use of control measures and adopted a resolution on control of endemic treponematoses that emphasized the need for prompt and vigorous action. I then encouraged the U.S. Agency for International Development and the Centers for Disease Control to send a team to West Africa to investigate the status of yaws and endemic syphilis. The team members accepted invitations to visit Ghana, Ivory Coast, Togo, and Mali in 1979. One result of that investigation was support for the yaws and yellow fever program, which began in Ghana in January 1981.

An understanding of the full significance of efforts to control yaws in Ghana was expressed by the late Dr. B. B. Waddy of the London School of Hygiene and Tropical Medicine, who worked for many years in the Gold Coast (Ghana) and was a major advocate of the now well-established regional effort to control river blindness (onchocerciasis) in West Africa. At a meeting of the Royal Society of Tropical Medicine and Hygiene in 1956, Dr. Waddy, who had then been in charge of the Medical Field Units in the Gold Coast for five years, stated:

...we must attack first the conditions which, without affecting population, cause farming inefficiency. These are above all, yaws, guinea worm and onchocerciasis. Yaws and guinea worm are under attack...onchocerciasis should be the next target... The forces available to combat rural ill-health are enthusiastic but small. They should not be dissipated on too many unattainable objectives, but concentrated ruthlessly on those that can be achieved, and which careful forethought considers will do the most good.

The endemic treponematoses pose a heavy burden to the affected individuals and to society. At the time Dr. Waddy began his great work in Ghana, the U.S. Department of State estimated that the mass treatment campaign against yaws in Haiti had
allowed some 100,000 persons who had been incapacitated to return to work, with a consequent increase in national production of some $5 million a year.

The burden of yaws, in causing incapacitation and permanent disfiguration in adults, is compounded by the suffering it causes in children. As a Nigerian proverb states: "A yaws sufferer cannot be happy save by the permission of flies."

'For the victims, it is no more possible to secure permission to be left in peace than it is to eradicate the ubiquitous flies. But we can do something about the yaws!'

RICHARD S. SCHWEIKER
SESSION I

The Control of Endemic Treponematosis

G. M. Antal and G. Causse

In the 1950s and 1960s, following a decision by the Second World Health Assembly in 1949, mass treatment campaigns against the endemic treponematosis were undertaken with the support of the World Health Organization and the United Nations Children's Fund. The control policy was based on recognition of the importance (1) of screening at least 90% of the target population; (2) of conducting periodic resurveys and treating missed, new, and imported cases; (3) of treating the entire treponemal reservoir (including latent cases and contacts); and (4) of using adequate dosages of long-acting penicillin (minimal dosages were recommended). Later, policies on the extent of contact treatment at different levels of endemicity were established. During these mass campaigns, >50 million clinical and latent cases and contacts were treated; prevalence of endemic treponematosis was reduced dramatically. The major reasons for resurgence of yaws and endemic syphilis in some areas are discussed. One important factor has been the failure of many countries to integrate active control measures into local health services after the mass campaigns. Yaws and pinta are continuing to decline to very low levels in the Americas. In West Africa, especially, incidence of yaws and endemic syphilis have returned to high levels. Few significant endemic areas remain in Asia except in Indonesia and Papua New Guinea.

The Prepenicillin Era

Mass campaigns against endemic treponematosis were already attempted in many tropical areas when therapy depended on multiple-dose regimens with arsenical agents and bismuth. However, at that time the epidemiologic concept that treatment was necessary for asymptomatic household contacts and persons with presumed latent cases as well as manifest cases had not yet evolved and the importance of complete population coverage had not been recognized. The treatment of large numbers of symptomatic persons, who served as sources of infection in the community, led to some reduction in disease transmission. But a short interruption of these treatment activities brought about a rapid reemergence of infectious cases as relapses with infectious lesions occurred in the untreated reservoir of persons with latent cases.

Development of Control Methodologies and Procedures

The introduction of low-cost, long-acting penicillin preparations that maintain a treponemical level in the blood and tissues for many weeks following a single injection made a mass treatment approach for treponemal infections a feasible technique in remote areas. The use of mass treatment techniques for eradication of yaws was first attempted in Haiti following trials that demonstrated the effectiveness of procaine penicillin in aluminum monostearate (PAM) in treatment of yaws lesions. These technical developments radically improved the prospects of combating yaws and other endemic treponematosis of childhood in developing countries. The acceptance by the Second World Health Assembly in 1949 of an epidemiologic rather than a narrow clinical approach for the control of endemic treponematosis set the scene for a technical assistance program of mass treatment campaigns against yaws, endemic syphilis, and pinta under the technical guidance of the World Health Organization (WHO) and with material support from the United Nations Children's Fund (UNICEF).

As a first step toward establishing an international technical policy for the control of endemic treponematosis, the First International Symposium on Yaws Control was held in 1952 in Bangkok, Thailand. The first experiences of field control projects were reviewed. On the basis of the knowledge of
epidemiology of yaws and endemic syphilis (especially of latency and clinical relapses), serologic latency, and the results of field trials confirming the effectiveness of PAM in the treatment of treponemal infections, a number of principles were established that were regarded as essential elements of programs for the control of endemic treponematoses: (1) the need to examine at least 90% of the target population in all screening surveys; (2) the need to undertake periodic resurveys of the population to treat persons who had escaped treatment during the previous treatment survey, those who were reinfected since, and those with imported cases from other endemic areas (these resurveys were to take place at intervals between six months to one year at the most, depending on the degree of endemicity observed during the preceding survey); (3) the need to treat the entire treponemal reservoir in the endemic area, which includes not only persons with clinical cases but also asymptomatic persons assumed on epidemiologic grounds to be in the early latency period with the potential for relapse and those assumed to be incubating the disease; and (4) minimal treatment dosage for adults with established disease was set at 1.2 million units of PAM and at one-half that dose for children younger than 15 years of age. The dosage set for adults assumed to be either in latency or incubating the disease was 0.6 million units of PAM and that for children was proportionally lower.

Twenty-seven years later the WHO Scientific Group on Treponemal Infections no longer saw a justification for giving half doses to contacts assumed to be in early latency or to be incubating the disease. Thus, the minimal treatment dose for adults with or without clinical disease is 1.2 million units of PAM or benzathine penicillin G and that for children 10 years of age and younger is 0.6 million units.

These four elements became—and still are—the principal components that must be applied in control programs against yaws, pinta, and the non-venerereal treponematoses.

The Second International Conference on Control of Yaws, held in 1955 in Enugu, Nigeria, established simple rules regarding the extent of contact treatment ("treatment policies") to be applied at different levels of endemicity and the associated magnitude of the treponemal reservoir in the population: (1) in hyperendemic areas (prevalence of active cases of >10%) the entire population should be treated (total mass treatment), (2) in mesoendemic areas (prevalence of active cases of 5%-10%) all children of prepubertal age in addition to adults with active cases and other obvious contacts of infectious cases should receive treatment (juvenile mass treatment); and (3) in hypoendemic areas (prevalence of active cases of <5%) treatment should be given to persons with active cases, their household contacts, and other obvious contacts of infectious cases (selective mass treatment).

These rules were rather loosely applied. In many campaigns the policy of total mass treatment was adopted whatever the prevalence of clinical cases. The additional cost of penicillin was a small part of the operational cost of the program, and this policy served to attract greater participation of the population and at the same time increased the effectiveness of the control on the treponemal reservoir.

Extensive immunologic studies conducted by WHO in areas where mass treatment had been applied have shown an epidemiologic situation that is signified by a few clinical cases arising from a large pool of cases in early latency, a finding that indicates the epidemiologic importance of the large reservoir of latent cases in maintaining disease transmission. Therefore, experienced field workers would apply treatment to contacts within a wide area around a person with an infectious case, including all children living at a distance of up to 0.5 km, those attending the same school class, and all members of the compound in which the infected person lives.

To promote an improved diagnostic standard and to facilitate a comparison of clinical data recorded during surveys within a country and between countries the Conference worked out an International Nomenclature of Yaws Lesions.

Field Campaigns

On the basis of pilot studies of yaws in Haiti, endemic childhood syphilis in Yugoslavia, and pinta in Mexico, mass treatment campaigns started in 1948 and extended to 46 countries in the context of the global WHO treponematoses program. These campaigns were purely national activities; on request countries could qualify to receive technical support from WHO and material supplies from UNICEF. From the onset of this program, UNICEF provided substantial assistance in the form of penicillin, supplies, transportation, and training for rural health workers that amounted to over $7 million (U.S.).

At the onset, mass campaigns against the en-
emic treponematoses were aimed at reducing the prevalence of these diseases to a level at which they would cease to be a public health problem. Encouraged by the impressive results obtained in the first years of campaigns, organizers changed their declared objective from "control" to "eradication," which would be achieved when no person with an indigenous active case had appeared in a large population group for a period of at least three years and no seroreactive child younger than five years old could be detected.

Not only were these mass treatment campaigns seen as effective tools in the control of endemic treponematoses and in the prevention of the disabilities they may cause, but they were also viewed as a spearhead for the promotion of health and social development among the most underprivileged population groups in developing countries. Indeed, in many remote communities these campaigns were an impressive first encounter with modern medicine and opened the road for further (health) development. It was recognized early in the development of the global program for the control of endemic treponematoses that vertical mass treatment campaigns could not continue indefinitely but needed to be integrated gradually into the work of the general health service. Therefore, plans for control of these diseases were to include the preparation of the rural health service for the integration of control and surveillance activities for reducing disease levels when continuation of periodic surveys by specialized teams was no longer economical. At which level of prevalence this integration was to take place depended on the level of preparedness of the rural health service for its new task and the potential for resurgence of these diseases in the area concerned.

In most countries mobile field teams were organized and carried out the attack phase of the program, i.e., initial treatment survey and subsequent resurveys, in a rather vertical fashion. In contrast, the yaws campaign in Indonesia was integrated into the rural health service from the beginning. The methods and procedures recommended by WHO frequently were adapted to suit local conditions without deviating from the basic principles established for control of endemic treponematoses. In West Africa, for instance, opportunity was taken of the mass screening program for endemic treponematoses to incorporate other public health activities into the functions of mobile teams, such as case finding for leprosy or sleeping sickness or for vaccination activities, without slowing down the progress of the attack phase. Total mass treatment was the preferred treatment policy, irrespective of the disease prevalence, and this approach greatly accelerated the reduction of the treponemal reservoir during the first years of the campaign.

It is estimated that in the course of the worldwide campaigns against endemic treponematoses, ~160

### Table 1. World Health Organization Treponematoses Programme: effect of mass penicillin treatment campaigns (1946–1963) on prevalence of infectious endemic treponematoses.

<table>
<thead>
<tr>
<th>Country or area</th>
<th>Period</th>
<th>Rural population involved (millions)</th>
<th>Initial treatment survey</th>
<th>Percentage with infectious yaws at last resurvey</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage with infectious yaws</td>
</tr>
<tr>
<td>Northern Nigeria</td>
<td>1954–1965</td>
<td>2.65</td>
<td>83</td>
<td>4.2</td>
</tr>
<tr>
<td>Togo</td>
<td>1956–1965</td>
<td>1.50</td>
<td>40</td>
<td>4.1</td>
</tr>
<tr>
<td>Midwestern Nigeria</td>
<td>1955–1964</td>
<td>1.49</td>
<td>77</td>
<td>3.2</td>
</tr>
<tr>
<td>Western Samoa</td>
<td>1955–1961</td>
<td>0.10</td>
<td>96</td>
<td>3.0</td>
</tr>
<tr>
<td>Eastern Nigeria</td>
<td>1954–1963</td>
<td>6.80</td>
<td>54</td>
<td>1.9</td>
</tr>
<tr>
<td>Western Nigeria</td>
<td>1956–1963</td>
<td>1.90</td>
<td>59</td>
<td>1.8</td>
</tr>
<tr>
<td>Ghana</td>
<td>1956–1965</td>
<td>4.20</td>
<td>. .</td>
<td>0.8</td>
</tr>
<tr>
<td>Northeastern Thailand</td>
<td>1952–1960</td>
<td>8.40</td>
<td>50</td>
<td>0.7</td>
</tr>
<tr>
<td>Southern Thailand</td>
<td>1952–1960</td>
<td>1.00</td>
<td>70</td>
<td>0.13</td>
</tr>
<tr>
<td>Philippines</td>
<td>1952–1960</td>
<td>2.40</td>
<td>33</td>
<td>0.1</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>1948–1954</td>
<td>0.83</td>
<td>80</td>
<td>0.4</td>
</tr>
</tbody>
</table>

* Includes a survey of children and a sampling survey.
† Includes noninfectious cases.
million persons were examined during initial treatment surveys and >300 million reexaminations were carried out during subsequent resurveys. In the course of these activities, ~50 million persons with clinical and latent cases and contacts were treated.

The immediate results of the mass treatment campaigns were impressive. Depending on the thoroughness and frequency of resurveys and on the degree of adherence to the recommended technical procedures, the prevalence of active clinical lesions was reduced to a fraction of the levels before the campaign (see table I). With the exception of Togo, where a low population coverage at the initial treatment survey and at resurveys necessitated a repetition of the mass treatment campaign, national campaigns were so successful that relatively low priority was given to the preparation of the rural health service for its new task on the conclusion of the mass campaign. Much of the optimism came from the expectation that improvement in hygiene and socioeconomic condition would take place and reduce disease transmission. Unfortunately, these hopes rarely materialized. Also, it was not realized at that time that, even in the virtual absence of infectious cases, a low level of transmission among children may still persist for many years—a situation that signifies a recurrence potential of the infection and that calls for continuous postcampaign surveillance through rural health centers, with a focus of attention on children at particular risk of infection.

From 1965 onward, mobile field teams were withdrawn from national endemic treponematoses programs and given new assignments in the smallpox campaign or in the cholera control program. Since the static rural health service usually did not have the means for outreach activities, i.e., screening and treatment of population groups in remote areas, satisfactory postcampaign surveillance was limited to health centers that received some support from multipurpose mobile teams or from experienced staff assigned from field teams.

The Present Situation

The failure by many countries to integrate continued active control measures into the functions of local health services (with the aim of consolidating the excellent results achieved by the mass treatment campaign) led to a gradual build up and extension of the treponemal reservoirs (tables 2, 3, and 4), with the occasional emergence of active cases at first; these cases would represent only the smallest fraction of a large number of active but latent infections in the community. In the absence of significant environmental improvement and with treatment limited to clinical cases where penicillin was available, the infection spread to neighboring areas that had previously achieved eradication. With the gradual increase of disease transmission, more overt clinical cases started to appear among children.

This situation is particularly precarious in the Sahelian region and western and central Africa, where over the last two decades untreated reservoirs of infection increased dramatically and mobile teams were either disestablished or given activities conceived to have higher priority.

In the southern parts of Ghana, Togo, and Benin, important yaws foci have formed in remote communities, where the prevalence of infectious cases approaches that during the precampaign era. It has been estimated that in Ghana 3.6 million children have been exposed to yaws, with the infection rate in 1979 ranging between 1% and 5%.

This resurgence led to the implementation in Ghana of a crash program (1981-1983) of anti-yaws activities, which was combined with yellow fever vaccination. There are yet unconfirmed reports of the detection of cases of yaws from the central area of Sierra Leone. A yaws hyperendemic area was detected among Pygmies in the Central African Republic by a WHO survey. At the initial treatment survey, >30% of the population suffered from active lesions; at the second resurvey the prevalence of clinical cases had approached zero. In Gabon, the presence of migrating population groups was the cause given for the renewal of yaws transmission in the country.

The incidence of endemic syphilis in the Sahel region of Africa approaches that of yaws in West Africa. It is estimated that ~2.8 million of the region’s 30 million inhabitants are at risk of infection. In high endemic areas of Senegal and Burkina Faso (formerly known as Upper Volta), 15%–40% of children gave serologic evidence of past or present infection with endemic syphilis and 2%–10% showed active clinical lesions.

In Indonesia, a serologic sample survey confirmed the complete interruption of transmission of yaws on some of the larger islands. Intensified activities in other areas have led to the detection of ~10,000 infectious cases of yaws annually since 1980. Most of these cases occurred in very remote areas and had
Table 2. Cases of yaws reported to the World Health Organization (WHO).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angola</td>
<td>75</td>
<td></td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benin</td>
<td>4,006</td>
<td>7,666</td>
<td>10,378</td>
<td>22,980</td>
<td>11,683</td>
<td>10,455</td>
<td>9,091</td>
<td>3,718</td>
<td></td>
</tr>
<tr>
<td>Central African Republic (inf)</td>
<td>MFU</td>
<td>MFU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chad</td>
<td>194</td>
<td>274</td>
<td>125</td>
<td>318</td>
<td>237</td>
<td>348</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congo</td>
<td>81</td>
<td>165</td>
<td>216</td>
<td>199</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabon (inf)</td>
<td>1,053</td>
<td>981</td>
<td>566</td>
<td>126</td>
<td>277</td>
<td>82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghana (inf)</td>
<td>51,432</td>
<td>59,926</td>
<td>71,765</td>
<td>53,875</td>
<td>44,836</td>
<td>47,944</td>
<td>59,317</td>
<td>27,210</td>
<td>34,279</td>
</tr>
<tr>
<td>Guinea</td>
<td>660</td>
<td>305</td>
<td>267</td>
<td>337</td>
<td>359</td>
<td>149</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea-Bissau</td>
<td></td>
<td>5</td>
<td>30</td>
<td>16</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivory Coast (inf)</td>
<td>14,176</td>
<td>14,887</td>
<td>15,506</td>
<td>13,018</td>
<td>10,671</td>
<td>13,200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mali (inf)</td>
<td>282</td>
<td>379</td>
<td>377</td>
<td>320</td>
<td>266</td>
<td>164</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niger</td>
<td>2</td>
<td>13</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td>981</td>
<td>521</td>
<td>279</td>
<td>1,197</td>
<td>277</td>
<td>331</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rwanda</td>
<td>1,172</td>
<td>649</td>
<td>659</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senegal</td>
<td></td>
<td>106</td>
<td>91</td>
<td>45</td>
<td>200</td>
<td>192</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sierra Leone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Togo (inf)</td>
<td>2,463</td>
<td>2,868</td>
<td>4,864</td>
<td>5,497</td>
<td>4,062</td>
<td>2,670</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uganda</td>
<td>6,934</td>
<td></td>
<td>10</td>
<td>219</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkina Faso (Upper Volta)</td>
<td>156</td>
<td>1,131</td>
<td>1,230</td>
<td>934</td>
<td>1,428</td>
<td>706</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Americas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guatemala</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panama</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colombia</td>
<td>22</td>
<td>55</td>
<td>131</td>
<td>144</td>
<td>127</td>
<td>64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecuador</td>
<td>857</td>
<td>868</td>
<td>185</td>
<td>100</td>
<td>53</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peru</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guyana</td>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suriname</td>
<td></td>
<td></td>
<td></td>
<td>29</td>
<td></td>
<td>26</td>
<td>12</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>118</td>
<td>131</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haiti</td>
<td>26</td>
<td>13</td>
<td>20</td>
<td>11</td>
<td>11</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antigua</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominica</td>
<td>32</td>
<td>7</td>
<td>3</td>
<td>28</td>
<td>7</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martinique</td>
<td></td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. Lucia</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. Vincent</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trinidad and Tobago</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia and Pacific</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuvalu</td>
<td></td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td></td>
<td></td>
<td></td>
<td>930</td>
<td>1,800</td>
<td>77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>5,237</td>
<td>3,506</td>
<td>2,781</td>
<td>5,233</td>
<td>5,577</td>
<td>6,817</td>
<td>13,190</td>
<td>10,520</td>
<td></td>
</tr>
<tr>
<td>Malaysia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>6</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>7</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Abbreviations: inf = infectious cases only; MFU = reported by mobile field units. Ellipses indicate that no information was available to WH0. Numbers in parentheses are number of months reported in year.

* Unofficial report by the Endemic Diseases Control Unit, 1975.
Table 3. Cases of endemic syphilis in Africa reported to the World Health Organization (WHO).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Senegal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mali</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31,476</td>
<td>21,423</td>
<td>19,352</td>
<td>15,567</td>
</tr>
<tr>
<td>Niger</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>454</td>
<td>1,578</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>10,528</td>
<td>4,658</td>
<td>4,061</td>
<td>6,148</td>
<td>4,705</td>
<td>3,890</td>
<td>1,849</td>
<td>949</td>
<td>2,486</td>
</tr>
</tbody>
</table>

NOTE. Numbers in parentheses are number of months reported in the year. Ellipses indicate that no information was available to WHO.

accumulated from the years when the control program was less active. A recent decline in reported cases may be a direct consequence of intensified control.

New foci of infection were recently identified in remote population groups in India and Thailand. There are some reports of persistent, low-level transmission of yaws in Malaysia, Papua New Guinea, and some Pacific islands. A recent serologic survey in Saudi Arabia identified elevated rates of seroreactivity among nomadic and seminomadic population groups from two distinct geographic areas.

In the Americas, incidence of reported yaws is very low, with small foci remaining in Brazil, Colombia, Ecuador, Guyana, Suriname, and some Caribbean islands. Reports suggest that pinta has virtually disappeared from countries of Latin America.

Even though statistical data on the extent of the problem of endemic treponematoses may not be completely accurate, governments usually are aware of the problem and its health implications. Realizing that renewed control activities would require considerable resources, countries requested in resolution WHA31.58 that WHO use its good offices to mobilize international support for the elimination of these diseases once and for all.

In view of the gradual extension of areas of endemic treponematoses, the earlier appropriate control measures can be implemented, the more cost-effective these measures are likely to be.

Table 4. Cases of pinta in the Americas reported to the World Health Organization (WHO).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>503</td>
<td>377</td>
<td>357</td>
<td>248</td>
<td>122</td>
<td>99</td>
<td>81</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Colombia</td>
<td>257</td>
<td>199</td>
<td>191</td>
<td>149</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Ellipses indicate that no information was available to WHO.

Future Control of Endemic Treponematoses

The principal approaches that were applied in programs of treponematoses control are still valid today. Because of a variety of factors, the epidemiologic situation regarding endemic treponematoses may now differ widely from area to area. Therefore, any serious effort to control these diseases should be preceded by a seroepidemiologic assessment of a carefully selected sample of the target population. These data should provide information on the extent of the symptomatic cases and the treponemal reservoir in different age groups and, thus, provide a sound basis for program planning.

Foci of endemic treponematoses that have a patchy distribution and are often located in medically underserved populations away from the network of health centers require for their control a mass treatment approach of a rather categorical nature. Wherever practical, treponematoses control activities should be integrated into other public health programs for the same target population. Particular emphasis must be given to the treatment of persons with infectious cases and a wide circle of their contacts, who are assumed to constitute a part of the treponemal reservoir. For disease transmission to be interrupted permanently, the mass treatment approach must be followed by periodic screening surveys of the child population and by subsequent long-term surveillance.
At an early stage of renewed program activities, the personnel of the static health service, including primary health care workers, school teachers, and other appropriate staff, should participate in the program in preparation for their eventual role in surveillance for these infections. At that stage cases need to be identified at the village level and reported to the health center for collaborative control action.

Because familiarity of medical personnel with nonvenereal treponematoses is waning, there is a need to train health staff to identify clinical cases and to take appropriate control actions at the local level. In support of these activities, long-acting penicillin preparations should be supplied to each health center in endemic areas, and a handbook of yaws, pinta, and endemic syphilis has been prepared for distribution by WHO [1].

Reference

Surveillance and Control of Resurgent Yaws in the African Region

R. Widy-Wirski

From the World Health Organization, Inter-Country Epidemiological Surveillance, Nairobi, Kenya

Yaws, once one of the most common infections in Africa, was expected to be eliminated in some countries and controlled in others after the mass treatment campaigns sponsored by the World Health Organization and the United Nations Children's Fund during the 1950s and 1960s and the implementation of improvements in education, sanitation, and other health-promoting activities. However, the curtailment of yaws control activity allowed the reservoir of untreated yaws to grow unchecked, and the number of reported cases of active yaws has increased in certain parts of Africa, especially in West Africa. In the Central African Republic, the prevalence of yaws is notably high among the Pygmies. Renewed programs for yaws control are under consideration. Mass campaigns are still necessary in some developing countries for the control of certain diseases but should be complementary to the development of general health services and should not be limited to the administrative borders of a given country.

Yaws was once one of the most common infections in Africa. It was a major cause of disability and mutilation, especially in rural areas. The World Health Organization (WHO) proposed and carried out in the 1950s and 1960s mass penicillin treatment campaigns in various yaws-endemic areas of the world, including many in Africa. The standard control methods that were developed proved to be enormously successful, the prevalence of yaws decreased dramatically, and in some countries the disease appeared to have been eliminated [1, 2]. The maintenance of effective yaws control, however, depended on continued expensive and time-consuming resurveys over a period of several years. This course proved difficult because of changing priorities in health care. Yaws surveillance teams began to deal with other disease problems, and the curtailment of yaws activity allowed the reservoir of untreated yaws to grow. The number of reported cases of active yaws (infectious and noninfectious) has again increased in certain parts of West Africa [3]. In the 1970s the incidence of yaws increased dramatically in countries such as Ghana, Ivory Coast, Benin, and Togo.

In 1976 the number of reported cases of yaws in Benin increased by 61.9% over that in the previous year; the number in Togo increased by 47.6%. Such increases could not be attributed solely to more effective case-finding activities. In fact, a steady increase in the number of reported cases was observed in this part of the area covered by the African Regional Office of WHO (WHO/AFRO). A resurgence of yaws in the northern part of Gabon was also noted. There, yaws was introduced by a massive emigration from Equatorial Guinea. In other African countries mass campaigns and general measures to promote health — e.g., health education, use of protective clothing, and better sanitation, including the liberal use of soap and water — reduced the incidence of yaws.

The Present Situation

Yaws is a notifiable disease in 35 of the 45 countries of the WHO/AFRO region (see table 1). In Equatorial Guinea, where yaws is not a reportable disease, it is known to be endemic [4]. Information is not available from Botswana, Comoros, Lesotho, Liberia, Mozambique, St. Helena, or Equatorial Guinea.

Seven countries reported >1,000 cases in 1982: Central African Republic, Congo, Benin, Ghana, Ivory Coast, Nigeria, and Togo. Data for 1983 are not yet available to WHO/AFRO except for Nigeria. This country reported 9,314 cases in 1983, as compared with only 1,201 in 1982 (an increase of more than sevenfold).

Table 1 shows the number of cases reported to WHO/AFRO during 1977–1982, and figure 1 shows the incidence per 100,000 population for 1982. Recently, there have been reports of pockets of yaws cases in two neighboring West African countries, Togo [5] and Ghana [6], at a level of 20–40 per 1,000 population; this figure contrasts with country aver-

Please address requests for reprints to Dr. R. Widy-Wirski, A/1 Armii W.P. 16/4, Warsaw, Poland.
### Table 1. Number of cases of yaws reported to the African Regional Office of the World Health Organization, 1977–1982, by country.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>NR</td>
</tr>
<tr>
<td>Benin</td>
<td>20,122</td>
<td>11,683</td>
<td>10,470</td>
<td>NR</td>
<td>NR</td>
<td>9,019</td>
</tr>
<tr>
<td>Botswana</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Burundi</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>347</td>
<td>203</td>
<td>167</td>
</tr>
<tr>
<td>Cameroon</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>Cape Verde</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>102</td>
<td>112</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1,085*</td>
</tr>
<tr>
<td>Chad</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>4*</td>
</tr>
<tr>
<td>Comoros</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Congo</td>
<td>815</td>
<td>579</td>
<td>343</td>
<td>864</td>
<td>2,157</td>
<td>1,433</td>
</tr>
<tr>
<td>Equatorial Guinea</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>137</td>
<td>225*</td>
</tr>
<tr>
<td>Gabon</td>
<td>1,824</td>
<td>814</td>
<td>1,082</td>
<td>229*</td>
<td>504</td>
<td>340</td>
</tr>
<tr>
<td>Gambia</td>
<td>1,426</td>
<td>153</td>
<td>291</td>
<td>NR</td>
<td>319</td>
<td>NR</td>
</tr>
<tr>
<td>Ghana</td>
<td>29,406</td>
<td>44,836</td>
<td>47,944</td>
<td>56,604*</td>
<td>44,023</td>
<td>41,939</td>
</tr>
<tr>
<td>Guinea</td>
<td>35,674</td>
<td>38,856</td>
<td>32,690</td>
<td>NR</td>
<td>5,612*</td>
<td>NR</td>
</tr>
<tr>
<td>Guinea-Bissau</td>
<td>30</td>
<td>16</td>
<td>11</td>
<td>218</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Ivory Coast</td>
<td>35,185</td>
<td>38,856</td>
<td>32,690</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Kenya</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>2,692</td>
</tr>
<tr>
<td>Lesotho</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Liberia</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Madagascar</td>
<td>0</td>
<td>346</td>
<td>NR</td>
<td>NR</td>
<td>15</td>
<td>NR</td>
</tr>
<tr>
<td>Malawi</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mali</td>
<td>169</td>
<td>291</td>
<td>162</td>
<td>186</td>
<td>203</td>
<td>47*</td>
</tr>
<tr>
<td>Mauritania</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mauritius</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mozambique</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Namibia</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Niger</td>
<td>NR</td>
<td>7,066</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nigeria</td>
<td>1,197</td>
<td>757</td>
<td>331</td>
<td>107</td>
<td>465</td>
<td>1,201*</td>
</tr>
<tr>
<td>Réunion</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Rwanda</td>
<td>687</td>
<td>577</td>
<td>490</td>
<td>489</td>
<td>455</td>
<td>531</td>
</tr>
<tr>
<td>St. Helena</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>São Tomé and Principe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Senegal</td>
<td>45</td>
<td>200</td>
<td>302</td>
<td>316</td>
<td>68</td>
<td>144*</td>
</tr>
<tr>
<td>Seychelles</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>122</td>
<td>154</td>
<td>1</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>NR</td>
<td>71</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>Swaziland</td>
<td>NR</td>
<td>NR</td>
<td>2,687</td>
<td>3,890</td>
<td>2,584</td>
<td>3,816</td>
</tr>
<tr>
<td>Togo</td>
<td>219</td>
<td>0</td>
<td>0</td>
<td>128</td>
<td>685*</td>
<td>198</td>
</tr>
<tr>
<td>Uganda</td>
<td>1,019</td>
<td>965</td>
<td>1,349</td>
<td>598</td>
<td>1,002</td>
<td>544</td>
</tr>
<tr>
<td>Upper Volta†</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Zaire</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Zambia</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96,551</td>
<td>112,727</td>
<td>99,497</td>
<td>64,515</td>
<td>65,115</td>
<td>61,691</td>
</tr>
</tbody>
</table>

**NOTE.** Table represents only reported cases. Data are from [4]. NR = no report.

* Data are provisional.
† Now known as Burkina Faso.

ages of 1.4 per 1,000 for Togo and 3.5 per 1,000 for Ghana. The numbers of cases in Ghana over the period 1969–1982 are shown in figure 2 [7].

There is a discrepancy between the number of cases in Ghana as reported to WHO and the number recorded nationally. It is known that the reported number of cases of yaws does not accurately reflect the actual total number. In Ghana it is estimated by
Afari [8] that for every reported case of yaws there are 10 unreported cases. In spite of this limitation, reporting certainly reflects the generally increasing trend.

Serologic surveys in selected villages in Ghana and the Ivory Coast suggested that for each case of active yaws there were two or more latent cases [9]. As expected, the cohort of children aged 10–14 years had the highest prevalence of yaws, and the majority of adults (persons older than 20 years) had Venereal Disease Research Laboratory (VDRL) serologic results that were reactive because of prior yaws infection. Most adults had received penicillin as treatment or prophylaxis during the earlier yaws campaigns.

In the Central African Republic, ~1,500 cases of yaws are reported yearly, but the true incidence is unknown. Yaws is endemic in the tropical forest region in the southern part of the country. It has been suggested that the very humid climate of the south favors the transmission of yaws, whereas the climate of the north is better suited for the spread of syphilis.

The rarity of syphilis in this region has usually been assumed to be due to the partial protection conferred by childhood yaws. Gonorrhea, a marker of venereal infection, is highly prevalent among the forest population of this region; for example, in a survey of the Pygmies’ camp in Lidjombo, 25% of male Pygmies were found to harbor gonococci [10]. During the period 1979–1982, extensive surveillance of treponemal diseases was carried out in the Central African Republic. Clinical and serologic surveys were conducted and serologic screening of prenatal patients was initiated in the capital, Bangui, and in five other major cities of the republic. It is estimated that only ~15% of the population of 2.5 million live in urban zones and have relatively easy access to health facilities. The results of this surveillance are shown in table 2.

In Bangui 35% of the genital ulcers seen are due to venereal syphilis and 10% to chancreoid. In rural areas the proportion is reversed, and in forest areas, which historically are hyperendemic for yaws, clinical venereal syphilis is not seen [11]. This pattern is consonant with the postulate of cross-immunity among treponemal diseases. However, the interpretation of serologic data, especially in the absence of clinical symptomatology, is extremely difficult in an area where more than one treponematosis is present [12].

As a result of surveillance (table 2), the Pygmies were identified as having an extremely high prevalence of treponemal infection. Of 486 Pygmies examined, 445 (91.6%) were reactive in both the VDRL test and the Treponema pallidum hemagglutination test. Among Pygmies older than 14 years, the proportion of positive seroreactors was 95.6%.

Active, contagious yaws is uncommon in other groups in the population of the Central African Republic. However, there is a particularly high level of yaws transmission among the Pygmies in that nation [13], in neighboring Cameroon and Zaire [14], and probably in the Congo. The Pygmies are ex-
Table 2. Treponemal seroreactivity in different population groups in the Central African Republic, 1979–1982.

<table>
<thead>
<tr>
<th>Area of residence, population group (sex)</th>
<th>No. of persons positive/no. examined* (percentage positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td></td>
</tr>
<tr>
<td>Routine testing</td>
<td></td>
</tr>
<tr>
<td>Prenatal patients (F)</td>
<td>2,644/20,560 (12.9)</td>
</tr>
<tr>
<td>Blood donors (M, F)</td>
<td>726/4,105 (17.9)</td>
</tr>
<tr>
<td>Venerable disease clinic gonorrhea patients (M)</td>
<td>1,307/6,498 (20.1)</td>
</tr>
<tr>
<td>Infants with possible congenital syphilis (M, F)</td>
<td>155/361 (42.9)</td>
</tr>
<tr>
<td>Prevalence screening</td>
<td></td>
</tr>
<tr>
<td>Civil servants (M)</td>
<td>15/170 (8.8)</td>
</tr>
<tr>
<td>Students (M)</td>
<td>101/614 (16.4)</td>
</tr>
<tr>
<td>Industrial workers (M)</td>
<td>40/212 (18.9)</td>
</tr>
<tr>
<td>Total</td>
<td>4,998/32,520 (15.4)</td>
</tr>
<tr>
<td>Rural savannah</td>
<td></td>
</tr>
<tr>
<td>Farmers (M)</td>
<td>136/661 (20.6)</td>
</tr>
<tr>
<td>Prenatal patients (F)</td>
<td>60/260 (23.1)</td>
</tr>
<tr>
<td>Total</td>
<td>196/921 (21.3)</td>
</tr>
<tr>
<td>Rural forest</td>
<td></td>
</tr>
<tr>
<td>Prenatal patients (F)</td>
<td>54/168 (32.1)</td>
</tr>
<tr>
<td>Farmers (M, F)</td>
<td>36/117 (30.8)</td>
</tr>
<tr>
<td>Farmers in contact with Pygmies (M, F)</td>
<td>232/265 (87.5)</td>
</tr>
<tr>
<td>Pygmies (M, F)</td>
<td>445/486 (91.6)</td>
</tr>
<tr>
<td>Total</td>
<td>767/1,036 (74.0)</td>
</tr>
</tbody>
</table>

NOTE. Data are from [10].
* Figures are based on positive results in both the Venerable Disease Research Laboratory (VDRL) test and the Treponema pallidum hemagglutination (TPHA) test.

Tremendously mobile, constantly crossing the borders to Zaire, the Congo, and Cameroon.

A mass treatment campaign could not entirely cover this population. Perhaps in the future, with the implementation of an adequate primary health care infrastructure, specific surveillance for yaws, which now requires mobile teams and very high expenditures, will be absorbed into the routine responsibilities of the rural health centers. In this way coverage of the population could be rendered more systematic and continuous. Since yaws, at present, affects primarily a remote forest population, the control program is given a low priority among the efforts made against communicable diseases in the Central African Republic.

The Future of Yaws Control in Africa

Largely because of the dramatic resurgence of yaws in parts of West Africa, the 31st World Health As-

sembley formally adopted a resolution in May 1978 urging member nations to take prompt and vigorous action to control treponematoses in general and yaws in particular. Renewed programs for yaws control are under consideration by several countries in West Africa and it is anticipated that they will be partially supported by WHO, the U.S. Centers for Disease Control, the U.S. Agency for International Development, the United Nations Children's Fund, and other agencies.

Several problems not seen in previous campaigns will be faced by a new yaws initiative [9]. (1) Although it is unlikely that Treponema pertenue has developed resistance to penicillin, the causes of penicillin treatment failure should be investigated and substantiated, and a study of quality-control measures for penicillin in Ghana should be included. (2) In earlier yaws campaigns most individuals given penicillin as treatment or prophylaxis for yaws were receiving this drug for the first time; thus, anaphylactic reactions were not expected and were rarely observed. In new yaws initiatives prophylaxis is recommended for monitoring possible anaphylactic reactions, and alternative therapies should be evaluated for penicillin-sensitive individuals. (3) Consideration should be given to the possibility that mass penicillin treatment may favor the selection and spread of penicillin-resistant bacteria such as gonococci, meningococci, and pneumococci. The areas of highest yaws prevalence in West Africa have in circulation strains of penicillinase-producing Neisseria gonorrhoeae. (4) Syphilis is notably uncommon in rural areas of the Central African Republic and Ghana. This fact supports the generally held belief that immunity to syphilis is produced by yaws. The possibility that the elimination of yaws and the associated herd immunity to treponemal infection may result in the replacement of yaws by syphilis must be considered. (5) Strategies for yaws control need to be considered on a regional basis. The practicality of integrating yaws control into other preventive health activities must also be assessed. New yaws control initiatives should enhance specific community awareness and health education at the time of the initial surveys and the resurveys. Local or village health workers should participate in all phases of the campaign against yaws so that they eventually can assume the responsibility for yaws surveillance and treatment.

This is by no means a complete list of the problems that may be involved in a new campaign against
yaws. The population at risk is not only much larger than in previous yaws campaigns but also much more mobile. Most authorities agree that yaws must be controlled soon if its disabling late complications, which are believed to occur in as many as 10% of untreated patients, are to be prevented. The resurgence of yaws in West Africa represents a failure to maintain the consolidation phase of the yaws campaign begun in the 1950s. Resources must be committed from the outset to the support of the difficult and expensive consolidation phase, possibly for as long as several decades, if yaws is finally to be controlled and eliminated.

**Is a Mass Campaign Still the Correct Approach?**

Many African countries have experienced epidemics of lethal diseases (trypanosomiasis, cerebrospinal meningitis), a high prevalence of crippling diseases (onchocerciasis, yaws), and very high child mortality from gastrointestinal and nutritional disorders. Such countries have suffered enormously, and these diseases have contributed largely to the limitation of social, economic, and health progress. Where endemic communicable diseases affect a significant proportion of the population, they are often best controlled en masse—i.e., through well-organized mass campaigns. Intensive mass campaigns have brought some of these diseases under control without eliminating the danger of their recurrence. There is abundant evidence that when vigilance is relaxed or surveillance activities are inadequate, these endemioepidemic diseases can and do recur, with disastrous effects on the socioeconomic life of the community.

These countries are thus faced with a difficult dilemma. There are two approaches to the control of such diseases. The first, generally known as the horizontal approach, tackles the various health problems on a long-term basis with multipurpose objectives. This approach involves the creation and development of a system of permanent units—the general health services. The so-called vertical approach seems more effective for urgent health problems. A vertical program usually consists of short-term, single-purpose applications of specific measures, commonly known as mass campaigns.

In some instances the best choice is a combination of the two approaches. We should not only consider the need to achieve maximal results with minimal means and resources and the socioeconomic benefits of such measures but also ensure the continuity and vigilance that only economically feasible, fixed health-care units can provide after the mass campaign has attained its objectives.

The control of human endemioepidemic diseases through mobile units first started in 1916, when Eugene Jamot realized the necessity of special intensive measures against trypanosomiasis in French Equatorial Africa. Some programs using mobile medical units were started with a single objective but sooner or later began to deal with several important diseases. Some of these programs were so successful that they actually stimulated the development of fixed rural health-care units.

Mass campaigns in some developing countries are still necessary for the control of certain communicable diseases but should not be regarded as an exclusive approach. On the contrary, they should be complementary to the development of general health services; that is, because mass campaigns provide only a temporary solution to the problem, an organized scheme for the establishment of rural health services should be put into action at the same time. The two important roles of mass campaigns are to stimulate the development of general health services and to reduce the high incidence of diseases to more manageable levels.

There is another alternative. A mass campaign may concentrate in its early stages on a single disease and then, during its later stages, attack another health problem while continuing with the maintenance and consolidation phases of the original campaign. The WHO Expert Committee on Venerable Infections and Treponematoses suggested that, during the late stages of a campaign against yaws, eradication measures might be included as part of a mass campaign against another disease. Mass campaigns involving this approach are known as sequential campaigns. The committee cited Bosnia as an example of an area where, after field teams were retrained, mycosis of the scalp was attacked on a mass basis but control of endemic syphilis (the original program) was maintained [15].

In Cambodia, Thailand, Haiti, and Nigeria, the mobile teams conducting surveys and resurveys of endemic treponematoses turned their attention during the consolidation phase to smallpox vaccination as well [16]. During the yaws campaigns some 30 million smallpox vaccinations were given between 1958 and 1963. Leprosy case-finding activities have been carried out during yaws campaigns in the British
Solomon Islands, Malaya, Togo, and other areas. Mass campaigns against yaws may still be needed in countries such as Ghana but should probably be combined with control or surveillance activities aimed at other diseases. The choice will of course depend on local epidemiologic patterns and priorities.

Since yaws is a disease of remote areas, it is frequently assigned a low priority in the health plans of affected nations. In 1979 a questionnaire was sent to all WHO/AFRO countries, and the response indicated that only Ghana was giving priority to yaws control. In many areas where yaws is endemic, there is also endemcity of parasitic diseases and hemorrhagic fevers. In the Pygmy population of the Central African Republic, surveillance of monkey-pox could be combined with the yaws control program [13]. If a combined mass campaign is used, it should not be limited to the administrative borders of a given country, since reintroduction of infection can be expected to occur.

References
8. Afari AE. A case study in which routine disease surveillance resulted in the detection of an important disease problem: infectious yaws in Ghana. Presented at the Third Annual WHO/AFRO/SHDS/CDC Disease Surveillance Conference, Sierra Leone, February 27-March 2, 1984
Yaws in Ghana

V. K. Agadzi, Y. Aboagye-Atta, J. W. Nelson,
D. R. Hopkins, and P. L. Perine*

From the Epidemiology Division, Ministry of Health, Accra,
Republic of Ghana; and the International Health Programs
Office, Centers for Disease Control, Atlanta, Georgia

The final results of a three-year campaign against yaws in the Republic of Ghana, which was introduced in an attempt to reduce an unusually high prevalence, are summarized. The campaign started in January 1981 and officially ended in December 1983. Serious economic and technical constraints slowed the progress of work after the first year and reduced the total population covered. In spite of the shortcomings, the program provided penicillin treatment to 77,818 patients with active yaws (4.04% of those examined during the campaign) as well as chemoprophylaxis for an additional 1,556,360 contacts. The campaign staff compiled detailed information on the epidemiology of yaws in Ghana. A second attack phase using simple equipment and vehicles such as motorcycles and bicycles could be implemented with greater efficiency and could reduce costs.

Yaws is endemic in the Republic of Ghana, although its severity varies from region to region, depending on the level of sanitation and overcrowding. Increasing prevalence of active yaws has been noticed in recent years. The epidemiologic pattern of yaws in Ghana was first described by Scott [1] from the results of a yaws control campaign in northern Ghana in 1956. He found the prevalence of infectious yaws in northern Ghana to be 1.5%, which decreased to 0.19% after an initial treatment survey. Subsequent campaigns assisted by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) were carried out in the Volta region in 1957 [2] and in the Brong-Ahafo region in 1960 [3]. The prevalence of infectious yaws was reduced from 1.69% to 0.17% in the Volta region and from 1.15% to 0.11% in the Brong-Ahafo region.

The prevalence of yaws was very low in Ghana between 1963–1969. In 1968, 6,593 active cases were reported and in 1969, 5,343 cases. During this time, yaws surveillance was actively pursued by mobile medical field units. After 1970, however, only sporadic case finding and treatment were performed because resources were diverted to activities for cholera control. Yaws prevalence began to increase because of insufficient surveillance and treatment, reaching a peak in 1976 (figure 1). The Ashanti, eastern, and central regions reported >80% of all yaws cases seen in 1975 and 1976 (table 1). Eighty-seven percent of all active cases reported occurred in children younger than the age of 15 years. This alarming increase in the number of cases prompted the government of Ghana to institute measures aimed at reducing yaws morbidity to manageable levels. An anti-yaws campaign commenced in January 1981 with the collaboration of international donor agencies.

Methods

The main objective of this campaign was to reduce morbidity due to yaws in Ghana. The goal was to attempt to reduce prevalence of yaws from an estimated rate of 400–500 cases per 100,000 to <100 per 100,000 by the end of 1983.

A systematic survey of all yaws cases (infectious and noninfectious) in endemic foci had been previously performed. The methods used in the campaign were the ones recommended by Hackett and Guthrie [4]. The country was first divided into a number of operational areas on the basis of the reported prevalence of disease. For example, in areas with high morbidity, i.e., >10% prevalence, mass treatment of all persons living in the areas (total mass treatment)
was carried out. In areas where prevalence ranged between 5% and 10%, all children younger than the age of 15 years were given penicillin injections (juvenile mass treatment). In areas with prevalences of <5%, only cases and contacts were treated (selective mass treatment) [4]. Benzathine penicillin (bicillin) or procaine penicillin in aluminium monostearate was used, depending on availability. Multipurpose mobile medical field teams were assigned the additional responsibilities of immunizing children younger than 10 years against yellow fever, those younger than five years against tuberculosis, those younger than two years against measles; and women of childbearing age against tetanus. The idea was to make the teams more useful and to avoid adopting the yaws campaign as a vertical program.

In all, 18 teams were deployed. Each consisted of four to seven technically qualified health personnel equipped with four-wheel-drive vehicles, Ped-O-Jet vaccine inoculators, and vaccines. The teams visited each village according to a previously prepared itinerary. The first visit, or initial treatment survey, was followed by a second or third visit (resurveys) three to six months later. The resurveys were designed to examine and treat those absent during the initial survey, treatment failures, and those reinfected. It was not always possible to resurvey villages because of logistic problems.

The doses of penicillin used varied according to the patient’s age; adults with active yaws received a single injection of 1.2 million units, children younger than 15 years received 600,000 units, and those younger than 6 years received 300,000 units. Patients and contacts received similar doses.

All yaws cases and contacts discovered during visits were recorded on village tally sheets, which were collated at the regional office of the mobile team. The summaries were forwarded to the national headquarters of the Epidemiology Division, where the final results were collated and analyzed.

### Results

A preliminary report in 1983 covering the first one and one-half years of operation [5] gives further progress of the campaign, whose attack phase was completed at the end of 1983. A total of 2,464 villages were visited during the initial treatment survey (table 2). A total of 1,733,872 persons were examined, and 65,602 (3.8%) patients with active yaws were treated. As the campaign progressed, the total number of persons expected to be examined declined. At the end of the first year of the campaign, 875,264 persons were seen, compared with 561,869 persons in the second year, which represented 65% of the initial coverage. During the third and final year, only 296,739 persons, or 34% of the initial coverage, were seen. These diminishing numbers were due to economic and technical constraints that affected the entire country.

The number of yaws cases reported in the exam-

---

### Table 1. Distribution of notified cases of yaws in Ghana: three hyperendemic regions compared with other regions.

<table>
<thead>
<tr>
<th>Year</th>
<th>Ashanti</th>
<th>Central</th>
<th>Eastern</th>
<th>Other regions*</th>
<th>Total</th>
<th>Percentage notified by three hyperendemic regions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1969</td>
<td>205</td>
<td>1,437</td>
<td>2,253</td>
<td>1,448</td>
<td>5,343</td>
<td>73</td>
</tr>
<tr>
<td>1975</td>
<td>15,944</td>
<td>16,901</td>
<td>15,329</td>
<td>11,755</td>
<td>59,926</td>
<td>80</td>
</tr>
<tr>
<td>1976</td>
<td>22,956</td>
<td>19,681</td>
<td>15,647</td>
<td>13,581</td>
<td>71,765</td>
<td>81</td>
</tr>
<tr>
<td>1979</td>
<td>10,020</td>
<td>11,876</td>
<td>13,194</td>
<td>12,854</td>
<td>47,944</td>
<td>73</td>
</tr>
<tr>
<td>1980</td>
<td>16,134</td>
<td>11,518</td>
<td>13,916</td>
<td>17,749</td>
<td>59,317</td>
<td>70</td>
</tr>
<tr>
<td>1981</td>
<td>10,135</td>
<td>14,824</td>
<td>10,534</td>
<td>10,004</td>
<td>45,523</td>
<td>78</td>
</tr>
<tr>
<td>1982</td>
<td>3,900</td>
<td>21,327</td>
<td>7,776</td>
<td>8,936</td>
<td>41,939</td>
<td>79</td>
</tr>
</tbody>
</table>

* Greater-Accra, Volta, western, Brong-Ahafo, northern, and upper regions.
Table 2. Number of villages visited, persons examined, and yaws cases diagnosed in Ghana during initial treatment and first resurvey, 1981–1983.

<table>
<thead>
<tr>
<th>Phase</th>
<th>No. of villages</th>
<th>No. of persons examined</th>
<th>No. of cases (%) of indicated type of yaws</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infectious yaws</td>
</tr>
<tr>
<td>Initial treatment</td>
<td></td>
<td></td>
<td>6,522 (0.75)</td>
</tr>
<tr>
<td>1981</td>
<td>1,263</td>
<td>875,264</td>
<td></td>
</tr>
<tr>
<td>1982</td>
<td>979</td>
<td>561,869</td>
<td>3,570 (0.64)</td>
</tr>
<tr>
<td>1983</td>
<td>222</td>
<td>296,739</td>
<td>1,089 (0.37)</td>
</tr>
<tr>
<td>Total</td>
<td>2,464</td>
<td>1,733,872</td>
<td>11,181 (0.64)</td>
</tr>
<tr>
<td>First resurvey</td>
<td>534</td>
<td>192,040</td>
<td>1,826 (0.95)</td>
</tr>
</tbody>
</table>

ined population was low. The total percentage of active yaws cases was as follows: 1981, 3.97%; 1982, 4.02%; and 1983, 2.77%. The percentage of total yaws cases among the persons examined during the three-year period was 3.8%.

The proportion of cases of infectious yaws seen during the survey was 17% of all cases. The percentage of infectious yaws cases seen at the initial treatment survey was 0.64%. Noninfectious cases of yaws were present primarily with hyperkeratotic plantar and/or palmar lesions. Of the 192,040 persons seen at the resurveys, 12,216 (6.36%) had evidence of yaws. The vast majority of these cases represented new cases that had not been examined or treated in the initial survey. They represented 0.95% of infectious and 5.41% of noninfectious yaws cases.

The prevalence of yaws among those younger than 15 years showed consistent trends (table 3). The mean prevalence of infectious yaws cases in this age group between 1981 and 1983 was 24.5% but was only 3.6% in those older than 15, a ratio of ~7:1. Conversely, there were more cases of noninfectious yaws among the adults than among the children, with a ratio of ~1:11.

Of 1,925,912 persons examined at both the initial surveys and resurveys, 77,818 (4.04%) received treatment because they had evidence of yaws. An additional 1,556,360 persons were contacts and were given prophylactic penicillin according to the guidelines recommended by WHO [4].

We calculated the total prevalence of yaws in Ghana using 1982 population estimates (12,567,859) projected from the 1970 populations census. The results were as follows: in 1981, the rate of yaws was 276 cases per 100,000 population; in 1982, 179 cases; and in 1983, 62 cases. These estimates are far less than the estimated rate of 400–500 cases per 100,000 population at the beginning of the campaign.

The average estimated cost of the program per patient with yaws increased from $1.41 (U.S.) in 1982 to $2.20 in 1983. This increase accounted for 56% of the initial cost of operations during the first one and one-half years and was due largely to increased costs of transportation.

Additional benefits of the three-year program included the following: a total of 1,475,554 children between one and 10 years of age, representing 42.3% of the eligible population, received yellow fever vaccine; 262,443 or 50.3% of the eligible children aged nine to 24 months were given measles vaccine; 558,453 or 24% of the women of childbearing age were given one dose of tetanus toxoid; and 494,791 or 21.3% of the eligible children (neonate to four years) received bacille Calmette-Guérin vaccine.

Discussion and Conclusions

Because of economic constraints, only a few of the mobile teams were able to do resurveys. Thus, the coverage achieved fell below expectations. Because the coverage achieved at the follow-up survey was low, it is difficult to state with certainty whether there will be any lasting change in the prevalence of yaws.


<table>
<thead>
<tr>
<th>Age, year of survey</th>
<th>No. of cases (%) of indicated type of yaws</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infectious yaws</td>
</tr>
<tr>
<td>&lt;15 years</td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>6,242 (30.6)</td>
</tr>
<tr>
<td>1982</td>
<td>3,460 (25.5)</td>
</tr>
<tr>
<td>1983</td>
<td>825 (17.5)</td>
</tr>
<tr>
<td>≥15 years</td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>280 (2.0)</td>
</tr>
<tr>
<td>1982</td>
<td>110 (1.2)</td>
</tr>
<tr>
<td>1983</td>
<td>264 (7.5)</td>
</tr>
</tbody>
</table>
in Ghana. The reduction in the prevalence of yaws—from an estimated 400–500 cases per 100,000 population before the survey to 62 cases per 100,000 population after the survey—shows that the target set before the campaign was accomplished satisfactorily.

There were initial misgivings about the validity of yaws control programs in Ghana because of its commitment to primary health care. Nevertheless, the multicomponent yaws and yellow fever program has managed to progress through a storm of economic and technical problems. No one expected that the campaign would treat 77,818 cases and 1,556,360 contacts when the campaign began. Indeed, most of the people examined and treated for yaws or immunized against yellow fever, measles, tetanus, and tuberculosis had no direct access to primary health care.

The success of combining the yaws control program with that of immunization using single-dose vaccine should be stressed. Although it is impossible to forecast the impact of such measures on the reduction of morbidity due to measles, tetanus, and tuberculosis, the mass vaccination campaign against yellow fever will prevent epidemics of this disease in vaccinated populations.

We anticipate that when primary health care is widely available in Ghana, local management teams will be responsible for the periodic examinations of schoolchildren at intervals of one to three years, particularly in areas where prevalence of active yaws has been reduced to <1%. The teams will use simple means of transportation to gain access to the remote villages and to reduce transportation cost. We anticipate that in certain areas health workers stationed in health centers and referral hospitals at the district level may undertake additional maintenance treatment and prophylaxis of cases and contacts.

Perhaps the most important requirement for a successful yaws control program is the availability of long-acting penicillin in sufficient quantities at all times and places. If this requirement is met, yaws will be reduced to the level where it will cease to be a major public health problem. The results of the present exercise have taught us a lesson; in spite of formidable economic and technical difficulties, it is possible to manage such a program, provided that medicine and vaccines are available and personnel can be motivated.

References
Some Epidemiologic Aspects of Yaws in the Ivory Coast

Konan N'Da

From the Ministry of Public Health, Abidjan, Ivory Coast

Because of the prevailing high levels of yaws, a mass treatment campaign was conducted in the Ivory Coast from 1956 to 1970. In 1970, at the end of the mass campaign, <30,000 cases of yaws were reported. After 1970, a program of detection and treatment of remaining foci of infection was carried out to control the disease. The number of cases reported annually continued to decline until 1974, when the number of reported cases began to rise. Since 1980, the annual reported incidence of yaws has declined. It is concluded that the mass campaign of 1956–1970 reduced the endemicity of yaws in the Ivory Coast. However, significant foci of the disease remain, and efforts to detect and treat yaws must be continued to prevent a resurgence of this infection in the Ivory Coast.

Yaws before 1956. Although documents on the endemicity of yaws in the Ivory Coast before 1956 were not available to us, the level of yaws was sufficiently high to warrant the organization of a mass campaign against the disease. This mass campaign, conducted between 1956 and 1970 by the Service de Grandes Endémies, was made possible through the assistance of the United Nations Children's Fund, the U.S. Agency for International Development, and the World Health Organization.

Mass campaign against yaws. In the first phase of the campaign (1956–1963), the only objective was the detection and treatment of all clinical cases of yaws. Standard treatment consisted of a single injection of long-acting penicillin, which was administered to patients and their contacts.

In the second phase of the campaign (1963–1970), this strategy was slightly modified. The objective was both the clinical and the serologic detection of yaws infection. Persons with clinical lesions or positive serologic results were treated with a total of three injections of long-acting penicillin given at 15-day intervals. Contacts received only a single injection. The mass campaign led to a decline in the endemicity of yaws.

Yaws control since 1970. Since 1970, the strug-


<table>
<thead>
<tr>
<th>Year</th>
<th>No. of reported contagious cases</th>
<th>Estimated population</th>
<th>No. of new and old cases</th>
<th>Prevalence per 1,000 population*</th>
<th>Incidence per 1,000 population*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970</td>
<td>29,600</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1971</td>
<td>17,027</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td>15,463</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1973</td>
<td>15,973</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td>13,176</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1975</td>
<td>28,581</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1976</td>
<td>?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977</td>
<td>?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1978</td>
<td>27,790</td>
<td>7,093,393</td>
<td>37,019</td>
<td>3.92</td>
<td></td>
</tr>
<tr>
<td>1979</td>
<td>32,690</td>
<td>7,313,288</td>
<td>39,023</td>
<td>4.47</td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td>35,422</td>
<td>7,540,000</td>
<td>30,387</td>
<td>5.18</td>
<td>4.70</td>
</tr>
<tr>
<td>1981</td>
<td>28,086</td>
<td>7,773,740</td>
<td>24,854</td>
<td>3.10</td>
<td>2.82</td>
</tr>
<tr>
<td>1982</td>
<td>22,576</td>
<td>8,014,182</td>
<td>10,030†</td>
<td>2.67†</td>
<td>1.75†</td>
</tr>
<tr>
<td>1983</td>
<td>7,248†</td>
<td>8,263,182</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Prevalence and incidence are calculated from estimated population data.
† Data are for the first six months of the year.
‡ The rates for the year are estimated from the number of cases for the first six months.

Please address correspondence to Dr. Konan N'Da, Directeur de la Santé Publique, Ministère de la Santé Publique, B.P.V. 16, Abidjan, Ivory Coast.
gle against yaws has been limited to the identification of existing reservoirs of infection and prompt treatment of affected individuals and their contacts. We were able to obtain interesting data on yaws in the Ivory Coast since 1970 from the Service Autonome des Statistiques Sanitaires et de la Documentation (table 1). The number of detected cases in all categories of yaws decreased from 1971 to 1974, a decline that can be interpreted as an indication of the success of the previous campaign against yaws. Endemicity of yaws recurred to some extent from 1975 to 1980; there was a noticeable increase in the number of cases of yaws registered during those years. The number of cases registered in 1981, 1982, and 1983 decreased progressively.

Incidence of yaws. It is difficult to determine the incidence of new cases of yaws in relation to the total population because of the problems of estimating the population of the Ivory Coast. The population increases from one year to another, and periodic censuses have proved to be complex. We obtained the following information from the statistics service. In 1980 the population of the Ivory Coast was 7,540,000, and the annual rate of population growth was 3.1%. We have extrapolated from these data to estimate the population from 1978 through 1983 (table 1).

Prevalence of yaws. The prevalence of yaws (the number of new cases plus the number of old cases in the population) was determined beginning in 1979 (table 1). The prevalence, like the incidence, has undergone a decline since 1980.

Conclusion. The campaign against yaws in the Ivory Coast that was in effect from 1956–1970 has decreased the endemicity of yaws. Although there was a slight recrudescence of yaws from 1975 to 1980, the situation improved in 1981–1982, and it appears that this trend continued into 1983. However, reservoirs of yaws remain, and the least slackening of control and treatment measures could result in the loss of the benefits of years of effort.
Endemic Treponematoses in the Sudan

Haidar Abu Ahmed Mohamed

Sudan is surrounded by eight countries and has marked movement of population across its borders. At one time yaws and syphilis were important public health problems in the Sudan. Following the wide use of penicillin, both diseases were much reduced in prevalence and were no longer public health problems. However, the extensive population movement and particularly the huge influx of refugees across the border pose important potential hazards. The rapid urbanization and the social and cultural changes that followed economic development affected family ties and community behavior and resulted in a marked increase in the prevalence of sexually transmitted diseases, including syphilis. It is difficult to know the true magnitude of the problem because of the poor health information system and coverage. Improvement of the surveillance system is urgently needed, and more attention needs to be paid to treponemal infections. This entails improvement in health services and training of health personnel.

The Sudan, with an area of 2.6 million square kilometers, is the largest country in Africa. The country is situated in the northeastern part of the continent, extends from latitude 6°N to 22°N and shares borders with eight African countries (Egypt, Libya, Chad, The Central African Republic, Zaire, Kenya, Uganda, and Ethiopia). The Nile traverses the country from south to north and is the main source of water.

The Sudan is dominated by a tropical continental climate, with a desert climate in the north and tropical jungles in the south. The annual rainfall varies from 25 mm in the north, which has a dry climate, to as much as 2,000 mm in the south, which has very high humidity.

According to the 1983 census, the total population is 21 million. More than 70% of the population live in rural communities. In the north and central parts, the population is a mixture of tribes of Arabic origin and are mostly Moslems. In the south there are predominantly Negroid tribes, who practice tribal religions, with minorities of Christians and Moslems [1].

The health services began during the colonial era as the Sudan Medical Service, which was established as the Ministry of Health after independence in 1956. Recently, in 1977, a National Health Programme was formulated, and priorities were established within this program. Availability of primary health care, especially in rural areas, was given high priority in the National Health Plan [2].

Treponemal Diseases in the Sudan

Syphilis. Syphilis has been reported in the Sudan since the inception of the medical services in 1904 [3]. The disease was at one time widespread in the north and central parts of the country [4]. The influx of laborers, traders, and peddlars from different parts of the country during the 1920s and 1930s into the Gezira area, where new agricultural schemes were being developed, and the effect of the quickly earned wages on sexual behavior facilitated the dissemination of syphilis. The disease was then second only to malaria as a cause of miscarriage and stillbirths. A serologic survey carried out in northern Sudan during the early 1930s showed a 9.4% positivity rate among pregnant women [5]. The prevalence was particularly high in eastern and western Sudan, where there was a larger immigrant population from the adjacent countries (Ethiopia and Chad) and where promiscuous behavior was common. The highest incidence recorded was during the early 1930s.

The incidence of syphilis declined following improvement in the health services coverage and the wide use of an antisyphilitic treatment (neosalvarsan), which was given in all hospitals from the 1920s until the 1950s. The extensive use of penicillin during the 1950s gave excellent results in the treatment of syphilis, and a dramatic decline in incidence was reported. In a study undertaken in Khartoum during the 1980s, which involved the administration of the Venereal Disease Research Laboratory (VDRL) test and the fluorescent treponemal antibody-absorption (FTA-ABS) test to 2,201 blood donors and 199 patients with sexually
transmitted diseases, a positive reaction was found for only a single patient, while none of the donors showed positive results [6]. This rate is far below that recorded generally among outpatients around the world [7]. However, it is difficult to draw conclusions from the serologic results reported in Khartoum. Since the data from the annual reports include all the sexually transmitted diseases, it is difficult to know the magnitude of the treponemal diseases.

Yaws. Although yaws has been endemic in the Sudan, the disease was never commonly reported north of the ninth parallel but was widespread south of that. Most cases were reported from the southern part of the Upper Nile province in the low-lying riverain part of Bahr El Gazal and Equatoria provinces. There is evidence that the disease has existed in those areas for generations. In the Sudan Medical Services Annual Report of 1927, yaws was described as the most widespread and most crippling disease affecting the Negroid people in the upper reaches of the White Nile and its tributaries.

Yaws is known as a disease of populations in tropical areas that have heavy rainfall and high humidity [8-10]. The disease is known to flourish best in rural communities, where there is poor sanitation, overcrowding, and poor personal hygiene [8-10]. Climatic prerequisites have largely determined the geographic distribution of yaws in the Sudan. The disease remains confined to the damp, swampy region of the upper Nile Basin, where overcrowding, lack of sanitation, communal feeding, the social practice of handing round the family pipe, and the plague of flies around the cattle camps provide good opportunities for its transmission.

The gloomy picture of the widespread disease reported during the 1920s and early 1930s has changed dramatically. Some of the epidemiologic characteristics of yaws facilitated its control. The facts that the disease is relatively easy to diagnose and that effective treatment is available offered good opportunities for gaining the confidence of the local communities. Similarly to what was advocated and practiced in some countries [11-13], the yaws campaign was known as a spearhead for the health services in the central areas in the Sudan.

Discussion
The treponemal diseases were not mentioned as a priority in the National Health Programme of 1977-1978 to 1983-1984 [14]. This does not mean that these diseases are not important health problems. However, the burden of other, more serious, diseases is so huge that the medical services are overwhelmingly occupied, and little attention can be given to problems of treponemal disease.

Syphilis, a sexually transmitted disease, is no doubt a health problem in the Sudan. Several factors led to the increase in its incidence. The fact that the Sudan has a long border and is surrounded by several countries exposes it to huge immigration movements. This situation has been further aggravated by political unrest and upheaval in the neighboring countries (Zaire, Uganda, Ethiopia, and Chad), which has resulted in a large number of refugees. Another factor is the breakup of the traditional pattern of social relationships and the marked decrease in parental control. The accelerated urbanization and migration of laborers into the rapidly expanding cities and into the new development areas have resulted in more promiscuity and a marked increase in the incidence of syphilis.

The exact magnitude of the problem of treponemal disease in the Sudan is not known. The information necessary for setting priorities and planning an effective control program is not available. The incidence figures are based on reports from health units. These statistics reflect the extent of case-finding practices, the latter depending on accessibility of services. There is poor coverage in many areas. The reported cases are no doubt only the tip of an iceberg. Statistics also reflect the extent of interaction between the available health services and the patients. In many of the conservative communities in the Sudan, social and cultural factors affect this interaction and usually result in underreporting of cases. The statistics on treponemal infections are also determined by the ability of the health workers to diagnose and treat the patients. The training of the paramedical health workers, who are responsible for running most of the health units, is not adequate to enable these workers to diagnose and treat such patients. The lack of supportive laboratory diagnostic facilities and the fact that serologic diagnoses are not possible result in underreporting.

Conclusion
The treponemal diseases are not considered a high priority among the health problems in the Sudan.
Because of the poor information about these diseases, it is not possible to know the magnitude of the problem. There is a potential danger of recrudescence of these diseases because of the increased migration to urban areas, the social changes that usually follow such migration, and the poor surveillance system available. These diseases need to be given special attention and should be kept under surveillance.

References
1. Sudan Al Manach, Khartoum, Sudan, 1962
4. Sudan Medical Services. Annual reports, 1926
5. Sudan Medical Services. Annual reports, 1935
14. Ministry of Health. The National Health Programme, Khartoum, Sudan: Ministry of Health
Endemic Treponematoses in Togo and Other West African States

Isak M. Touré

In 1970 an alarming increase in the number of cases of treponematoses in general and yaws in particular began to be apparent in sub-Saharan Africa, yet official reports usually underestimate the extent of these diseases. Thus, a clinical and serologic investigation of the prevalence of yaws was conducted in May 1981 in Togo. The proportion of examined persons found to have clinical yaws lesions varied from 1% to 3.9%; all of the four cantons with a prevalence of ≥3% are located near Ghana, where the disease is endemic. Children one to 14 years old (and especially those five to 14) were most frequently affected by yaws. The results confirm that yaws is underreported and that it persists and is even resurgent in many areas of Togo and in other French-speaking countries in West Africa. Because of the prevalence of migration and nomadism, a regional (as opposed to national) effort to combat the treponematoses is essential.

Contrary to general belief, yaws and endemic syphilis (bejel) continue to be significant problems in sub-Saharan Africa. In Benin [1] studies conducted between 1955 and 1958 revealed clinically active disease in an average of 7%-10% of the persons examined; in Burkina Faso (formerly known as Upper Volta) [1-3] positive serologic (Kline test) results were found in 35%-68% of inhabitants of the Black Volta River area [1, 4]. Similar results were obtained in Ivory Coast, Niger, Senegal, Togo, and northern Mali [1, 2, 4].

With the assistance of several organizations (the United Nations Children’s Fund, the World Health Organization, and the U.S. Agency for International Development, the Services des Grands Endémies of the states involved and the Organisation de Coordination de Cooperation pour la lutte Contre les Graines Endémies (OCCGE) mounted mass campaigns against yaws and endemic syphilis between 1958 and 1961. These efforts resulted in a spectacular decline in the prevalence of both diseases. In every case, studies conducted between 1962 and 1964 revealed the prevalence of treponemal illness to be <1%. In 1970, however, an alarming increase in the number of cases of treponematoses in general and yaws in particular began to be apparent in sub-Saharan Africa. In addition, official reports of cases usually underestimate greatly the extent of these diseases. This paper reports on clinical and serologic studies undertaken in the past few years to help evaluate the situation epidemiologically.

Methods
An investigation of the prevalence of yaws was conducted in May 1981 at the request of the Ministry of Public Health of the Republic of Togo in three districts of the country: Vogan and Tabligbo in the coastal region and Bassar in the central region. The investigations were limited to six cantons in the Vogan district (Akoumape, Badouge, Dagbati, Klologo, Massepe, and Sevagan), three cantons in the Tabligbo district (Kouve, Tchehpoodedepoe, and Tometi-Kondji), and six cantons in the Bassar district (Baghan, Bangeli, Dimori, Kabou, Katchamba, and Namo) [5, 6]. All inhabitants of the cantons selected were invited to give a brief medical history and to undergo clinical examination by the team physician. Serologic examinations (quantitative and qualitative Kline tests) were administered to a randomly selected sample of attendees (20%). Persons with positive serologic results were recontacted to confirm the existence or nonexistence of symptoms of yaws.

Results
Clinical and serologic findings in the three districts are summarized in Table 1. No cases of gansosa or goundou were seen. The proportion of examined persons found to have clinical yaws lesions in the 14 can-
Table 1. Summary of results of the 1981 yaws survey in Togo.

<table>
<thead>
<tr>
<th>District, canton</th>
<th>Clinical results*</th>
<th>Serologic results†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vogan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Badouge</td>
<td>14/465 (3.0)</td>
<td>9/90 (10)</td>
</tr>
<tr>
<td>Sevagan</td>
<td>16/540 (3.0)</td>
<td>4/80 (5)</td>
</tr>
<tr>
<td>Akosombo</td>
<td>15/730 (2.0)</td>
<td>20/125 (16)</td>
</tr>
<tr>
<td>Klogo</td>
<td>14/665 (2.1)</td>
<td>17/120 (14.2)</td>
</tr>
<tr>
<td>Dagbati</td>
<td>8/550 (1.0)</td>
<td>10/70 (14.3)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>84/3,865 (2.2)</td>
<td>60/485 (12.4)</td>
</tr>
<tr>
<td>Tabligbo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tcheckpodelekooe</td>
<td>18/672 (2.7)</td>
<td>15/130 (11.5)</td>
</tr>
<tr>
<td>Kouve</td>
<td>29/144 (3.9)</td>
<td>8/122 (6.6)</td>
</tr>
<tr>
<td>Tomesti-Kondji</td>
<td>7/328 (2.1)</td>
<td>7/65 (10.8)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>54/1,744 (3.1)</td>
<td>30/317 (9.5)</td>
</tr>
<tr>
<td>Bassar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimori</td>
<td>34/1,087 (3.1)</td>
<td>28/80 (35)</td>
</tr>
<tr>
<td>Baghan</td>
<td>10/483 (2.1)</td>
<td>9/30 (30)</td>
</tr>
<tr>
<td>Bangeli</td>
<td>29/1,672 (1.7)</td>
<td>15/75 (20)</td>
</tr>
<tr>
<td>Namo</td>
<td>38/1,250 (3.0)</td>
<td>44/130 (33.9)</td>
</tr>
<tr>
<td>Katchamba</td>
<td>17/1,473 (1.2)</td>
<td>7/90 (7.8)</td>
</tr>
<tr>
<td>Kabou</td>
<td>13/1,529 (0.9)</td>
<td>6/90 (6.7)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>141/7,494 (1.9)</td>
<td>109/495 (22.0)</td>
</tr>
</tbody>
</table>

* Results are expressed as the number of persons with clinical evidence of yaws/number examined (percentage with clinical yaws).
† Results are expressed as the number of Kline test-positive serum samples/number tested (percentage positive).
‡ Data for the canton of Massepe were not available.

Discussion

Extrapolation of the percentages of persons found to have clinical yaws to the total population of the areas concerned suggests that in the Vogan, Tabligbo, and Bassar districts ~2,970, 2,236, and 2,068 persons, respectively, actually had clinical yaws in May 1981. Similarly, if our sample results are representative, some 18,063, 6,149, and 24,222 persons—if tested—would have had positive serologic results in the three respective districts at that time. However, only 2,584 cases of yaws were officially reported in all of Togo in 1981 (J. Soneman, unpublished observations and [7]).

Clearly, the endemicity of the treponematoses varies substantially among different cantons in Togo. Since the cantons studied in this survey are mainly rural, all (or nearly all) of the treponematoses detected by serologic means are almost certainly endemic forms—especially yaws—and not venereal syphilis. It must be recalled, however, that the serologic tests used do not distinguish among the different treponemal infections.

This investigation confirms that yaws persists in several areas and is even resurgent in some. The contact we noted between Togolese and inhabitants of Ghana and Benin in border areas is typical of that found in border areas in general.

Other studies conducted in Bobo Dioulasso[3], Burkina Faso, revealed the following rates of serologic positivity among representative groups of the population and their children (pregnantal women, blood donors, job applicants, driver's license candidates, students, soldiers, and ill persons believed to have venereal or endemic syphilis): 8.2% in 1978, 9.6% in 1979, and 8.0% in 1980. In Timbuctu, Mali, a similar investigation in 1980 with the Kline and Treponema pallidum hemagglutination tests revealed a much higher average positivity rate in one area (author's unpublished observations). Bejel was the main treponemal problem in the areas of Mali studied (author's unpublished observations and[8]), where 80% of the population is nomadic.

Conclusion

Yaws and endemic syphilis have often been considered in recent years to have been eradicated or to be in the process of being eradicated. Our investigations confirm, however, that these diseases persist and are even resurgent in some regions of the OCCGE coun-
tries. Because of the prevalence of migration and nomadism, a campaign against yaws and endemic syphilis in one of these countries cannot succeed without a concurrent campaign in neighboring countries. Such a struggle will require logistic, financial, and human resources. A strategy for combating these diseases should include (1) epidemiologic evaluation, with the use of clinical and serologic surveys; (2) ongoing surveillance, with the help of traditional chiefs, schoolchildren, teachers, etc., in reporting suspected cases; (3) health education for affected populations; (4) mass treatment of persons in endemic zones with long-acting penicillin; (5) reevaluation of persons by repeat surveys in zones where treatment has been provided; and (6) issuance of the *Handbook of Endemic Treponematosis* developed by the World Health Organization to public health workers in endemic areas [9].

References


5. Centers for Disease Control. OMS cours de formation pour les responsables nationaux des programmes d'antibiotiquel de vaccination. Module 4: évaluer le degré d'atteinte des objectifs. Atlanta: Centers for Disease Control, 1978


Yaws in Southeast Asia: An Overview

Albert Zahra

A summary is presented of yaws control programs, from their initiation up to the present, in India, Indonesia, and Thailand. In all three countries, the prevalence was spectacularly reduced. From 1950 to 1961, in Java and Bali the rates fell from 11.34% to 0.72%, and comparable results were achieved in India and Thailand. In all programs, resurveys were carried out after the original mass treatment campaigns, and quite successful efforts were made to integrate the yaws control activities into more general health services. Although a small number of active cases of yaws in localized foci are still found, with the rapid expansion of primary health services and continuing surveillance for yaws and the appropriate use of selective or juvenile mass treatment approaches, it should be possible to achieve eradication in the foreseeable future.

The World Health Organization (WHO) was founded on the goodwill and collaboration of its Member States. It will be recalled that on April 7, 1948, the Constitution of WHO came into force, and at the First World Health Assembly top priority was given to venereal diseases and treponematoses, along with malaria, maternal and child health, tuberculosis, nutrition, and environmental sanitation. Special attention was given to the need for control of early syphilis, but during the first two years of WHO programming (1948–1950), the serious public health problem posed by nonvenereal treponematoses, and particularly by yaws, was gradually recognized as deserving high priority by three countries in Southeast Asia: Indonesia, Thailand, and India. In Ceylon, yaws had ceased to be a problem from about 1940 (before the advent of penicillin)—probably because of the use of parenteral arsenical preparations from the 1920s onward and of general improvements in communications and environmental health such that the inaccessibility of many rural areas virtually ceased to be a problem. Scattered pockets of yaws were reported in Burma but certainly presented no health problem; the reason for this was never satisfactorily explained.

Yaws in the 1950s

This review confines itself to the history of the WHO-assisted yaws control programs in Indonesia and Thailand from 1949 onward and in India from 1952 [1].

Work in the early 1950s resulted in the following estimates: in 1954 [2], in Indonesia there were 10 million cases of yaws among a total population of some 75 million, with a prevalence of >20% in some districts; in Thailand, out of a population of 18.3 million, ~60% (or ~11 million) lived in areas of endemic yaws, where there were some 1,430,000 cases; and in India there were endemic pockets, mainly in parts of the states of Madhya Pradesh and Andhra Pradesh.

The estimated figures, especially for Thailand and Indonesia, and also for India, showed that huge quantities of long-acting penicillin would be needed for mass campaigns. One program in Southeast Asia that was assisted by WHO reported as early as 1951 that >90,000 ml of penicillin were being used monthly [3]. Assistance from WHO and the United Nations Children's Fund (UNICEF) was therefore directed toward the establishment of the local manufacture of long-acting penicillin within this region to be used not only for the sake of yaws control but also to supply the general health services as a whole. Indeed, as it turned out, for years difficulties in the manufacture prevented the production of the long-acting procaine penicillin G with 2% aluminum monostearate (PAM) needed for major yaws campaigns, and UNICEF has provided PAM for internationally assisted programs in the region. Long-acting benzathine penicillin was subsequently produced in India in the 1960s.

Programs for the control of treponematoses also required the support of diagnostic facilities, and WHO assisted in the local production of the cardio-lipin needed for serologic tests; by 1955, Venereal Disease Research Laboratory (VDRL) antigen be-
came available from an institute in Calcutta to all Member States in Southeast Asia.

By the end of 1953, the statistics of the three WHO-assisted programs in India, Indonesia, and Thailand were as follows. In India, 85% of the population of 79,813 in 556 villages had been examined; 3,789 cases of yaws (5.6%) had been found, and those persons who had lesions or a history of yaws, as well as their contacts, had been treated. In Indonesia, a total of 6,745,515 persons had been examined, and 1,079,224 had been treated. In Thailand, 2,581,879 had been examined, and 317,892 had been treated [2]. Some indication of the cost of the program is given in Table 1.

The activities of the yaws control project in India extended into what were then three adjoining states, Madhya Pradesh, Hyderabad, and Madras (the two latter areas were later incorporated into the new state of Andhra Pradesh). WHO provided a medical officer "coordinator" for one year starting in late 1952.

From May 1950, WHO continued to assist yaws control programs with international staff on the spot—in Indonesia until the end of 1955 and in Thailand with a team until August 1962.

**Yaws in the 1960s**

At the Second Asian Yaws Conference, sponsored by WHO and held in Bandung, Indonesia, in October-November 1961, the data presented on Indonesia and Thailand showed the following. In the years of the Indonesian program (from May 1950 to June 1961), the islands of Java and Bali had been well covered: 56,973,149 persons had been examined at least once, 8,738,762 courses of treatment had been given, and the prevalence of yaws had been reduced from 11.34% to 0.72%. In Thailand, during the same years, 22,165,149 persons had been examined in initial surveys and resurveys, 3,139,043 courses of treatment had been given, and the prevalence of yaws had been reduced from 12.8% in the most heavily infected provinces to an average of 1.3% (infectious and active cases) [4]. A few cases were occasionally encountered in Burma and Ceylon.

During the campaign against yaws in India from 1952 to 1964, in the four states Orissa, Andhra Pradesh, Maharashtra, and Madhya Pradesh, ~0.2 million cases of yaws were detected and treated and ~9 million persons were estimated to be at risk in 1961. As a result of the campaign, disease transmission in many areas was interrupted to an extent that yaws eradication seemed to be a possibility for the foreseeable future.

Thus, in these years of WHO/UNICEF assistance, yaws had been virtually eliminated from Thailand and from the most thickly populated parts of Indonesia. More work remained to be done in India and in many of the outer islands of Indonesia. Activities were extended by the national staff to the smaller islands of Indonesia with the use of a motor launch named PAM provided by WHO. However, in general, the disease had ceased to be a public health problem in the Southeast Asia region.

**Rural Health Services and Mass Campaigns Against Yaws**

Since yaws is essentially a disease of rural areas, the mass campaigns offered a unique opportunity for promoting the improvements of rural health services. When rural peoples with little previous experience of health services saw how one injection of penicillin could make extensive skin lesions disappear in a matter of days, they began to desire better health in general and broader community health services.

As early as 1954, WHO was urging Member States to recognize the need for immediate planning and development of rural health services so that the yaws

<table>
<thead>
<tr>
<th>Program areas</th>
<th>Government</th>
<th>UNICEF</th>
<th>WHO</th>
<th>Total</th>
<th>Government (%)</th>
<th>Cost per person examined</th>
<th>Cost per person treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>369,832</td>
<td>259,511</td>
<td>33,534</td>
<td>662,877</td>
<td>55.8</td>
<td>0.43</td>
<td>2.76</td>
</tr>
<tr>
<td>Indonesia</td>
<td>718,310</td>
<td>855,200</td>
<td>19,317</td>
<td>1,592,827</td>
<td>45.1</td>
<td>0.39</td>
<td>2.33</td>
</tr>
<tr>
<td>Total</td>
<td>1,088,142</td>
<td>1,114,711</td>
<td>52,851</td>
<td>2,255,704</td>
<td>48.2</td>
<td>0.41</td>
<td>2.54</td>
</tr>
</tbody>
</table>

NOTE. Data are from [2].
### Table 2. Status of the Treponematoses Control Programme (TCP) in Indonesia and population covered, by province, at the end of 1976.

<table>
<thead>
<tr>
<th>Province</th>
<th>Total no. of kecamatan</th>
<th>No. of kecamatan with TCP team</th>
<th>No. of indicated type of survey performed</th>
<th>No. of persons covered/total population (× 10⁶)</th>
<th>Percentage covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Java</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Java Timur</td>
<td>538</td>
<td>525</td>
<td>...</td>
<td>540</td>
<td>23,547/26,400</td>
</tr>
<tr>
<td>B. J. Jogjakarta</td>
<td>72</td>
<td>72</td>
<td>...</td>
<td>74</td>
<td>2,71/2,711</td>
</tr>
<tr>
<td>Java Tengah</td>
<td>492</td>
<td>492</td>
<td>...</td>
<td>501</td>
<td>22,268/22,268</td>
</tr>
<tr>
<td>Jakarta Raya</td>
<td>27</td>
<td>26</td>
<td>...</td>
<td>26</td>
<td>4,256/4,324</td>
</tr>
<tr>
<td>Java Barat</td>
<td>365</td>
<td>353</td>
<td>...</td>
<td>362</td>
<td>19,887/20,583</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>1,494</strong></td>
<td><strong>1,468</strong></td>
<td><strong>...</strong></td>
<td><strong>1,503</strong></td>
<td><strong>72,669/76,286</strong></td>
</tr>
<tr>
<td>Off Java</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bengkulu</td>
<td>23</td>
<td>22</td>
<td>...</td>
<td>21</td>
<td>308/318</td>
</tr>
<tr>
<td>Sumatra Selatan</td>
<td>85</td>
<td>78</td>
<td>...</td>
<td>57</td>
<td>3,472/3,578</td>
</tr>
<tr>
<td>Lampung</td>
<td>61</td>
<td>61</td>
<td>...</td>
<td>46</td>
<td>2,062/2,062</td>
</tr>
<tr>
<td>Sumatra Barat</td>
<td>85</td>
<td>80</td>
<td>...</td>
<td>65</td>
<td>2,240/2,848</td>
</tr>
<tr>
<td>Jambi</td>
<td>38</td>
<td>38</td>
<td>...</td>
<td>33</td>
<td>915/915</td>
</tr>
<tr>
<td>Riau</td>
<td>69</td>
<td>51</td>
<td>...</td>
<td>34</td>
<td>1,131/1,156</td>
</tr>
<tr>
<td>Sumatra Utara</td>
<td>176</td>
<td>163</td>
<td>...</td>
<td>99</td>
<td>5,552/6,094</td>
</tr>
<tr>
<td>Aceh</td>
<td>133</td>
<td>111</td>
<td>...</td>
<td>83</td>
<td>1,671/2,005</td>
</tr>
<tr>
<td>Kalimantan Barat</td>
<td>106</td>
<td>81</td>
<td>...</td>
<td>7</td>
<td>1,585/1,942</td>
</tr>
<tr>
<td>Kalimantan Tengah</td>
<td>70</td>
<td>55</td>
<td>...</td>
<td>5</td>
<td>609/610</td>
</tr>
<tr>
<td>Kalimantan Selatan</td>
<td>97</td>
<td>96</td>
<td>...</td>
<td>66</td>
<td>1,984/2,008</td>
</tr>
<tr>
<td>Kalimantan Timur</td>
<td>57</td>
<td>37</td>
<td>...</td>
<td>36</td>
<td>758/1,037</td>
</tr>
<tr>
<td>Sulawesi Utara</td>
<td>79</td>
<td>75</td>
<td>...</td>
<td>54</td>
<td>1,455/1,594</td>
</tr>
<tr>
<td>Sulawesi Tengah</td>
<td>62</td>
<td>56</td>
<td>...</td>
<td>40</td>
<td>935/959</td>
</tr>
<tr>
<td>Sulawesi Selatan</td>
<td>169</td>
<td>155</td>
<td>...</td>
<td>108</td>
<td>4,681/5,053</td>
</tr>
<tr>
<td>Sulawesi Tenggara</td>
<td>46</td>
<td>43</td>
<td>...</td>
<td>43</td>
<td>1,127/1,179</td>
</tr>
<tr>
<td>Maluku</td>
<td>55</td>
<td>51</td>
<td>...</td>
<td>18</td>
<td>913/969</td>
</tr>
<tr>
<td>Irian Barat</td>
<td>104</td>
<td>51</td>
<td>...</td>
<td>41</td>
<td>304/921</td>
</tr>
<tr>
<td>N.T. Barat</td>
<td>57</td>
<td>57</td>
<td>...</td>
<td>64</td>
<td>2,410/2,410</td>
</tr>
<tr>
<td>N.T. Timur</td>
<td>80</td>
<td>79</td>
<td>...</td>
<td>51</td>
<td>2,544/2,680</td>
</tr>
<tr>
<td>Bali</td>
<td>47</td>
<td>44</td>
<td>...</td>
<td>45</td>
<td>1,834/2,139</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>1,699</strong></td>
<td><strong>1,484</strong></td>
<td><strong>...</strong></td>
<td><strong>546</strong></td>
<td><strong>38,472/42,837</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3,193</strong></td>
<td><strong>2,952</strong></td>
<td><strong>...</strong></td>
<td><strong>546</strong></td>
<td><strong>111,151/119,123</strong></td>
</tr>
</tbody>
</table>

**NOTE.** Kecamatan are districts. ITS = initial treatment survey; RS = resurvey; C = consolidation; and M = maintenance. Data are from the Subdirektorate of Yaws and Veneral Disease Control, Director of Center for Disease Control, Indonesia, 1976. * The total number of TCP teams is greater than the number of kecamatan with a TCP team because larger kecamatan may have two operating teams.

Control programs could be incorporated into the general public health services for purposes of surveillance.

The first step, pending the eventual establishment of a network of rural health centers, was for the mobile teams that were carrying out treponematoses resurveys to undertake additional responsibilities, particularly with respect to smallpox vaccination, leprosy case finding, and primary care.

During consolidation and surveillance activities, the yaws project in Thailand, for example, administered 1,679,656 primary and 11,251,456 secondary smallpox vaccinations, 244,400 combined cholera and typhoid immunizations, and 162,700 courses of treatment for conjunctivitis; and some 2,000 cases of leprosy were diagnosed between the years 1959 and 1963 [5]. In Indonesia, the public health services in Java participated in surveillance of yaws in rural areas from the very start of the campaign, and by 1962 surveillance was being carried out by rural dispensaries in the 1,989 subdivisions of the island where yaws control was in progress; at that time these dispensaries covered 72% of the population. The specially trained yaws scouts (djirupsakets), while undertaking population resurveys, also notified cases of leprosy found during community screening, and
there was greater utilization of the yaws workers on a multipurpose basis at the peripheral level of the health services. The combination of case-finding duties was directly stimulated by the WHO medical officers associated with the yaws and leprosy control projects in both Thailand and Indonesia.

Whereas in Indonesia, by 1962 there was already an adequate network of rural health services to take over from the specialized yaws control programs in both Java and Bali, the health coverage in Thailand was thinner, and WHO added to the team a public health officer and a nurse, who were later to assist in training and expansion of the rural health services. When the WHO adviser on yaws was withdrawn in 1962, the WHO public health officer remained. The team was expanded, and this assistance is still being given. By 1965, yaws surveillance in Thailand had been integrated into the general health services in all 46 provinces in which the disease had been endemic.

In India, mass treatment of the remaining foci in the areas endemic for yaws, as partly revealed by a WHO consultant provided in 1966-1967, continued to be undertaken by the primary health centers; at the same time attention was concentrated on infectious foci rather than on resurveying burnt-out foci.

Yaws in the 1970s and 1980s

The Treponematosis Control Programme (TCP) in Indonesia was assessed by WHO consultants in 1968, 1971, 1975, 1977, and 1981. By 1971, the data available indicated the existence of several small, isolated foci, with active transmission in some parts of Java and Madura. In the areas of Kalimantan that were visited, no signs of yaws transmission were found, however. By 1976, the point of eradication was reached in very large areas of the country, except for some residual foci in Pekalongan, Pemalang, Tegal, and Brbes Kabupaten. The phase reached by the TCP at the end of 1976 is shown in table 2 and that reached in 1981-1982 in table 3. By then the general health policy was to persist, with integration of the TCP teams into the primary health care services and supplementation of these programs with crash programs for yaws control aimed at decreasing yaws prevalence sufficiently that by the end of the third five-year development program yaws would be practically eradicated and residual surveillance could be taken over by the health centers. The choice of juvenile mass treatment or selective mass treatment would depend on the epidemiologic situation.

To assess the current status of yaws in India in the four erstwhile endemic states of Orissa, Madhya Pradesh, Andra Pradesh and Maharashtra, WHO conducted a rapid survey in the second half of 1981, bearing in mind that, after expectations that eradication would be approached in the late 1960s, there was a resurgence of yaws in a district of Madhya Pradesh in 1977, an outbreak that was dealt with.

The findings in 1981 were as follows. In Orissa, eight cases of the disease were detected in Phulbani district, four cases in Koraput, and seven cases in Mayurbhanj. In Bastar district of Madhya Pradesh, the populations of two villages were examined, as well as people in a marketplace, but no cases of yaws were found. In the Chandrapur district of Maharashtra, no cases of yaws were found. In four villages of Khammam district of Andhra Pradesh, five cases were detected.

From the above observations, it would appear that "last yaws cases" may sporadically occur, and therefore a close and continued watch for yaws must be maintained in some areas of the country if this infection is to be eliminated completely.

As mentioned earlier, by 1966 yaws surveillance in Thailand had been totally integrated into the general health services in all 46 provinces in which the disease had been endemic, while a skeleton of "watch-dog" teams who were experts in yaws control were retained for supervision and training purposes. By the early 1970s, only isolated sporadic cases of yaws were being reported, while a close surveillance was maintained in the previously endemic areas of north, northeast, and southern Thailand. Information based on the reporting of yaws cases from mid-1970 onward became difficult to obtain from official reports; it is assumed that this difficulty indicates that, for practical purposes, interruption of transmission had occurred.

The most recent reports were in October 1983 and January 1984, when the Division of Epidemiology was notified of a suspected outbreak of yaws in the Narathiwat Province in the south. A total of seven children and two adults with skin lesions were found to have positive treponemal serologic tests. After the above investigation, in January 1984 it was reported that a five-year-old child with multiple papillomas and a VDRL titer of 1:128 was found in another village of the same Narathiwat Province. Treatment of
Table 3. Frequency of yaws in Indonesia, by province, April 1981 through March 1982.

<table>
<thead>
<tr>
<th>Province</th>
<th>Total population (x 10^3)</th>
<th>No. of examinations</th>
<th>No. of noninfectious cases</th>
<th>No. of infectious cases</th>
<th>Prevalence of infectious cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Java Timur</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>D.I. Jogjakarta</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Java Tengah</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>D.K.I. Jaya</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Java Barat</td>
<td>27,418</td>
<td>33,981</td>
<td>9</td>
<td>11</td>
<td>0.032</td>
</tr>
<tr>
<td>Bali</td>
<td>2,470</td>
<td>27,871</td>
<td>6</td>
<td>51</td>
<td>0.182</td>
</tr>
<tr>
<td>N.T. Barat</td>
<td>2,855</td>
<td>100,938</td>
<td>2</td>
<td>26</td>
<td>0.025</td>
</tr>
<tr>
<td>D.I. Aceh</td>
<td>2,610</td>
<td>764,578</td>
<td>911</td>
<td>507</td>
<td>0.056</td>
</tr>
<tr>
<td>Sumatera Utara</td>
<td>8,350</td>
<td>462,289</td>
<td>970</td>
<td>851</td>
<td>0.184</td>
</tr>
<tr>
<td>Sumatera Barat</td>
<td>3,203</td>
<td>872,162</td>
<td>1,804</td>
<td>869</td>
<td>0.099</td>
</tr>
<tr>
<td>Riau</td>
<td>2,163</td>
<td>252,856</td>
<td>639</td>
<td>674</td>
<td>0.256</td>
</tr>
<tr>
<td>Jambi</td>
<td>...</td>
<td>162,582</td>
<td>...</td>
<td>818</td>
<td>0.503</td>
</tr>
<tr>
<td>Sumatera Selatan</td>
<td>4,626</td>
<td>403,438</td>
<td>2,548</td>
<td>1,287</td>
<td>0.319</td>
</tr>
<tr>
<td>Bengkulu</td>
<td>767</td>
<td>79,905</td>
<td>294</td>
<td>264</td>
<td>0.330</td>
</tr>
<tr>
<td>Lampung</td>
<td>4,587</td>
<td>655,274</td>
<td>88</td>
<td>216</td>
<td>0.032</td>
</tr>
<tr>
<td>Kalimantan Barat</td>
<td>2,988</td>
<td>187,975</td>
<td>494</td>
<td>1,162</td>
<td>0.618</td>
</tr>
<tr>
<td>Kalimantan Tengah</td>
<td>971</td>
<td>105,040</td>
<td>46</td>
<td>20</td>
<td>0.019</td>
</tr>
<tr>
<td>Kalimantan Selatan</td>
<td>...</td>
<td>513,863</td>
<td>114</td>
<td>76</td>
<td>0.014</td>
</tr>
<tr>
<td>Kalimantan Timur</td>
<td>...</td>
<td>62,001</td>
<td>444</td>
<td>71</td>
<td>0.114</td>
</tr>
<tr>
<td>Sulawesi Utara</td>
<td>2,159</td>
<td>621,790</td>
<td>1,086</td>
<td>1,247</td>
<td>0.200</td>
</tr>
<tr>
<td>Sulawesi Tengah</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Sulawesi Selatan</td>
<td>6,079</td>
<td>657,328</td>
<td>11</td>
<td>14</td>
<td>0.002</td>
</tr>
<tr>
<td>Sulawesi Tenggara</td>
<td>888</td>
<td>163,793</td>
<td>999</td>
<td>116</td>
<td>0.070</td>
</tr>
<tr>
<td>N.T. Timur</td>
<td>2,786</td>
<td>184,004</td>
<td>1,871</td>
<td>565</td>
<td>0.307</td>
</tr>
<tr>
<td>Maluku</td>
<td>1,410</td>
<td>24,246</td>
<td>103</td>
<td>18</td>
<td>0.074</td>
</tr>
<tr>
<td>Irian Jaya</td>
<td>1,151</td>
<td>125,536</td>
<td>1,451</td>
<td>2,551</td>
<td>2.011</td>
</tr>
<tr>
<td>Timor Timur</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>77,481</td>
<td>6,461,370</td>
<td>13,890</td>
<td>11,414</td>
<td>0.176</td>
</tr>
</tbody>
</table>

NOTE. Data are from the Subdirectorat of Yaws and Venereal Disease Control, Director of Center for Disease Control, Indonesia, 1982.

* Number of infectious cases per 100 examinations.

Conclusion

The tremendous enthusiasm in the countries of Southeast Asia for accelerating national programs based on primary health care within the framework of their “National Strategy for Health For All by the Year 2000” is bringing about major efforts toward the augmentation, within the available resources, of health services coverage and the provision of an integrated package made up of the eight elements considered essential to primary health care. A significant development is the recognition of and increasing commitment to the intensification of national efforts to promote community participation and involvement through the mobilization and training of villagers/guides, health workers, and motivators from within the community and the greater involvement of nongovernmental agencies. Through the new global WHO collaborative programs as part of maternal and child health services, the expanded programs on immunization and control of diarrheal diseases are progressively covering the vulnerable age groups (younger than five years old) in the rural populations. Apart from efforts at developing simple and effective logistic systems, these and other multidisciplinary approaches as part of primary health care are increasingly focusing on health education of the mother as the frontline health worker in the family and the community at large.

It is in the above context of rapid expansion of primary health care in Southeast Asia that full advantage should be taken for creating once again an awareness and national commitment and pride.
that the residual foci of yaws in erstwhile endemic areas of Indonesia, Thailand, and India should be and can be eradicated. Eradication of yaws in these three countries is feasible. Eradication calls for a global, regional, and national drive to re-educate the community and workers at all levels in health, education, and social welfare services about yaws—its epidemiology, ease of recognition, and effective treatment and control. A simplified and well-illustrated guidebook should prove a big help. Surveillance is one "must," and provision for immediate action, whether through selective mass treatment or juvenile mass treatment, as warranted, is another.

1 Incidentally, so is the eradication of guineaworm in those states of India where guineaworm is endemic.


References

Yaws in Malaysia

Eddy K. C. Lo

From the Department of Health Services (Epidemiology), Ministry of Health, Selangor, Malaysia

In 1954, with the assistance of the World Health Organization and the United Nations Children’s Fund, a campaign against yaws was initiated in Malaysia with the formation of a yaws elimination unit in the Ministry of Health. Between 1954 and 1975, the reported annual incidence of yaws fell from 140.85 to 1.25 per 100,000 population. When rates dropped to less than two per 100,000, the program was merged with the general health services. Currently when cases are reported, contacts are traced, school and village surveys are carried out, and appropriate treatment is given. The major problems facing the control program today are a loss of interest in control activities; a smaller number of health workers experienced in the diagnosis, management, and control of the disease; and a growing reluctance to treat asymptomatic contacts with penicillin for fear of anaphylactoid reactions. Despite these problems, it is not an unreasonable expectation that, with continued stimulation from the individuals responsible for infectious disease control, yaws will eventually be eliminated.

Yaws has been an endemic, rural disease of importance to public health in Malaysia for many decades. The number of reported cases of yaws has tended to vary with the nature and extent of the health services rendered and the efficiency of the reporting system, both of which have varied over time.

The first recorded campaign against yaws in Malaysia was carried out in 1920 by Viswalingam [1], who treated overt cases of yaws with novarsenobillon (neoaarsphenamine) in the states of Negeri Sembilan, Pahang, Perak, and Selangor. The median number of cases of yaws reported annually from 1921 through 1935 was 12,200, with a range of 197-31,135. After the Second World War and immediately preceding the initiation of the yaws elimination campaign in 1954 (from 1947 to 1953), the median number of cases reported annually was 44,000 (range, 35,657-104,702).

Distribution of Cases of Yaws

As is true elsewhere, yaws in Malaysia is predominantly a childhood disease. Turner [2] stated in 1959 that the incidence of yaws in localities was erratic, with many factors other than climate entering the picture. Among the cases reported, 88% of the affected individuals are younger than 15 years, and 94% are younger than 20. The male-to-female ratio is ~2:1. There is also a considerable difference in incidence among the various ethnic groups; the ratio of affected individuals of Malay, Chinese, and Indian backgrounds is 30:5:1. Yaws is primarily a rural disease and is reported only rarely in urban areas. A review of the monthly reports of cases during the period 1964-1976 supported the common impression that the incidence of yaws is higher during the rainy seasons and is associated with the two intermonsoonal periods of northeast and southwest Malaysia.

Manifestations of Yaws in Reported Cases

In Malaysia, the classification of clinical cases is based on the recommendations of the World Health Organization (WHO) [3]. Cases are divided into two categories: infectious and noninfectious. The infectious category comprises WHO groups I-IV (initial lesions, multiple papillomas, plantar and palmar papillomas, and other early skin lesions, respectively), and the noninfectious category comprises WHO groups V-IX (hyperkeratosis; gumma, ulcers, and gangosa; bone and joint lesions; latent yaws; and other manifestations, respectively). Of the cases reported, ~92% are in the infectious category, the most common type being multiple papillomas. Among noninfectious cases with clinical manifestations, the most commonly encountered types of disease include ulcers and bone and joint lesions. Individuals in all groups, except those with latent yaws (WHO group VIII), are designated active cases.
Table 1. Reported cases of yaws and incidence per 100,000 population in Malaysia, by year (1958—1982).

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
<th>Incidence per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958</td>
<td>9,462</td>
<td>140.85</td>
</tr>
<tr>
<td>1959</td>
<td>6,954</td>
<td>101.44</td>
</tr>
<tr>
<td>1960</td>
<td>5,523</td>
<td>78.96</td>
</tr>
<tr>
<td>1961</td>
<td>3,523</td>
<td>49.36</td>
</tr>
<tr>
<td>1962</td>
<td>2,043</td>
<td>27.70</td>
</tr>
<tr>
<td>1963</td>
<td>1,455</td>
<td>19.13</td>
</tr>
<tr>
<td>1964</td>
<td>825</td>
<td>10.56</td>
</tr>
<tr>
<td>1965</td>
<td>560</td>
<td>6.97</td>
</tr>
<tr>
<td>1966</td>
<td>420</td>
<td>5.06</td>
</tr>
<tr>
<td>1967</td>
<td>401</td>
<td>4.70</td>
</tr>
<tr>
<td>1968</td>
<td>335</td>
<td>3.81</td>
</tr>
<tr>
<td>1969</td>
<td>325</td>
<td>3.60</td>
</tr>
<tr>
<td>1970</td>
<td>690</td>
<td>7.75</td>
</tr>
<tr>
<td>1971</td>
<td>613</td>
<td>6.81</td>
</tr>
<tr>
<td>1972</td>
<td>268</td>
<td>2.98</td>
</tr>
<tr>
<td>1973</td>
<td>339</td>
<td>3.30</td>
</tr>
<tr>
<td>1974</td>
<td>156</td>
<td>1.48</td>
</tr>
<tr>
<td>1975</td>
<td>136</td>
<td>1.25</td>
</tr>
<tr>
<td>1976</td>
<td>198</td>
<td>1.78</td>
</tr>
<tr>
<td>1977</td>
<td>138</td>
<td>1.21</td>
</tr>
<tr>
<td>1978</td>
<td>94</td>
<td>0.87</td>
</tr>
<tr>
<td>1979</td>
<td>85</td>
<td>0.78</td>
</tr>
<tr>
<td>1980</td>
<td>77</td>
<td>0.69</td>
</tr>
<tr>
<td>1981</td>
<td>33</td>
<td>0.29</td>
</tr>
<tr>
<td>1982</td>
<td>15</td>
<td>0.12</td>
</tr>
</tbody>
</table>

**NOTE.** Data are from the Malaysian Ministry of Health.

Yaws Control Activities

The campaign against yaws in Malaysia started in 1954 with the assistance of WHO and the United Nations Children’s Fund. A yaws elimination unit in the Ministry of Health was set up to oversee the program. Those states with a high prevalence of yaws that were covered by the campaign included Kedah, Kelantan, Pahang, Penang, Perak, and Trengganu.

The program started with an initial mass survey and treatment campaign. Infected individuals and their contacts were given single intramuscular injections of procaine penicillin with 2% aluminum monostearate (PAM). Individuals aged 15 years or older received 1.2 million units if they had active yaws lesions and 0.6 million units if they had latent yaws or were contacts. Persons in the same categories but younger than 15 years received 0.6 million and 0.3 million units, respectively. This phase of the campaign was followed by annual resurveys and treatment of patients and contacts as appropriate. Table 1 shows the number of cases of yaws and the incidence per 100,000 population for the years 1958 through 1982. During this period the reported number of cases decreased from 9,462 to 15 per year, and the incidence per 100,000 population dropped from 140.85 to 0.12.

As the rates decreased during the consolidation phase, the activities of the program were changed. When the proportion of active yaws cases decreased to <2% and that of infectious cases to <0.5% in an area, modified school surveys were carried out every six months. In locations where infectious cases were found in a school survey, the entire village was examined, and patients and contacts were treated.

When the incidence decreased to less than two per 100,000 population, yaws control activities were integrated into the general health services. Under this plan, all health workers are trained to recognize cases of yaws. Whenever a case is detected and reported, the health staff in charge of epidemiologic services immediately initiates an investigation. Family contacts are traced, and school and village surveys are done if indicated. Patients and contacts are given PAM as appropriate, and follow-up examinations are performed.

During the period 1954–1975, the total cost of the campaign against yaws slightly exceeded 2,200,000 Malaysian dollars (~$1,000,000 U.S. dollars). The cost since that time cannot be readily determined since yaws-related activities have been merged into the general health services.

**Current Problems of Yaws Control in Malaysia**

Although the mass campaign resulted in a greatly diminished incidence of yaws, this approach is time consuming and relatively expensive. Fortunately, the disease is generally easily recognized, and single-dose treatment with PAM is remarkably effective. These facts make it possible, where populations are well served by primary health-care facilities, to integrate yaws control activities into the general health services. However, as the incidence of yaws falls, there is a loss of interest in and support for sustained surveillance, which is essential for the successful maintenance of the consolidation phase. This pattern exists not only among members of appropriating bodies but even among health workers, who see yaws as a health problem of relatively low priority. Furthermore, as cases of yaws become rare, fewer and fewer health workers gain experience in the diagno-
sis, management, and control of the disease, both in the individual and in the community. If a resurgence of yaws is to be avoided, health personnel and administrators must be constantly reminded of the existence of this disease and the necessity of providing for its surveillance and control until it is eliminated from Malaysia.

A problem more recently coming to the fore is the growing lack of enthusiasm on the part of many health workers for the treatment of contacts who have no clinical manifestations of yaws. This lack of enthusiasm is partially a result of the fear of anaphylactoid reactions to penicillin and partially an example of a general reluctance to give therapy to individuals with no clinical evidence of disease.

Despite these problems, the program in Malaysia has been, on the whole, a real success. With continued stimulation of the government and health establishment by authorities in infectious disease control, the eventual disappearance of yaws from Malaysia is not an unreasonable expectation.

References
Yaws in Papua New Guinea: Extent of the Problem and Status of Control Programs

M. Sophie Reid

From the Dermatology Unit, Port Moresby General Hospital, Boroko, Papua New Guinea

Yaws was a significant health problem in Papua New Guinea until the nationwide total mass treatment campaign, which took place from 1953 to 1958. The number of cases reported annually fell to <300 during the 1960s. In the early 1970s outbreaks occurred in East New Britain and Bougainville but were effectively controlled. A larger outbreak in 1977–1978 on Karkar Island was more difficult to bring under control despite the clinical appearance of the cases, which were less florid than those seen in the 1950s. The latter outbreak raised questions about decreased response to penicillin, lack of ability to develop effective immunity, and increased susceptibility to yaws. Smaller outbreaks were reported in 1983 and 1984 in remote areas, but the current extent of yaws in Papua New Guinea is not fully known. Action is being taken to rectify this situation and to ensure that reports of yaws are fully investigated and that cases are properly managed.

The independent country of Papua New Guinea (figure 1) consists of the eastern half of the island of New Guinea and many offshore islands, including New Britain, New Ireland, and Bougainville. The nation extends from the equator to 12° south latitude in the east and from 141° to 160° east longitude. The country is made up of 20 provinces, and the total population at the last census (1980) was just over 3 million. The pattern of population density is shown in figure 2.

Yaws was a significant health problem in Papua New Guinea until the late 1950s (see table 1). Thus, a nationwide total mass treatment campaign was conducted from 1953 through 1958 [1, 2]. The health report [1] for the administrative year ending June 30, 1961, indicated that although some foci of infection remained in remote, isolated areas because of the failure of some primitive mountain people to visit clinics and the difficult terrain, these problems would probably be dealt with as the influence of the administration of Papua New Guinea spread to these areas.

Records for the years 1960–1966 are incomplete (table 1), but Vines, who was doing the fieldwork for his epidemiologic sample survey [4] from 1963 to 1966, reported seeing no cases of active yaws. From 1967 to 1971 very few cases were reported annually [3]. From 1971 to 1978 the number of cases was recorded monthly from each province, and the total annual figure—along with those [5] for provinces with significant recrudescences—are shown in table 2. During this period most outbreaks were on the New Guinea islands and mainland. From 1971 to 1978 fewer than 40 cases were reported from the whole of Papua and only 90 from the highlands region. These small outbreaks were readily brought under control.

In 1978 the Papua New Guinea Department of Health was advised that, in the interest of simplifying the reporting of diseases, the number of diseases reported should be reduced. As a result, yaws was removed from the list, and no official figures exist for 1979 and later. The figures given in table 2 for 1983 and 1984 represent cases seen by members of the Dermatology Unit at Port Moresby General Hospital in Boroko or reported to us because of our expressed interest in this condition.

Yaws on Karkar Island

The recrudescence on Karkar Island in Madang Province is worthy of special consideration because it was the largest recent outbreak reported, was seemingly the most difficult to bring under control, and raised some interesting questions. Karkar is a volcanic island situated ~64 km north of the Madang coast; it has an area of ~470 km². Its narrow coastal plain rises to a mountainous interior. The island has
an annual rainfall of >300 cm and rich, fertile soil supporting coconut and cocoa plantations on the coast and vegetable gardens further up the mountain slopes. It has a good road system and a good health service, and its population has increased from ~9,000 in 1947 to 22,000 in 1980. Boats travel regularly between Karkar and the Madang coast, and there is daily air service to and from the town of Madang.

Karkar Island, where yaws has been a problem since before World War II, has been the scene of many campaigns against yaws; neoaarsphenamine and bismuth injections were used in the late 1940s and penicillin thereafter. The 1955 total mass treatment campaign, which was part of the national campaign, appeared to be effective in that no cases of yaws were reported for five years thereafter, but by 1962 a rising incidence occasioned a selective mass treatment campaign in which people with yaws were sought and they and their contacts treated. From 1963 to 1975 fewer than 20 cases were reported annually, but the work of Garner et al. [6] on serum samples taken in 1969 (mainly from the people of Kaul Village) showed that 67.5% of the individuals studied had serologic evidence of treponemal infection. Of persons younger than 15 years to whom the Venereal Disease Research Laboratory (VDRL) test was administered, 18% had titers of ≥1:8; only 0.4% showed clinical evidence of early yaws. Among tested adults, 3% had titers of ≥1:8, none showed signs of early yaws, and three showed signs of late yaws. Thus, although the total mass treatment and selective mass treatment campaigns were successful in eliminating the bulk of infectious cases, eradication was not achieved and a low level of endemicity persisted.

An impressive rise in the number of reported cases of yaws in 1977 caused Edwin Tscharke, the officer in charge of Gaubin Hospital in the southern part of Karkar Island and a man with 30 years of experience with yaws in Karkar, to organize his own yaws treatment campaign early in 1978 [7]. In this campaign, 1,800 of the island’s population of 22,000
persons were treated. The estimated prevalence of yaws varied markedly from place to place, from zero at best to 27% at worst. Tscharke thought that the response to penicillin was poorer in 1978 than in the 1950s, despite the administration of adequate doses of procaine penicillin G with 2% aluminium monostearate (PAM) for five consecutive days. A survey, which was limited in extent but had the facilities for dark-field microscopy and also for processing and storage of serum for later testing, was conducted in August 1973; it showed a prevalence of infectious yaws varying from 2% in one area to 22% in another and the existence of latent cases. A total mass treatment campaign, in which the overall prevalence of yaws was estimated at 4.7%, took place in December 1973. However, despite the claim [8] that 92%–95% of the population were treated, significant numbers of cases continued to be reported by the trainee aid post orderlies who were doing the annual reviews under the supervision of Mr. Tscharke.

A more comprehensive survey was done in October 1981. Table 3 shows the combined results for Waskia (the northern part of the island) and Takia (the southern part). Even in light of the tremendous variation in prevalence from place to place and the fact that the villages surveyed were randomly selected (with two severely affected villages in Takia excluded), the prevalence was low. What is now required, therefore, is that the local health service remains aware that yaws still exists and that it thoroughly investigates, adequately treats, and monitors all patients and contacts.

The experience in Karkar raises a number of interesting points. First, the clinical appearance of cases in this outbreak was less florid than that of the cases described and photographed in the 1950s. I can recall only three patients in this outbreak who were "covered with papillomas"; strangely, two of these were brothers, of whom the first presented in 1978 and the second in 1982. Only two plantar papillomas were seen, and the only other early lesions noted on the soles of the feet of patients at Karkar.
### Table 1. Number of reported cases of yaws in Papua New Guinea, 1953–1970.

<table>
<thead>
<tr>
<th>Period*</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1953–1954</td>
<td>15,985</td>
</tr>
<tr>
<td>1954–1955</td>
<td>18,778</td>
</tr>
<tr>
<td>1955–1956</td>
<td>13,589</td>
</tr>
<tr>
<td>1956–1957</td>
<td>6,013</td>
</tr>
<tr>
<td>1957–1958</td>
<td>2,858</td>
</tr>
<tr>
<td>1958–1959</td>
<td>2,056</td>
</tr>
<tr>
<td>1959–1960</td>
<td>2,352</td>
</tr>
<tr>
<td>1960–1962</td>
<td>NA†</td>
</tr>
<tr>
<td>1962–1963</td>
<td>56</td>
</tr>
<tr>
<td>1963–1964</td>
<td>244</td>
</tr>
<tr>
<td>1964–1965</td>
<td>NA</td>
</tr>
<tr>
<td>1965–1966</td>
<td>274‡</td>
</tr>
<tr>
<td>1966–1967</td>
<td>206‡</td>
</tr>
<tr>
<td>1968</td>
<td>NA</td>
</tr>
<tr>
<td>1969</td>
<td>167</td>
</tr>
<tr>
<td>1970</td>
<td>132</td>
</tr>
</tbody>
</table>

**NOTE**: The nationwide total mass treatment campaign was concluded in 1958. Data are from [1–3].

* For the years 1953–1967, data are reported for July 1 to June 30; for 1968–1970, data are reported for the calendar year.
† NA = data not available.
‡ Data are for New Guineans only.

were macules associated with some loss of keratin. No hyperkeratoses were seen on palms or soles. Only two patients showed evidence of bone involvement. Not surprisingly, no manifestations of late yaws were seen in association with this outbreak.

Second, it is strange that a place that is not really remote and has a good road system and a good health service should be the scene of an outbreak as exten-

### Table 3. Prevalence of yaws on Karkar Island, October 1981.

<table>
<thead>
<tr>
<th>Type of yaws</th>
<th>Villages</th>
<th>Schools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>3.6 (0–33)</td>
<td>5.4 (0–34)</td>
</tr>
<tr>
<td>Latent</td>
<td>21 (0–125)</td>
<td>35 (0–250)</td>
</tr>
<tr>
<td>Previous</td>
<td>474 (0–825)</td>
<td>435 (0–933)</td>
</tr>
</tbody>
</table>

* Across villages or schools.

sive and difficult to bring under control as this one was. The patients were most cooperative; any reluctance to appear for an examination was attributed to apathy resulting from a failure to remember or to be informed about the unpleasant deformities associated with late yaws.

Third, the question was raised as to whether penicillin was as effective in curing yaws in 1978 as in the 1950s. In April 1978 a boy was seen with a dark-field-positive papilloma on the leg. His records indicated that he had had five injections of PAM for the treatment of yaws one month previously. In October 1981 treponemes were seen on dark-field microscopy of exudate from a papilloma on the shoulder of a boy who had completed a five-day course of therapy with aqueous procaine penicillin 96 hr before. After penicillin therapy — even with aqueous procaine penicillin — a treponemical serum level would be expected to be maintained for 96 hr. The easiest but not necessarily the most correct explanation for these two cases is that the penicillin preparation had been improperly stored or — in the case

### Table 2. Number of reported cases of yaws in Papua New Guinea and selected provinces, 1971–1978 and 1983–1984.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total no. of cases in Papua New Guinea</th>
<th>New Britain</th>
<th>Bougainville*</th>
<th>Madang</th>
<th>Sepik</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>East</td>
<td>West</td>
<td></td>
<td>East</td>
</tr>
<tr>
<td>1971</td>
<td>135</td>
<td>34</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1972</td>
<td>406</td>
<td>180</td>
<td>0</td>
<td>115</td>
<td>23</td>
</tr>
<tr>
<td>1973</td>
<td>354</td>
<td>216</td>
<td>40</td>
<td>580</td>
<td>12</td>
</tr>
<tr>
<td>1974</td>
<td>526</td>
<td>34</td>
<td>8</td>
<td>441</td>
<td>13</td>
</tr>
<tr>
<td>1975</td>
<td>421</td>
<td>66</td>
<td>32</td>
<td>215</td>
<td>7</td>
</tr>
<tr>
<td>1976</td>
<td>326</td>
<td>71</td>
<td>5</td>
<td>163</td>
<td>34</td>
</tr>
<tr>
<td>1977</td>
<td>930</td>
<td>77</td>
<td>17</td>
<td>41</td>
<td>777</td>
</tr>
<tr>
<td>1978</td>
<td>883</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>652</td>
</tr>
<tr>
<td>1983</td>
<td>NA†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>1984</td>
<td>NA†</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>16</td>
</tr>
</tbody>
</table>

* This province is now designated North Solomons.
† NA = data not available.
of the PAM — that it did not meet the international standard.

Fourth, questions about variations in susceptibility and immunity were raised by the observation of the two previously mentioned brothers who presented four years apart with very florid infections and by the cases of two young girls who were adequately treated for proven yaws in 1978 but developed new papillomas in 1980. The VDRL titers of the girls fell in 1979 and rose again at the time of reinfection, and their fluorescent treponemal antibody absorption and Treponema pallidum immobilization tests remained reactive throughout the period of study. Our observations suggest that some individuals may be more susceptible to yaws and that some may be less capable of developing effective immunity following infection. It would be interesting to pursue the reason for these differences.

**Yaws in Other Provinces of Papua New Guinea**

As of February 1984 the full extent of the yaws problem in Papua New Guinea was not known. During January and February our dermatology unit saw cases in (or received reports of cases from) East Sepik Province (the Wogamush and April River areas), West Sepik Province (Yilui, Pes, Paup, and Ossina), and East New Britain Province (Uka, Maso, Inahele, and Taupua). The diagnoses were confirmed by darkfield microscopy of exudate or, where dark-field facilities were unavailable, by biopsy and serologic study. It is probable that yaws still persists in Madang Province (on Karkar Island); new cases were seen there in October 1983.

The number of cases seen in the Wogamush and April River areas was small, but only one-half of the population of these areas was seen. The health workers of the areas should have been able to see and treat the people with yaws and their contacts as part of their regular patrol. Unfortunately, the area is very sparsely populated, the people are nomadic, and no health worker resides in the region.

The outbreak at Yilui, an isolated village, was managed by the medical officer in charge of the Raihu Health Centre (Aitape). His report stated that of the population of 433 persons, 193 patients and 216 contacts were treated; the remaining 24 village residents were seen by the nurse on her next patrol. Because the available supply of benzathine penicillin was sufficient to treat only 58% of patients with infectious cases, the remaining patients and the contacts received aqueous procaine penicillin and oral probenecid. PAM is no longer available in Papua New Guinea.

The other patients from West Sepik Province were isolated, and they and their contacts were appropriately treated. Reports of cases, as yet unconfirmed, came from Aitape as children returned to school after the long vacation.

The outbreak in East New Britain occurred in villages served by the Uvol Health Centre and involved only 11 persons, mostly children. This outbreak was investigated and managed by the provincial health officer of the area at the request of the nurse in charge.

It is unlikely that yaws is present in only four provinces and not in the others (at least in remote areas). Thus, in an assessment of the full extent of the problem, aspects other than those that are purely geographic must be considered.

First, there is a lack of awareness of yaws, partly because it is no longer a notifiable disease and partly because the majority of the present generation of health workers have never seen the condition. (It has been more than 20 years since yaws was highly prevalent in Papua New Guinea.) Second, health personnel capable of investigating and managing an outbreak of yaws are not readily available, not because they do not exist, but because they are occupied with their normal, full-time jobs. Third, the average health worker in the field does not fully appreciate that a single im dose of aqueous procaine penicillin and a single dose of PAM do not result in the maintenance of adequate serum levels for the same length of time. Therefore, when a case of yaws is diagnosed, inadequate treatment may be given and the anticipated cure may not be achieved.

The national Department of Health now realizes that yaws is recurring throughout the country and that the extent of the problem is unknown. Specific action is being taken to rectify this situation by the formulation of an appropriate control program. Most importantly, yaws is being returned to the list of notifiable diseases, and the already-existing program concerned with educating undergraduate and graduate health workers is being intensified. The existing education program, which has been conducted by the Dermatology Unit at Port Moresby General Hospital since 1978, has included the showing of color slides and a brief discussion of yaws and its management in every course of lectures given to undergraduate health workers, including trainee aid
post orderlies, nurse's aides, nurses, health extension officers, and physicians. Such information has also been included whenever the unit has been invited to address gatherings of graduate health workers, particularly during its interprovincial visits. The unit has considered especially valuable the opportunity to address special workshops where the officers in charge of remote health centers are gathered together. For example, in March 1984 a presentation was made at the annual meeting of medical officers in charge in the provinces (i.e., provincial health officers) on the subject of yaws and its correct management. Should compulsory reporting of cases and intensification of the education program reveal an extensive yaws problem, health personnel capable of investigating and managing an outbreak can be made available for a limited period.

**Conclusion**

Accurate estimates of trends in the incidence and prevalence of yaws over the past 30 years cannot be made for many reasons. The data regarding the number of cases of yaws reported during the period of the total mass treatment campaign (1953-1958) represented the results of a survey of the entire population. Data for the ensuing 20 years came from case reports only, which were modified to a variable extent by the knowledge and interest of the health workers concerned. Certainly there was considerable underreporting. After cessation of the requirement for reporting in 1978, the sources of data were a series of surveys: (1) August 1978 — a limited, random survey of five areas of Karkar Island; (2) December 1979 — a survey associated with the total mass treatment campaign on Karkar Island; (3) October 1981 — a random survey covering one-third of the population of Karkar Island; (4) January 1984 — a survey and treatment program in Yilui, West Sepik Province; and (5) January 1984 — a survey of the Wogamush and April River areas of East Sepik Province. Thus, the current extent of yaws in Papua New Guinea clearly is not known. However, documented reports of small outbreaks in isolated areas over the last few years and experience with the larger epidemic on Karkar Island in 1978 have caused the health department to take steps to deal with the problem. The education program will be intensified to make health workers more aware of the disease, more skilled in its diagnosis and in the management of patients and contacts, and more sensitive to the importance of reporting. These improvements should make it possible to determine with reasonable accuracy the extent and distribution of yaws cases. The nucleus of a team capable of investigating and correctly managing outbreaks exists, and, should the problem prove to be of sufficient magnitude, more health workers will be trained and assigned to yaws control activities.

**References**

7. Reid MS, Talbot EN, McNamara KM, Garner MF. Fluctuations in antibody levels in infection with *Treponema pertenue* following a four-year follow-up of Karkar islanders with early yaws. Australian Journal of Dermatology 1982;24:71-8
8. Winnyard GPA. The investigation and management of an outbreak of yaws in Papua New Guinea. Paper submitted to the Faculty of Community Medicine, University of London, 1980:71

*Although the references are accurate, some may be difficult to locate. The sources of data regarding the total mass treatment campaign and reported cases of yaws were official reports of the Commonwealth of Australia [1, 2] that were reviewed in the special New Guinea collection of the Medical Library of the University of Papua New Guinea. Official reports of the Department of Public Health of Papua New Guinea [3, 5] were reviewed at the headquarters of that department.*
Endemic Nonvenereal Treponematosis (Bejel) in Saudi Arabia

George Csonka and Joseph Pace

From The John Hunter Clinic, St. Stephen's Hospital, London, England; and King Abdul Aziz Hospital, Tabuk, Saudi Arabia

A total of 2,515 individuals attending a large military hospital in Saudi Arabia who had appropriate radiologic evidence of treponematosis were studied clinically and serologically. The indications are that nonvenereal treponematosis (bejel) exists in considerable numbers among the nomadic communities living in rural areas. In contrast, venereal syphilis is less common in this population and is found almost exclusively in urban populations. Some of the high-risk regions for bejel have been identified. Many individuals from nomadic communities complained of persistent pain in the lower limbs, which was often associated with radiologic evidence of osteoperiostitis of the long bones. It also appears that within the last 30 years bejel has become clinically attenuated, with the majority of seropositive individuals having latent disease. A hypothesis is put forward that persistent lesions are sustained by superinfection and that improvements in hygiene have resulted in a decrease in the incidence of reexposure. Measures to control the infection are outlined.

Endemic syphilis, called bejel in the Middle East, is a nonvenereal treponematosis that has its onset in early childhood and is transmitted from child to child by close skin-to-skin contact, by kissing, and possibly by fomites such as communal drinking vessels.

Major features of bejel and venereal syphilis are compared in Table 1. The classic form of bejel is easily recognized as a clinical entity; the initial infectious mucous patches in the mouth usually are followed by the appearance of a generalized nonirritating rash such as that seen in syphilis but much more marked and persistent. In some patients a late stage develops during which gummata of the skin, bone, and cartilage progress, sometimes resulting in the formation of destructive lesions, especially of the nose and palate. Painful osteoperiostitis of the tibia and fibula is common. This florid form was first described by Hudson in Syria [1], and the description was later amplified by Hudson [2] and Csonka [3] in Iraq. Bejel has been reported from Yugoslavia, where it has now been completely eradicated [4]. The disease is still present in parts of Africa and Southeast Asia [5]. It is confined to nomadic and seminomadic communities living in the remote rural areas, where the standard of hygiene is low and access to static health services is limited. The florid form of this disease appears to have been significantly modified in a generation, having been replaced by a milder form in which the number, severity, and duration of both early and late lesions are reduced. The reason for this change is not clear. Since the sera of individuals with bejel are positive for lues to a degree that is similar to that for individuals with venereal syphilis at the same stage, a simple serologic survey of rural communities should provide the epidemiologic data essential for mapping the location of endemic foci, information that can serve as a basis for the introduction of control measures.

In a recent report the World Health Organization (WHO) linked the patchiness of the distribution of areas with persistent nonvenereal treponematosis not only to inadequate medical services but also to the increase in the number of atypical and latent cases, which are not identified by clinicians unfamiliar with these forms of the disease [5]. While bejel was contained in parts of the Middle East after the introduction of treatment campaigns in the 1950s, persistent foci of the infection were reported in 1954 by a team from WHO [6] and again in 1979 by Sebai and Baker [7] and have been confirmed by us [8]. Such information is important, as the social consequences of mistaking nonvenereal bejel for venereal syphilis can be catastrophic. These considerations encouraged us to extend our investigations. We compared evidence (anamnestic, clinical, serologic, and radiologic data) on treponematoses for those attending the hospital who were nomads and those who were born and bred in towns.
Table 1. Major features of bejel compared with those of venereal syphilis.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Venereal syphilis</th>
<th>Bejel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative organism</td>
<td><em>Treponema pallidum</em></td>
<td><em>T. pallidum</em></td>
</tr>
<tr>
<td>Geographical distribution</td>
<td>Worldwide</td>
<td>Middle East, Africa, Southeast Asia</td>
</tr>
<tr>
<td>Climate</td>
<td>Any</td>
<td>Hot and humid or dry</td>
</tr>
<tr>
<td>Transmission</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Venereal</td>
<td>Yes</td>
<td>No*</td>
</tr>
<tr>
<td>Congenital</td>
<td>Very rare</td>
<td>Yes</td>
</tr>
<tr>
<td>Nonvenereal contact</td>
<td>Very rare</td>
<td>Yes</td>
</tr>
<tr>
<td>Contaminated families</td>
<td>Mostly young adults</td>
<td>Young children</td>
</tr>
<tr>
<td>Age group infected</td>
<td>Males predominate</td>
<td>Females predominate</td>
</tr>
<tr>
<td>Sex</td>
<td>Early genital sores, open skin and mucous membrane lesions</td>
<td>Mucous patches in the mouth, early open skin lesions; status during early latency undetermined</td>
</tr>
<tr>
<td>Infectious lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Becoming very rare</td>
<td>Becoming rare</td>
</tr>
<tr>
<td>Skeletal</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Yes</td>
<td>No*</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Yes*</td>
<td>No*</td>
</tr>
<tr>
<td>Stages of disease</td>
<td>If present, clearcut and separated by time</td>
<td>If present, less clearcut, persists with overlapping</td>
</tr>
<tr>
<td>Predominant course of untreated</td>
<td>Latency often leads to cure</td>
<td>Latency often leads to cure</td>
</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eradication by mass treatment</td>
<td>Not applicable</td>
<td>Possible—achieved in Yugoslavia</td>
</tr>
<tr>
<td>Response to penicillin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early stages</td>
<td>Excellent</td>
<td>Excellent</td>
</tr>
<tr>
<td>Late stages</td>
<td>Variable</td>
<td>Variable</td>
</tr>
</tbody>
</table>

* Generally assumed, but certain proof is not available.

Subjects and Methods

**Subjects**. In a first retrospective study, the medical records of 105 seropositive patients seen at Abd al Aziz Hospital (Tabuk, Saudi Arabia) between 1976 and 1980 who had a diagnosis of venereal syphilis were assessed, and the findings for nomads and urban dwellers were compared. In a second prospective investigation, 527 women attending the antenatal clinic and 263 of their husbands were examined, and clinical findings and rates of seropositivity among nomads and urban dwellers were compared. In a third prospective study, 1,620 nomadic patients who came from all parts of the country to attend the primary care unit of the hospital were screened. Patients found to have venereal syphilis received 2.4 million units of benzathine penicillin im once a week for three weeks. Patients thought to have bejel were given a single im injection of 1.2 million units of benzathine penicillin.

**Serologic tests**. The Venereal Disease Research Laboratory (VDRL) and the *Treponema pallidum* hemagglutination (TPHA) tests were used routinely for antibody determinations. The fluorescent treponemal antibody-absorption (FTA-ABS) test was used when results of other tests were inconclusive.

Results

When the medical records of 105 seropositive patients were reviewed in the prospective study, it appeared that all 99 nomadic patients had endemic nonvenereal syphilis and that all six city dwellers had venereal syphilis. The rates of seropositivity (by the FTA-ABS test) for the 790 Saudi nationals attending the antenatal clinic in Tabuk were 0.3% (two of 609) for the city dwellers and 19.3% (35 of 181) for the nomads. No cases of "congenital" bejel were observed in infants born of untreated, seropositive nomadic mothers. The rate of seropositivity was greater among the female than the male nomads attending the primary care unit in Tabuk; 20.5% (133
of 648) of the females and 14.7% (143 of 972) males were seropositive. The majority of the patients in this group were between 15 and 35 years of age. The domiciles of seropositive patients in this group are shown in figure 1; there is clustering in two areas. Radiographs of the long bones of the lower limbs and occasionally of the forearms were taken selectively for the first 200 of these patients, but thereafter radiology of the tibia and fibula was part of the routine examination; 15% of these patients showed evidence of osteoperiostitis. Some of the characteristic radiologic features (figure 2) are similar to those in a patient with active bejel in Iraq who was seen by one of us 30 years ago (figure 3). The majority of patients with radiologic changes complained of nocturnal pain in their lower limbs, and pain was sometimes severe enough to interfere with work and even to curtail all activities. Other late lesions were observed comparatively rarely; these included gummatha of the skin and destruction of the palate. One patient, a Bedouin woman with long-standing hoarseness was thought to have tuberculous laryngitis but did not respond to antitubercular therapy. Results of her serum VDRL and FTA-ABS tests were positive, and the biopsy specimen showed granulomatous lesions compatible with treponemal infection. Symptoms cleared promptly with penicillin therapy. Another seropositive patient presented with extreme destruction of the face and naso-oropharynx and is at present undergoing a series of plastic repair operations (figure 4).

Discussion
The evidence for the 2,515 individuals in this study, 418 (16.6%) of whom were seropositive, suggests that the incidence of positive serology is significantly higher among nomads than among persons born and living in towns. The absence of young children attending the hospital may have been in part responsible for the absence in this series of patients with early lesions of mucous membranes in the mouth.
and early generalized rash. In our experience in neighboring Iraq during the height of the bejel epidemic a generation ago, skin lesions often continued into adolescence; therefore, there appears to have been a genuine decrease in the incidence of clinically obvious early lesions. In a small survey undertaken by one of us in Saudi Arabia in 1978, which included the screening of a number of nomadic children, the absence of frank clinical lesions in children who were seropositive was noted [8]. In contrast, recent reports from the two largest cities in Saudi Arabia, Riyadh and Jeddah, show that classic primary and secondary syphilis and latent syphilis for which there was a history of early venereal syphilis appeared to be the only cause of treponemal infection [9, 10].

The incidence of seropositivity among nomads in the present series is of interest; a larger percentage of females than males were seropositive, a preponderance that is typical of endemic nonvenereal treponematosis. For venereal syphilis males are much more frequently affected. It is therefore becoming clear that one is dealing with two different populations at risk of treponemal infection: the nomadic or seminomadic Bedouins, who appear to have a high incidence of endemic treponematosis; and the people born and bred in towns, who do not get endemic treponematosis but may develop venereal syphilis because the opportunity of exposure is much greater than among the nomads. The present findings suggest that in the nomadic communities bejel accounts for the majority of positive serum reactions and that in the country as a whole bejel probably outweighs venereal syphilis.

Bejel seems to have undergone a change, and more recently fewer clinically observable lesions are observed; this phenomenon has also been reported from areas of the world with other types of endemic nonvenereal treponematoses, but the reason for this change is not known [5].

The only common late manifestation noted by us was painful chronic osteoperiostitis of the tibiae and fibulae. Interestingly, many such patients considered the pain to be due to bejel, which they remember having had in early childhood.

Penicillin was given to patients with skeletal lesions, but it is too early to assess its efficacy; past experience in Iraq indicated that, whereas penicillin halted progression of these lesions, its influence on

Figure 2. Osteoperiostitis of the tibia and fibula of a seropositive patient in Saudi Arabia, 1981.
Figure 3. Osteoperiostitis with some osteolytic changes involving mainly the tibia in an Iraqi patient with bejel, 1951.

Pain was variable. Destructive lesions of the palate and nasal septum are particularly distressing features of untreated bejel; they are commonly associated with difficulties in speech and eating and are disfiguring. Such an extreme case as that illustrated in

Figure 4. "Mutilating bejel," with almost complete destruction of the nose, nasal septum, and palate, in a patient in Saudi Arabia.

Figure 4 appears to be very rare, but a similar case in an adolescent boy with bejel in Iraq was reported by Jones [11].

We feel that the time has come to start field studies in Saudi Arabia, since we have identified several high-risk communities. The inhabitants of these areas, including all children, should be systematically screened clinically and serologically to establish the prevalence of bejel and to determine the chain of infection under present circumstances. The most suitable serologic test is the quantitative VDRL reaction, which correlates well with activity. In our hands, however, this test results in false-negative results in 20% of cases and should therefore be paired with a specific test such as the TPHA. If our assumption from the available evidence is correct—that ≤5% of individuals living in endemic areas will have early active disease—such patients and their immediate
contacts should be treated. The treatment recommended by WHO consists of a single im injection of 1.2 million units of benzathine penicillin for adults and 0.6 million units for children younger than 10 years of age. In the event of there being >5% of such patients in a community, they, their household contacts, and all children younger than 10 should receive treatment. Annual resurveys are essential until proof of eradication has been obtained. A factor that was not significant in the past is people's increasing mobility, which can lead to the spread of the infection across frontiers; thus cooperation of all countries adjacent to an area with endemic treponematosis is necessary to limit such extension. While field studies are proceeding, nomads attending the major hospitals of the country should be screened for endemic treponematosis by the simple VDRL and TPHA tests and the results should be entered on a master map. One can expect to have soon a fairly complete picture, which by constant updating can show the main foci of endemic treponematosis and be used for planning screening and treatment campaigns. It is likely that after such campaigns the infection will have been contained or even eradicated in Saudi Arabia. Some observers question the wisdom of eliminating endemic nonvenereal treponematosis, since this might remove some immunologic protection against venereal syphilis, i.e., by functioning as a sort of natural vaccination. We believe that one should eradicate endemic nonvenereal treponematosis, which can cause avoidable chronic ill health, and treat venereal syphilis as it arises.

The intriguing question, as yet unanswered, is why bejel—and indeed all other nonvenereal treponematoses—have become attenuated within a generation even in communities that until recently have rarely been exposed to antibiotics. It is possible that the early persistent lesions were sustained by frequent superinfection and that with improvement in hygiene such repeated contacts have become uncommon, a change that has resulted in a decline in the frequency, severity, and duration of early lesions. As regards late lesions, there is good evidence that for patients who have had untreated endemic treponematosis, reexposure to fresh infection years later precipitates late lesions [4]. Consequently, as the chances of reexposure diminish so does the development of late lesions. It might be argued that, if this is true, raising the standard of hygiene would by itself eliminate nonvenereal treponematoses. This may be the case in the long run, but the intelligent use of penicillin now, when we know it is still fully effective, can be expected to speed this process. Furthermore, the opportunity given by treatment campaigns can be used to improve hygiene for the benefit of all.

References
5. Treponemal infections. WHO Tech Rep Ser 1982;674:16-20
Yaws in the Americas

Ronald K. St. John

From the Epidemiology Unit, Pan American Health Organization, Washington, D.C.

Until the middle of this century, yaws was a major public health problem in the Americas Region of the World Health Organization. All countries located between the tropics of Cancer and Capricorn reported cases of yaws. From 1950 to 1957, major programs for the eradication of yaws were implemented throughout the region, and yaws rapidly ceased to be a threat. As of 1983, sporadic cases continued to occur in limited geographic areas of Colombia, French Guyana, Guyana, and Suriname.

The earliest reference to yaws in the Americas is cited by Dr. Vargas Cuellar in his treatise titled "Yaws and Other Pathologies in the Cauca Valley" [1]. He reported that Captain Don Gonzalo Fernandez de Oviedo Valdez, writing in The General and Natural History of the Indians, circa 1510, describes a yaws-like illness in local Caribbean Indians. It should be noted that black slaves did not arrive in Colombia until the end of the 16th century. The disease described by Captain Fernandez is characterized as follows:

The Indian naturally has the entire or major portion of the skin ulcerated with a skin lifted up in a hardened scar. They appear ugly but more commonly are robust with considerable strength until they become shriveled and this wrinkling is the disease that is finished when the itching or disease has changed the whole skin of the person.

It is confirmed that this disease is contagious and is taken in many ways such as a healthy person using the clothes of the sick, as in eating and drinking in his company, or using plates and cups which the sick have used for eating and drinking. . . . The truth is that it is a true plague of this land and as common to the Indians as other diseases are common in other peoples.

Dr. Cuellar goes on to note that this disease does not resemble leprosy, syphilis, or scabies.

In the interval between that early description and the mid-1950s, it is difficult to obtain systematic information on the occurrence of yaws and the magnitude of the problem. Sporadic reports based on special studies of selected populations or on incomplete passive case-reporting systems offer a partial picture of the extent of this disease. For example, Cuellar [1] analyzes the age, sex, racial, geographic, and socioeconomic distribution of 1,281 persons with yaws diagnosed between July 1938 and March 1939.

He found that a total of 45.1% (579 of 1,281) of cases occurred in children 15 years of age or younger.

Yaws in the Mid-1950s

When the discovery of penicillin was coupled with the widespread availability of serologic screening of large populations, research on the extent of the problem of yaws was stimulated and surveillance was intensified. Aided by the successes of pilot programs sponsored by the World Health Organization (WHO) for the control and/or eradication of yaws [2], systematic surveys were undertaken and extensive case-reporting mechanisms were established. Prevalence data, which were collected by the Epidemiology and Statistics Section of the Pan American Health Organization (PAHO) and published by Samame in 1952 [3], are summarized in Table 1. Active, organized yaws control programs were underway in Haiti and the Dominican Republic, and data from these countries probably reflect the severity of the problem quite accurately. Nevertheless, these data underestimate the severity of the problem in many countries since the denominator utilized in the calculations is the entire population, not the population at risk. The data also do not differentiate active and inactive cases. Samame noted the complete absence of yaws transmission in Argentina, Chile, Paraguay, Uruguay, Canada, and the United States.

By the mid-1950s, a more complete picture was emerging, in part due to the initiation or extension in many countries of yaws control programs. Bica and Roman [4] analyzed information on yaws country by country, subregion by subregion. Their data are reproduced and summarized in figure 1 and tables 2 and 3.

The geographic distribution of yaws as of December 31, 1956, is illustrated in figure 1. Yaws was...
Table 1. Prevalence of yaws per 100,000 population in selected countries of the Americas Region, 1952.

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colombia</td>
<td>43.5</td>
</tr>
<tr>
<td>Ecuador</td>
<td>3.4</td>
</tr>
<tr>
<td>Haiti</td>
<td>4,982.0</td>
</tr>
<tr>
<td>Panama</td>
<td>35.8</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>319.1</td>
</tr>
<tr>
<td>Venezuela</td>
<td>183.7</td>
</tr>
<tr>
<td>Guyana</td>
<td>26.4</td>
</tr>
<tr>
<td>French Guyana</td>
<td>413.0</td>
</tr>
<tr>
<td>Jamaica</td>
<td>330.0</td>
</tr>
<tr>
<td>Trinidad and Tobago</td>
<td>10.4</td>
</tr>
</tbody>
</table>

NOTE: Data are from [3].

Endemic in almost all countries located between the tropics of Cancer and Capricorn. Again, no cases of yaws were reported in Canada, United States, and Mexico in the north or in Chile, Argentina, Uruguay, and Paraguay in the south. Although no cases of yaws were found in Mexico, another treponematosis, pinta, was widespread.

Bica and Roman [4] noted the focal nature of yaws in Central America and Panama. Sporadic cases were reported from seven provinces in Guatemala, and no cases were noted in El Salvador, Honduras, or Belize. Yaws was not considered to be a problem in Nicaragua, and in Costa Rica only six cases were notified from 1951 to 1956. Before the initiation of a countrywide yaws control program, yaws in Panama was described as common (see table 1), but the incidence was reduced dramatically, and sporadic cases were occurring in three provinces only.

Table 2 summarizes data from the Caribbean area. By 1956, yaws had already disappeared from many islands, e.g., Bahamas, British Virgin Islands, Curaçao, and Puerto Rico. Among the countries in the Caribbean, only in Jamaica were the cases divided into infectious (4,600) and noninfectious (3,900) cases. The prevalence rates for the total number of cases of yaws are remarkably high in some of the islands, specifically Dominica, Grenada, and St. Vincent. Haiti is mentioned briefly by the authors.
<table>
<thead>
<tr>
<th>Country, year</th>
<th>Total no. of cases</th>
<th>Prevalence</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigua and Barbuda</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1953</td>
<td>53</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1954</td>
<td>70</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1955</td>
<td>46</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases reported</td>
</tr>
<tr>
<td>Aruba</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases reported</td>
</tr>
<tr>
<td>Bahamas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases reported</td>
</tr>
<tr>
<td>British Virgin Islands</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases reported after successful campaign</td>
</tr>
<tr>
<td>Cuba</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1937-1953</td>
<td>1,682</td>
<td>NA</td>
<td>Cases discovered through special campaigns</td>
</tr>
<tr>
<td>1953</td>
<td>2,000-4,000</td>
<td>NA</td>
<td>Estimated no. of cases based on sample surveys; disease confined to eastern provinces</td>
</tr>
<tr>
<td>Curacao</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases reported</td>
</tr>
<tr>
<td>Dominica</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1954</td>
<td>1,469</td>
<td>3,000</td>
<td>12 years previously survey revealed prevalence of 6%</td>
</tr>
<tr>
<td>1955</td>
<td>1,031</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Dominican Republic 1955-1956</td>
<td>3,827</td>
<td>NA</td>
<td>Total no. of cases discovered during a 13-month period</td>
</tr>
<tr>
<td>Grenada</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950-1953</td>
<td>1,500*</td>
<td>7,000</td>
<td>Includes Carriacou, Petit Martinique, and Grenadines</td>
</tr>
<tr>
<td>Guadeloupe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950-1953</td>
<td>100*</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Jamaica</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1953</td>
<td>8,500</td>
<td>NA</td>
<td>Based on survey of health districts representing 70% of the population</td>
</tr>
<tr>
<td>Nevis, Anguilla, and St. Kitts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>NA</td>
<td>5,000</td>
<td>Serosurvey of 87% of population revealed 33.4% had positive VDRL†</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>0</td>
<td>0</td>
<td>No cases since 1946</td>
</tr>
<tr>
<td>St. Lucia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950-1953</td>
<td>2,800</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1955</td>
<td>578</td>
<td>660</td>
<td></td>
</tr>
<tr>
<td>St. Vincent and Grenadines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>1,117</td>
<td>NA</td>
<td>Cases discovered in pilot program represent 22.5% of population examined</td>
</tr>
<tr>
<td>Trinidad and Tobago</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1945-1953</td>
<td>9,808</td>
<td>NA</td>
<td>Cases represent 4% of all patients seen at medical center clinics</td>
</tr>
<tr>
<td>U.S. Virgin Islands</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>NA</td>
<td>NA</td>
<td>No cases since 1930</td>
</tr>
</tbody>
</table>

Note. No data were available for Barbados, Cayman Islands, Martinique, Monserrat, Turks, and Caicos. Data are from [4].

NA = data not available.

* Numbers are estimates.

† VDRL = Venereal Disease Research Laboratory test.
and is not included in the table since a model PAHO/WHO yaws eradication program had been implemented since 1950. By 1956, Rao [5] reports that prevalence was zero in most areas and was only 1%–2% in some geographic sectors.

The data from South America are summarized in table 3. In contrast to the Caribbean, where entire populations were affected, in most countries of South America, yaws was confined to particular geographic areas noted for their poverty and tropical climates. In endemic areas, the prevalence of active cases could reach 5%–10%, and up to 75% of the population had positive serologic tests. Because of larger populations at risk, the sheer number of cases was considerable. Control measures were often more difficult to carry out because of geographic isolation.

**Eradication of Yaws in St. Vincent**

Before reviewing the current status of yaws in the Americas, I will illustrate briefly the nature of the measures taken to combat yaws by summarizing a typical program that was implemented in the mid-1950s. The eradication program in St. Vincent and the Grenadines is an excellent example of the successful campaigns carried out in the Americas. The approaches used were based on experience gained in Haiti, which had been the site for a PAHO/WHO-sponsored pilot program for yaws eradication beginning in 1950.

Before the program, yaws was widespread in St. Vincent and the Grenadines [6]. In a combined population of 72,622, careful preliminary surveys revealed an estimated 5,420 infectious cases, 3,842 in children younger than 13 years old. A total of 14,725 active

---

**Table 3.** Number of cases of yaws and prevalence per 100,000 population in South America as of December 1956, by year and country.

<table>
<thead>
<tr>
<th>Country, year</th>
<th>Total no. of cases</th>
<th>Prevalence</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colombia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>2,000</td>
<td>NA</td>
<td>Yaws confined to Pacific Coast, where prevalence before campaign was 75%</td>
</tr>
<tr>
<td>Bolivia</td>
<td>NA</td>
<td>2,400</td>
<td>Yaws confined to small focus in eastern Andes; no subsequent data after 1946</td>
</tr>
<tr>
<td>Brazil</td>
<td>1956</td>
<td>530,000*</td>
<td>6,000</td>
</tr>
<tr>
<td>Ecuador</td>
<td>1956</td>
<td>4,000*</td>
<td>NA</td>
</tr>
<tr>
<td>French Guyana</td>
<td>1954</td>
<td>8</td>
<td>NA</td>
</tr>
<tr>
<td>Guyana</td>
<td>1952-1953</td>
<td>90</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>1954-1955</td>
<td>110</td>
<td>NA</td>
</tr>
<tr>
<td>Peru</td>
<td>1951</td>
<td>1,148</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>1955</td>
<td>555</td>
<td>NA</td>
</tr>
<tr>
<td>Venezuela</td>
<td>1951-1955</td>
<td>10,235</td>
<td>NA</td>
</tr>
</tbody>
</table>

NOTE. No data were available for Suriname. Data are from [4]. NA = data not available.

* Numbers are estimates.

**Table 4.** Results of the yaws eradication program in St. Vincent and the Grenadines, 1955-1958.

<table>
<thead>
<tr>
<th>Resurvey (year)</th>
<th>No. of persons examined</th>
<th>No. of active cases found</th>
</tr>
</thead>
<tbody>
<tr>
<td>First (1956)</td>
<td>73,000</td>
<td>8</td>
</tr>
<tr>
<td>Second (1957)</td>
<td>66,643</td>
<td>5</td>
</tr>
<tr>
<td>Third (1958)</td>
<td>23,189</td>
<td>5</td>
</tr>
</tbody>
</table>

NOTE. The total number of persons treated in St. Vincent and the Grenadines was 68,125 and 4,293, respectively. The total number of children treated in these same countries was 26,989 and 1,927, respectively.
cases were estimated, and 50% of the entire population were classified as contacts of cases.

In 1953 a proposal for eradication was presented to PAHO/WHO and the United Nations Children's Fund (UNICEF). In addition to the utilization of procaine penicillin G with 2% aluminum monostearate (PAM) for the entire population, the elements of the program included carefully conducted, statistically valid surveys; community health education; mass treatment utilizing therapy teams that moved from house to house; evening clinics; and yearly evaluation. The program began in 1955. The

Table 5. Number of cases and incidence of yaws per 100,000 population in Colombia, by geographic zone, 1980–1983.

<table>
<thead>
<tr>
<th>Geographic zone</th>
<th>1980 (No. of cases)</th>
<th>1981 (No. of cases)</th>
<th>1982 (No. of cases)</th>
<th>1983 (No. of cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quibdó</td>
<td>22 (29)</td>
<td>26 (30)</td>
<td>23 (40)</td>
<td>13 (22)</td>
</tr>
<tr>
<td>Buenaventura</td>
<td>24 (219)</td>
<td>64 (176)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tumaco</td>
<td>7 (10)</td>
<td>19 (23)</td>
<td>3 (5)</td>
<td>16 (28)</td>
</tr>
<tr>
<td>Total</td>
<td>53 (35)</td>
<td>109 (53)</td>
<td>3 (5)</td>
<td>16 (28)</td>
</tr>
</tbody>
</table>

NOTE. Data are from [7]. NA = data not available.

Table 6. Number of cases of yaws in Suriname reported through Medical Mission by year, 1979–1983.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>26</td>
</tr>
<tr>
<td>1980</td>
<td>12</td>
</tr>
<tr>
<td>1981</td>
<td>16</td>
</tr>
<tr>
<td>1982</td>
<td>45</td>
</tr>
<tr>
<td>1983*</td>
<td>21</td>
</tr>
</tbody>
</table>

NOTE. Medical Mission is a private medical organization providing medical care in the interior of Suriname for ~10% of the population. Data are from [8].

* For the first 28 weeks only.
Table 7. Number of reported cases of pinta in Mexico by five-year periods, 1960–1983.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960–1964</td>
<td>191,864</td>
</tr>
<tr>
<td>1965–1969</td>
<td>73,658</td>
</tr>
<tr>
<td>1975–1979</td>
<td>351</td>
</tr>
<tr>
<td>1980–1983*</td>
<td>175</td>
</tr>
</tbody>
</table>

NOTE: Data for 1984 were not available. Data are from [10].

results are summarized in table 4. Fully 93% of the population was treated with PAM during the three-year program. The first resurvey taken at the conclusion of the mass treatment campaign uncovered only eight cases, seven of which were infectious, early cases. The five cases that were found one and two years later during the second and third resurveys, respectively, were uniformly distributed throughout the country and had no common sources. Six of the patients had not been treated during the initial phase of the program. Subsequently, cases of yaws ceased to occur in this country.

Yaws in the Mid-1980s

The current status of yaws can be summarized rapidly. Figure 2 shows the probable current geographic distribution of yaws in the Americas in 1983. A few areas—specifically Suriname and Colombia—continue to report sporadic cases. The data from Colombia are summarized in table 5. The disease is confined principally to three geographic regions. In February 1984, Colombia reviewed and revised its entire yaws program with an overall objective of eradication.

In 1981, PAHO supported two consultants to review the situation in Suriname. Sporadic cases of yaws continue to occur (table 6), although no systematic surveillance for yaws exists for the entire country. During the extensive evaluation in 1981 [9], no active cases of yaws were seen by either consultant. They concluded that yaws is not "a serious health problem in Suriname at this time and is unlikely to become one in the future if the present level of health services available to those at risk for yaws is continued." At present, patients are treated but treatment of contacts and/or selective mass treatment of yaws foci are seldom implemented.

Unofficial anecdotal reports indicate that yaws occurs occasionally in French Guyana. Sporadic cases that are not confirmed by laboratory testing are reported to the Ministry of Health of Haiti by the Dermatology Service of the Hospital of the University of Haiti. No cases have been noted in all of Central America since 1970. From the Caribbean, observers in Jamaica and the Turks and Caicos Islands have not seen a case in five years or more.

Before concluding this general review of yaws in the Americas, brief mention should be made of the success of the program in Mexico for the control of pinta. The results of extensive campaigns carried out in Mexico from 1960 to 1983 are summarized in table 7. Pinta has ceased to be a major public health problem in Mexico.

Summary

The last 30 years have witnessed a dramatic decline in what was at one time a serious public health problem. Specific campaigns that often involved house-to-house searches for cases of yaws and penicillin treatment of entire populations were enormously successful in all countries where yaws was endemic. With very few exceptions, in all countries in this hemisphere the disease has been eradicated. Even where yaws has continued to be transmitted, it has failed to regain its previous prominence as a major public health problem.

References


Yaws in Suriname

P. L. A. Niemel,* S. Sadal, and J. J. van der Sluis

Frambesia tropica, or yaws, is still prevalent in the urban population of some of the districts in Suriname. In 1911 a campaign against yaws, probably the first such campaign in the world involving treatment with salvarsan, was organized. It resulted in the rapid cure of all hospitalized patients. As a consequence of this success, the disease became less important to the medical authorities in the country. After introduction of penicillin (1945) for the treatment of yaws, the disease almost disappeared in Suriname. After 1970 new cases were diagnosed, and the resurgence of yaws in Suriname became apparent. The symptoms in these cases were attenuated in comparison to those described in standard handbooks. A survey of yaws in the different districts of Suriname was undertaken to determine the prevalence of the disease and its spread through the country in order to plan a new treatment campaign.

Suriname is located on the northeastern coast of the mainland of South America between 2° and 6° north latitude and 54° and 58° west longitude. The country, a former colony of The Netherlands, became an independent republic in 1975. The climate is tropical and humid (rainfall per year, 2,200 mm; average temperature, 27°C). The population of 430,000 comprises a mixture of imported laborers and their descendants. Blacks, whites, Hindustani (Indian), and Javanese (Indonesian) predominate; and native Indians and Chinese are two of the minority groups.

Frambesia tropica (yaws) and syphilis are endemic in Suriname; yaws is predominant in rural areas and syphilis is more or less restricted to the capital town of Paramaribo [1, 2] (table 1).

A decline in the incidence of yaws was first observed in 1951 (table 2); the change probably reflected the introduction of penicillin in these remote communities and an increased awareness of the problem of yaws [1, 2].

In 1976–1977 a study of yaws among 2,971 schoolchildren four to 16 years of age was undertaken in the Saramacca district. Each pupil was examined for skin lesions and had a blood sample taken. A positive reaction in the Venereal Disease Research Laboratory (VDRL) test was found for 398 (12.4%), and yaws lesions were observed in 34 (1.1%) of these children. The families (a total of 563 individuals) of 187 of those children with positive VDRL tests were investigated, and 301 (53.4%) had a positive result in the VDRL test [1–5].

In 1981 a follow-up study was done in the same region [4]. A total of 111 children in the lower grades (six to eight years old) and older grades (11–13 years old) were examined. Among the children six to eight years old, no active cases of yaws were found. Results of serologic tests were negative for all of the children. Among the 11- to 15-year-old children, no active cases of yaws were found. For five children the results of the VDRL test were positive (titers, 1:1–1:4) and correlated with the results of the treponemal hemagglutination (TPHA) test. Two of these children were already known to be seropositive from the 1976 survey (VDRL titer, 1:32 and 1:128, respectively, and both TPHA positive). Two children had been seronegative in 1976. One child had not been included in the 1976 survey.

In 1979 a survey of 1,500 schoolchildren in the Paramaribo region was undertaken following the diagnosis of yaws in a Bush Negro girl. Each child was examined for skin lesions and had a blood sample...
Table 1. Incidence of syphilis and yaws diagnosed at the Dermatological Service in Paramaribo, Suriname.

<table>
<thead>
<tr>
<th>Year</th>
<th>Syphilis</th>
<th>Yaws</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973</td>
<td>87</td>
<td>3</td>
</tr>
<tr>
<td>1974</td>
<td>78</td>
<td>20</td>
</tr>
<tr>
<td>1975</td>
<td>124</td>
<td>11</td>
</tr>
<tr>
<td>1976</td>
<td>124</td>
<td>12</td>
</tr>
<tr>
<td>1977</td>
<td>175</td>
<td>8</td>
</tr>
<tr>
<td>1978</td>
<td>146</td>
<td>2</td>
</tr>
<tr>
<td>1979</td>
<td>96</td>
<td>6</td>
</tr>
<tr>
<td>1980</td>
<td>81</td>
<td>7</td>
</tr>
<tr>
<td>1981</td>
<td>91</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Number of registered cases of yaws in Suriname, 1949 – 1962.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1949</td>
<td>1,339</td>
</tr>
<tr>
<td>1950</td>
<td>1,436</td>
</tr>
<tr>
<td>1951</td>
<td>506</td>
</tr>
<tr>
<td>1952</td>
<td>462</td>
</tr>
<tr>
<td>1953</td>
<td>312</td>
</tr>
<tr>
<td>1954</td>
<td>341</td>
</tr>
<tr>
<td>1955</td>
<td>269</td>
</tr>
<tr>
<td>1956</td>
<td></td>
</tr>
<tr>
<td>1957</td>
<td>644</td>
</tr>
<tr>
<td>1958</td>
<td>799</td>
</tr>
<tr>
<td>1959</td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td>914</td>
</tr>
<tr>
<td>1961</td>
<td>491</td>
</tr>
<tr>
<td>1962</td>
<td>581</td>
</tr>
</tbody>
</table>

Table 3. Results of surveys for yaws in Suriname.

<table>
<thead>
<tr>
<th>Area, no. of persons examined</th>
<th>Year</th>
<th>No. (%) seropositive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saramacca, 2,971</td>
<td>1976</td>
<td>398 (13.3)</td>
</tr>
<tr>
<td>Kaaimaanton, 68</td>
<td>1976</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Djoemoe, 83</td>
<td>1977</td>
<td>12 (14.4)</td>
</tr>
<tr>
<td>Nieuw Aurora, 41</td>
<td>1977</td>
<td>23 (56.1)</td>
</tr>
<tr>
<td>Djoemoeoe, 328</td>
<td>1979</td>
<td>8 (2.4)</td>
</tr>
<tr>
<td>Paranam, 1,687</td>
<td>1979/80</td>
<td>18 (1.1)</td>
</tr>
<tr>
<td>Blauwgrond, 1,383</td>
<td>1980</td>
<td>3 (0.2)</td>
</tr>
<tr>
<td>Botopasi, 204</td>
<td>1980</td>
<td>10 (4.9)</td>
</tr>
<tr>
<td>Lefanti, 229</td>
<td>1980</td>
<td>68 (29.9)</td>
</tr>
<tr>
<td>Kambaloa, 64</td>
<td>1980</td>
<td>12 (18.7)</td>
</tr>
<tr>
<td>Dam, 43</td>
<td>1980</td>
<td>14 (32.5)</td>
</tr>
<tr>
<td>Manlobi, 235</td>
<td>1980</td>
<td>99 (41.1)</td>
</tr>
<tr>
<td>Saramacca, 111</td>
<td>1981</td>
<td>5 (3.5)</td>
</tr>
<tr>
<td>Commewijne, 1,469</td>
<td>1981</td>
<td>23 (1.6)</td>
</tr>
<tr>
<td>Nickerie, 300</td>
<td>1981</td>
<td>2 (0.6)</td>
</tr>
</tbody>
</table>

In 1981, in the district of Commewijne, an area known to have endemic yaws in the past (circa 1940), 1,463 pupils (ages, four to 16 years) from six schools were examined, but no active cases of yaws were detected. Results of the VDRL and TPHA tests were positive in 23 (1.6%) cases.

In the Blauwgrond area north of Paramaribo—also noted for high prevalence of yaws in 1940—a total of 1,383 pupils of primary-school age were examined. In three (0.22%) results of both the VDRL and TPHA tests were positive.

In the district of Nickerie on the Guyana border, 300 school children were examined. Only two (0.67%) were found to be seropositive by the VDRL and TPHA tests (table 3).

All the surveys were performed by specially trained nurses, laboratory assistants, and doctors in integrated campaigns for the detection of yaws, leprosy, leishmaniasis, and other dermatoses [4]. All individuals who were seropositive for spirochete infection were treated with benzathine penicillin in dosages proportionate to their age and/or weight [1, 3, 5, 6]. The full dosage for an adult was 2.4 million units. The family history was studied to rule out the possibility of congenital syphilis. Where feasible, all contacts were treated at the same time as the patient in an effort to break the chain of transmission.

The symptomatology of yaws now seen in Suriname seems to be attenuated in comparison to that of the disease usually described in the literature [1–3, 7, 9]. According to the classic descriptions, yaws lesions are frambesiform, elevated, appear mostly in large numbers, present all over the body, and some-
times cause mutilating scars [7, 9, 10]. The symptoms observed in this study were extremely mild compared to those described for cases of yaws in Suriname in 1911 [8]. We observed these classic features in only a few patients from the interior of the country.

The cause of this apparent attenuation in the symptoms of yaws in our Surinamese patients is not known. The attenuated pattern might be related to low endemicity [7]. A constant monitoring of symptoms and prompt treatment of affected individuals with antibiotics possibly could result in alterations in the symptoms of incubating disease. Antibiotics administered for other infections also might affect the treponemes and result in a change in the symptoms or even in the cure of an incubating case of yaws. The practical consequence of this change in symptomatology is that the diagnosis of yaws may easily be overlooked. The medical and paramedical personnel in the field should be aware of the changing patterns of yaws in these attenuated, atypical cases. Serologic studies in suspected cases associated with this attenuated disease is essential to a correct diagnosis.

Despite earlier successful mass campaigns against yaws, this disease is still prevalent in many tropical countries [6, 11, 12] from which many people emigrate to Europe and the United States [13]. In such situations in which children present with skin lesions, yaws should be considered. Positive serology in an immigrant from these yaws-endemic countries could be an indication of late, latent yaws and not necessarily a syphilis infection. An in-depth epidemiologic analysis could be worthwhile. The diagnosis in these cases should not be one of latent syphilis but one of latent treponematosis.

References

Yaws in Colombia

William Rodriguez Uribe

From the Yaws Section, Ministry of Health, Bogota, Colombia

By the beginning of this century, yaws was a well-known endemic disease in Colombia. Colombian authorities estimated that by early 1930 there were 70,000 active cases of yaws, most of which were located in the Pacific coastal regions. With the advent of penicillin therapy, Colombia organized an anti-yaws campaign, which began in 1950. The campaign relied on the use of penicillin and house-to-house case finding. From 1950 to 1953 more than 111,000 persons with active cases of yaws and 125,000 of their contacts were treated with penicillin. The reported incidence of yaws declined dramatically, and by 1973 only 573 cases were reported in the endemic areas. By 1983 this number had fallen to 31. Because of the persistence of small foci of yaws activity, the anti-yaws campaign has been reorganized to provide a firm basis for the final eradication of the disease in Colombia.

The Era Before Penicillin

By the beginning of the 20th century, yaws was a well-established disease in Colombia. It has been estimated that in the early 1930s there were 70,000 active cases of yaws throughout the country. Although data are not available for an in-depth analysis of the geographic distribution of the cases, most of them were located in the Pacific coastal areas. The various social and demographic factors that influenced the acquisition of the disease included extreme poverty, crowding, and an unsanitary environment.

The Early Campaign Years

With the advent of penicillin therapy, Colombia organized a formal anti-yaws campaign, which began in 1950. The campaign relied on the use of penicillin G with 2% aluminum monostearate (PAM) and house-to-house visits for detection and treatment of individuals with active cases and of their immediate contacts. In the early years—from 1950 through 1953—approximately 111,000 persons with active yaws and 125,000 of their immediate contacts were treated. Subsequently, there was an immediate and rapid decline in the incidence of yaws throughout the country. By 1967, 8,622 cases of suspected yaws were registered. Most of these cases were found in the Pacific coastal regions; the annual in-

Table 1. Incidence of yaws in the Pacific coastal region of Colombia, 1973–1983.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
<th>Estimated population reached by the program*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973</td>
<td>573</td>
<td>463,924</td>
</tr>
<tr>
<td>1974</td>
<td>379</td>
<td>366,279</td>
</tr>
<tr>
<td>1975</td>
<td>319</td>
<td>180,635</td>
</tr>
<tr>
<td>1976</td>
<td>220</td>
<td>283,864</td>
</tr>
<tr>
<td>1977</td>
<td>169</td>
<td>290,109</td>
</tr>
<tr>
<td>1978</td>
<td>118</td>
<td>597,639</td>
</tr>
<tr>
<td>1979</td>
<td>130</td>
<td>614,104</td>
</tr>
<tr>
<td>1980</td>
<td>53</td>
<td>631,021</td>
</tr>
<tr>
<td>1981</td>
<td>109</td>
<td>648,404</td>
</tr>
<tr>
<td>1982</td>
<td>24</td>
<td>666,267</td>
</tr>
<tr>
<td>1983</td>
<td>31</td>
<td>684,648</td>
</tr>
</tbody>
</table>

NOTE. The yaws campaign has been concentrated in the states on the Pacific coast. Cases of yaws in Colombia are confined almost exclusively to states in this area.

* These figures are estimates of the population covered by the yaws program. They are not total population figures.

The incidence rate, based on the population at risk, was 26 per 1,000 population.

The Current Era

Because yaws has always been concentrated in the coastal region of Colombia, incidence data collected by the yaws campaign—which concentrates its active case-finding efforts in the Pacific region—provide a reasonable approximation of the trend in this disease. Table 1 summarizes the number of reported cases in the population covered by the program for the years 1973 to 1983. A steady decline
Table 2. Reported cases of yaws in Colombia, by political administrative subdivision, 1975–1983.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guajira</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Magdalena</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesar</td>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td>12</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atlántico</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bolívar</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucre</td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Córdoba</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>68</td>
<td>10</td>
</tr>
<tr>
<td>Pacific</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choco</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valle</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cauca</td>
<td>2</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nariño</td>
<td>3</td>
<td></td>
<td>9</td>
<td>28</td>
<td>7</td>
<td>17</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antioquia</td>
<td>5</td>
<td>6</td>
<td></td>
<td>10</td>
<td>2</td>
<td>3</td>
<td></td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Norte Santander</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Santander</td>
<td>1</td>
<td>21</td>
<td></td>
<td></td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Caldas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Quindío</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risaralda</td>
<td></td>
<td>14</td>
<td>58</td>
<td>52</td>
<td>17</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cundinamarca</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>10</td>
<td>32</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bogota D.E.</td>
<td></td>
<td>2</td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td>1</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Tolima</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huila</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Boyaca</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meta</td>
<td>1</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National territories</td>
<td>73</td>
<td></td>
<td>7</td>
<td>12</td>
<td>6</td>
<td>64</td>
<td></td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>131</td>
<td>144</td>
<td>127</td>
<td>64</td>
<td>153</td>
<td>83</td>
<td>56</td>
<td>16</td>
</tr>
</tbody>
</table>

NOTE. Data are from the Yaws Section, Ministry of Health, Colombia. Data for 1983 are preliminary.

in the number of cases is obvious. Cases are confined almost exclusively to the four states on the Pacific coast: Choco, Valle, Cauca, and Nariño.

Additional cases are reported from health departments throughout the country through a surveillance system that is independent of the anti-yaws campaign. These reports are summarized in table 2. The reports reflect the tendency of the Pacific population to migrate to the central and northern portions of the country in search of work. Thus, in 1983 areas other than those on the Pacific coast reported 14 cases of yaws.

Conclusions

The tremendous decline in the incidence of yaws in Colombia, especially in the high-risk areas of the Pacific coast, is well documented. Nevertheless, some problems remain. The yaws campaign continues to be a vertical program. Knowledge of the program and its activities is limited to the personnel who work in the yaws program; the medical and paramedical professions of the country who work at the level of the health districts are unaware of the program.

Since the yaws control program has limited its activities to a traditionally endemic area, one cannot say with certainty that transmission does not occur in other regions. On the basis of this consideration and others, the program has recently been reorganized and some consideration is being given to focusing the control program on a slightly larger target population.
SESSION II

Mass Treatment Campaigns Against the Endemic Treponematoses

R. R. Willcox

From St. Mary's Hospital, London; and Royal South Hants Hospital, Southampton, England

In pre-antibiotic times, mass campaigns against the endemic treponematoses required multiple injections of arsenicals and bismuth. The essentiality of a population census, an examination of the total population, and the treatment of clinical and latent cases were all appreciated, as was the value of a multipurpose approach. It was also recognized that, in combination with the anticipated slow correction of economic circumstances and attitudes, chemotherapy was the chief weapon against disease but that this weapon, even if successful in a particular area, could not prevent later reintroduction of infection. With the introduction of single-dose penicillin therapy and the impetus of worldwide, internationally assisted mass campaigns came a dramatic reduction in incidence. However, in some areas continued surveillance by the local health services did not materialize. Thus, there has been not just a low-level continuum of disease but a resurgence, particularly in Africa, where a return to mass therapy has once again proved necessary—this time combined with multipurpose immunization.

For at least two centuries, mercury was one of the most efficient remedies for yaws [1], although, during the time of slavery, iron rust and lime juice were frequently employed to dry up yaws lesions rapidly [2]. By the end of the 19th century in the West Indies, mercury—often combined with the fairly recently discovered potassium iodide—was used by most medical workers, but iron and inorganic arsenic were still given by a considerable number, and even sarsaparilla by some [2].

With the limitations of available treatment, any attempts at the control of the disease were based on isolation, segregation, and compulsion. In the late 17th century, all well-managed estates had “yaws hospitals” in which patients with yaws and leprosy were confined [2, 3]. With an apparent increase in the dissemination of yaws after the slaves were emancipated, the proposed methods of control remained traditionally based on isolation, disinfection, and destruction of houses; notification and registration of cases; restriction of movement of patients; and establishment of a dispensary system. Mass treatment was not proposed, but the suggestion was made that a special overseer for yaws-control officers be appointed [2].

The Arsenic and Bismuth Era

The New Drugs

The introduction of arsphenamines around 1910 and the popularization of bismuth after World War I brought about a radical change in the treatment of both syphilis and yaws. The two agents were used singly or together against yaws. The lower efficacy of bismuth than of arsenical preparations was offset by the much lower cost of bismuth and the fact that bismuth could be injected intramuscularly by nonprofessional personnel. With both drugs, multiple injections were necessary (five to 10 commonly being given for yaws); this requirement created considerable operational problems.

The Use of Mass Campaigns

In order to bring these new drugs to the many people who were unable to attend the small number of clinics and dispensaries, special teams were formed. During the 30 years after World War I, campaigns of mass treatment with these drugs were carried out, with varying degrees of intensity, in many areas. Campaigns against yaws were conducted in Asia, commencing early on in Ceylon and Indonesia [1], Africa [4, 5], the Pacific islands [6], and the Caribbean [3, 6]; campaigns against endemic syphilis were carried out in the USSR [7] and present-day Yugoslavia [8].
[1, 3, 4, 6]. The results were best if mass treatment by mobile teams was followed by the provision of numerous permanent treatment dispensaries so that no patient had to walk long distances (defined in Africa as more than 10 miles) and by home visits by a yaws attendant for the detection of cases in the villages and referral of the affected patients to the dispensary for treatment [6]. But the campaigns failed for other reasons as well, not the least of which was the disruption resulting from World War II [1, 8]. Additional factors included the lack of simultaneous and uninterrupted efforts in all endemic areas [8] (with a virtual impossibility of preventing reintroduction from outside [6]), the lack of systematic examination of an entire region, the lack of emphasis on epidemiologic aspects (especially tracing and treatment of contacts), the persistence of low health and economic standards, and the unavailability of antibiotics, which were soon to be introduced.

The Antibiotic Era

The Introduction of Penicillin

Following the first report of its efficacy in the treatment of syphilis in 1943 [11], penicillin was almost immediately applied to the treatment of yaws [12, 13], endemic syphilis [13, 14], and pinta [13]. With the arrival of repository penicillin—first penicillin in oil-beeswax, then procaine penicillin in oil with aluminum monostearate (PAM), and later benzathine penicillin—few or only single injections were necessary. The mass application of penicillin in so-called eradication projects in limited areas of Africa and in some Pacific atolls demonstrated the simplicity of the method, the nontoxic nature of the antibiotic, and the rapid epidemiologic control that followed treatment. As a result of these successes, an expert committee of the World Health Organization (WHO) in Washington, D.C., in 1949 urged early implementation of a program against syphilis and yaws in Haiti and the Dominican Republic and a program against bejel in Iraq [15].

Such campaigns rapidly extended to many countries. Within three years more than 15 million people had been examined [16]; ultimately, a reported 200 million people in 45 countries were examined and 50 million treated with penicillin [17].

Aims of Mass Campaigns

The goals of the mass campaigns were the following: (1) to control the reservoir of infection first revealed by a survey of the entire population of the area; (2) to interrupt the spread of yaws by rendering early cases noncontagious, preventing infectious recurrences, and aborting incubating disease by means of mass treatment; (3) to detect by means of postcampaign surveys any missed cases or new infections and to treat these cases promptly [17]; and (4) to make the preliminary decision to undertake health activities after the campaign ended [18]. The more optimistic individuals hoped ultimately to eradicate yaws from the community and not merely to reduce endemicity to an ill-defined level [18, 19].

The Framework of Yaws Control

The proposed framework for the control of yaws was (1) an orientation and preliminary analysis of the problem; (2) the development of methodology; (3) a demonstration survey and training phase (including study of a "control" or "research" area); (4) an expansion phase, or mass treatment campaign; and (5) a consolidation phase, in which provision was made for permanent medical facilities and for well-trained national personnel to consolidate the gains already made [20]. This framework involved the active participation of residents of endemic areas in securing 95% coverage rapidly, in conducting regular posttreatment surveys, and in developing better permanent health services [21].

The Strategy of Mass Campaigns

Dose of penicillin. With cost an important consideration, single doses of only 300,000 units of PAM were used and were found to be satisfactory in decreasing the reservoir of venereal syphilis in the area next to the Himalayan boundary in India [22]. In Haiti a single dose of 600,000 units of PAM for adults was used for the treatment of yaws, with the objective of decreasing transmission rather than curing every individual case. This goal, which was considered adequate for mass treatment [23], was later determined to have been achieved [24]. However, in a number of areas, at least at the outset, multiple injections were given for the treatment of yaws [13], endemic syphilis [8], and pinta [25].
When variations were found in the serum levels of drug that were attained with different preparations [23], WHO established minimal dose requirements. In 1952 the recommended minimal dose to be given to infected adults in one injection in mass campaigns against the endemic treponematoses was 1.2 million units of PAM. Proportionately less was to be administered to children, and contacts were to be given less than half of the minimal dose [26]. (In fact, it was later decided that contacts should receive the same dose as infected patients; see section on mass campaigns in the 1980s.) These recommendations received full support in a number of campaigns [21, 27, 28].

**Treatment of contacts and patients with latent disease.** Treatment of active cases only came to be recognized as insufficient when the importance of missed latent cases that later underwent infectious relapse became obvious [27]. These latent cases were often diagnosed by serologic tests, which were required in defined research areas to establish the extent of the problem and the progress being made [1, 8, 23]. As a campaign expanded, however, with an inevitable dilution of the most experienced staff, the use of serologic tests slowed down the rate of work [29] and discouraged attendance of patients [30].

Less identifiable were contacts incubating the disease. Although contacts of yaws patients were treated in some campaigns [23], it was the campaign against endemic syphilis in Yugoslavia [8] that made obvious the necessity of their treatment. As a result, a WHO expert committee recommended that contacts without overt signs of disease receive preventive (or "abortive") treatment with PAM wherever treponemal diseases constituted a major public health problem [26].

Where the minimal dose was administered to patients with active cases, WHO also recommended the following: (1) that in hyperendemic areas, where the prevalence of active cases exceeded 10%, the rest of the population should be regarded as having latent cases or as contacts and should be given penicillin (a policy known as total mass treatment); (2) that in areas of medium prevalence (5%-10%), all prepubertal children and other obvious contacts should receive treatment (juvenile mass treatment); and (3) that in areas of low prevalence (<5%) all household and other obvious contacts of patients with infectious cases should receive treatment (selective mass treatment) [27].

**Techniques of operation.** Descriptions of the mass campaigns of previous years, including the annual reports of the Jamaica Royal Commission in 1932–1936, were technically helpful in planning new programs [20]. Although multipurpose programs were often debated [29], the inclusion of other activities was always unavoidable and basic attachment to a polyclinic was favored [1, 23, 29, 30]. However, the restriction of treatment to patients voluntarily attending clinics was not a successful policy [27, 31]; rather, house-to-house surveys clearly proved to be the best approach [31], with the actual treatment administered either on the spot or later at a delineated treatment point.

**Results of Mass Campaigns**

In areas where coverage was adequate at the time of the initial survey, clinical and serologic follow-up observations made several years after adequate therapy showed a generally satisfactory situation [32]. By 1968 the initial rapid decrease in the number of individuals with clinical lesions had been followed by very slow serologic recession, but in only one large area had an endemic treponematosis of childhood been eradicated; elsewhere, isolated clinical cases of yaws continued to occur, and residual foci persisted [33]. The sole exception to this rule was in Bosnia, where intensive treatment had been applied to all cases of endemic syphilis detected by repeated, systematic clinical and serologic screening of patients, family members, and other contacts [34]. It is significant that this campaign was carried out against a background of socioeconomic change along with the evolution of modern health services throughout the area involved [34]. Despite the overall picture, the conclusion to be drawn from this single example was clear. Early infectious disease could be eliminated and the transmission of treponemal infection interrupted by a vigorous and carefully conducted mass campaign supported by the organization of an efficient health service and a concomitant improvement in socioeconomic conditions [34].

**The Current Situation**

**The Overall Problem**

For a number of reasons—not the least of which are complacency generated by the success of the earlier campaigns, greater competition for finite budgets,
population increases [35], and political changes—both on-the-spot surveillance and the hoped-for expansion of health services have been prematurely discontinued in many areas, and yaws has not been eradicated from any large geographic area [35, 36]. Although it is no longer a major public health problem in many areas, such as the Americas [37], yaws still smolders at a low level of incidence and is in fact resurgent in some countries. It was estimated in 1976 [38] that there were at least one to two million cases worldwide (compared with 50–100 million in the 1950s [38]). In some areas, including especially parts of central and western Africa [35, 38], the prophecy of a replacement of yaws by venereal syphilis has been fulfilled [39]. Endemic syphilis likewise remains a considerable problem in the sub-Saharan region [35].

Mass Campaigns in the 1980s

The climate in which WHO-assisted activities operated earlier has changed, and the previous approach may not be applicable or acceptable today. Nevertheless, the solution to the problem of endemic treponematoses can lie only in the reestablishment of regular surveillance of individual households and treatment of patients plus their domestic and other contacts [38] (i.e., selective mass treatment). Indeed, an intensive campaign involving juvenile mass treatment, organized along the lines earlier recommended by WHO, is being conducted in Ghana, where in 1.5 years some 1.25 million people have been examined and nearly 800,000 have received penicillin [40]. However, some differences or modifications are significant. (1) Four different international organizations are now involved. (2) The 18 teams, each consisting of four to seven qualified health workers, are operating across regional boundaries. (3) In the initial treatment survey, both PAM and the more stable benzathine penicillin have been given to patients and contacts in double the doses previously used (i.e., for active yaws cases: 2.4 million units in adults, 1.2 million units in children younger than 15 years, and 0.6 million units for those younger than six years). Both patients and contacts receive the same dose. This higher dose had been suggested previously elsewhere [17]. Recent WHO recommendations continue to support the use of a minimum of half this amount [35]. (4) The initial treatment survey is followed in three to six months by a further survey for the detection and treatment of missed cases and treatment failures. (5) Follow-up yaws surveillance is being incorporated into the emerging primary health care system. (6) Finally, and perhaps most important, the campaign has incorporated other preventive-medicine activities for selected groups, including the use of yellow fever, measles, and bacille Calmette-Guerin vaccine and tetanus toxoid [40].

Discussion

The declared goals of the campaign in Ghana include only a reduction in the incidence of yaws as opposed to the actual eradication of yellow fever, to which end immunization is available. One day, perhaps, it will be possible to vaccinate against the treponematodes. Until then, another coordinated international effort using antibiotic treatment is required. With all such campaigns, there will remain a built-in risk of ultimate failure unless the arrangements for post-campaign surveillance are adequate and secure.

References

Integration of Yaws Control and Primary Health Care

André Meheus

From the Department of Epidemiology and Social Medicine, University of Antwerpen, Antwerpen, Belgium

Where a primary health care (PHC) system (e.g., a community health worker and a health center as the first referral level) is fully operational, control activities for yaws should be part of PHC. Where the whole population is adequately covered, the PHC system is responsible for early detection of cases of active clinical yaws, treatment and follow-up of these cases, treatment and follow-up of contacts, and health education related to yaws control. In circumstances where PHC is not as yet fully implemented, the structure for a yaws control program must be different. In areas with adequately functioning static health services or with a nascent PHC system, yaws control could be started as a vertical program—initial treatment survey and resurvey by a yaws team working in close collaboration with a health worker selected by the community. Subsequently, active yaws surveillance is taken over by that worker who also assumes the other functions of primary health care. In areas with nonexisting or poorly functioning static health services, a program for yaws control should not be implemented because control and effectiveness are likely to be poor.

At the beginning of this century, whole populations in many tropical countries suffered from yaws. During the 1920s and 1930s, mass treatment campaigns against yaws with use of injections of arsenical preparations and bismuth were launched at hospitals or, more often, by means of mobile units. Results of yaws treatment (often combined with smallpox control measures) were spectacular, and a system of rural dispensaries was established to consolidate results obtained by the mobile teams. In this way, yaws control in central Africa was the starting point for the system of basic health services in this region [1].

This injection treatment for yaws also firmly established the success of Western-style medicine in tropical countries and brought large numbers of people to dispensaries and hospitals [2]. However, effective surveillance was not always accomplished, and by 1950 it was estimated that there were still 50 million cases of yaws, in all its forms, in the world [3]. With penicillin available as a public health weapon, many countries organized mass treatment campaigns in collaboration with the World Health Organization and the United Nations Children’s Fund. Long-acting penicillins (procaine penicillin G in oil with aluminum monostearate [PAM] and benzathine penicillin), administered as single im injections, were especially valuable during these campaigns [3-7]. Services for yaws control were implemented as a vertical program; once the prevalence of disease was reduced almost to the point of eradication, control activities were integrated into the general health care system.

The mass treatment approach was successful in Southeast Asia, Central and South America, and many African countries. Before the penicillin era, prevalence rates of active clinical yaws ranged from 5.6% (Cameroon) to 30% (Liberia) in Africa, from 2.5% (Brazil) to 50% (Haiti) in the Americas, from 3.1% (Thailand) to 17.2% (Indonesia) in Southeast Asia, and from 3.6% (Laos) to 40% (New Hebrides) in the western Pacific region. In the 1950s, in three to five years’ time, the implementation of treatment surveys resulted in a decrease in the prevalence of yaws to very low levels: from 11.3% to <0.001% in western Samoa, from 37.5% to 1.0% in Haiti, and from 11.9% to 0.9% in East Java, Indonesia [3, 7]. However, yaws returned to parts of West and central Africa mainly because of inadequate facilities for screening, for prophylactic treatment of contacts, and for follow-up [7-9].

Control efforts for yaws need to be implemented again, but innovative approaches are needed. A vertical program is problematic because additional financial and human resources for such a program are rarely available. Furthermore, most countries aim at a balanced and comprehensive approach toward “Health for All” through a system of primary health care [10].
Primary Health Care

Most countries aimed for wide coverage of their population by health care services and planned to have basic health services (health centers) for every 10,000-30,000 inhabitants [11]. These health centers were to be staffed with at least one well-trained medical professional (nurse, medical assistant, or even a medical doctor in some countries) who also would be the leader of the health team, which would include a variable number of medical auxiliaries. Tasks were not only the delivery of curative services but also preventive and promotive health activities. This system in many countries did not reach its goals. Wide population coverage by health services and health promotion were always achieved because of nonexistent or insufficient participation of the community in health activities and the failure to reallocate resources in personnel, money, and medicine to the areas of greatest need, mainly the rural areas. The bias toward more sophisticated urban hospital medical care remained unchanged or was even accentuated in many areas of the developing world [11].

In the new concept of primary health care (PHC), the local community organization has to be actively involved in health matters and has five functions: it establishes priorities; it organizes community action for problems that cannot be resolved by individuals; it controls the PHC service by selecting and appointing the community health worker; it assists in financing services and/or in sharing the labor involved; and it links health action with broader community goals [12].

A common element is the use of a community health worker, who frequently is a villager selected by the community and trained locally for two to three months. He or she can be an unpaid volunteer or partially or totally supported by the official health services or by the village people in cash or in kind. The health worker must receive initial training from the health service, and this training must be practical and given near his home. The official health services also appoint a supervisor, who should give much of the instruction and be responsible for continued on-the-spot or cyclical training.

The work of the health worker covers both health care and community development. Duties depend on the health problems he or she meets, which vary from one country to another. There are, however, problems or concerns common to all countries, and, thus, a working guide and guidelines for training health workers were developed [13]. The PHC system is made up of the health centers together with the community activities personalized through the community health worker. In most countries the health worker serves a population of between 500 and 2,000 people. The functions of the health worker are (1) to care for the sick, promote health of the people, and look after community hygiene; (2) to give care and advice to anyone who consults him; (3) to refer patients to the nearest health center or hospital; (4) to visit all dwellings (disease prevention, hygiene); (5) to make regular reports to local authorities; (6) to keep close contacts with the supervisor; and (7) to promote community development activities [13].

Important points in the whole system are the support from the community for the health services of the health worker, his supervision and continuing education, and the close collaboration between health workers at the first referral level, which is the health center.

Serious concern has been expressed regarding the actual state of the PHC movement in many countries, where it is sometimes more rhetoric than reality. PHC is ineffective if implemented as small projects or as a new vertical program and should therefore be forged into substantive national programs as part of the development process [14].

Strategies for Yaws Control: Past Experience

Strategies for control of yaws include population screening combined with mass treatment, case finding and diagnosis at the consultation combined with contact tracing and treatment, health education, and professional training [15].

Population screening. In screening for yaws, cross sections of whole populations or subgroups only—for example, schoolchildren—are examined for the presence of yaws lesions. Screening of children younger than 15 years of age is particularly important since they are the main reservoir of the infection. Few children with early yaws complain about the lesions, which are usually asymptomatic unless they appear on the hands or feet, involve bone, or become superinfected. But even so, many parents do not have the time or money to bring their children to a distant health facility [9]. Where the prevalence of clinically active cases is >10%, total mass treatment is given, i.e., the entire population receives the recom-
mended treatment. Where the prevalence is 5%-10%, patients and their contacts receive full doses, and juvenile mass treatment is carried out; all children younger than 10 years old are given 0.6 million units of benzathine penicillin G, and those aged 10 years and older, 1.2 million units. Where the prevalence is <5%, patients as well as household and other obvious contacts should be given the full recommended doses (selective mass treatment).

The aim of these screening programs is the early detection and treatment of cases and particularly the reduction in size of the infectious reservoir and the interruption of transmission. These screening programs were the cornerstone of the vertical programs against yaws. Once the prevalence of clinically active yaws decreased to <2% and of infectious cases to <0.5%, the program passed into the consolidation phase. Population screening was continued but integrated into the overall activities of existing rural health centers [16].

Case finding and diagnosis of patients. Case finding is the examination for possible yaws in patients who have sought medical care for any reason [17]. It is a more comprehensive assessment of health in a patient. In diagnosis, the patient is examined and, eventually, tests are done in order to identify the exact cause of the patient’s chief complaint.

The recognition of yaws in patients coming to the consultation with “skin problems” (diagnosis) or a check for yaws lesions in other patients (case finding) is the cornerstone of yaws control in integrated health care systems. Cases of yaws found in this way should be the starting point of selective mass treatment. A problem with this approach is the lack of experience in recognition of yaws by many health workers and/or the failure to treat contacts of patients.

Health education. The population must be informed and should participate in the population surveys; people will accept treatment most readily if given the epidemiologic basis. In integrated health care systems, they should be encouraged to come forward with their skin problems. The health service must be able to respond adequately to this demand; the health worker at the health center should be able to distinguish between yaws, leprosy, and other skin conditions and should have means for adequate management.

Yaws Control and Primary Health Care

As explained above, the PHC system has a community dimension added to the health care activities of the static health services (dispensaries, health centers). In areas where yaws still is or has become again an important health problem (active clinical yaws, prevalence >2%), control measures for yaws can be implemented by means of several health care structures (figure 1).

In areas where PHC is not yet implemented, yaws
control could be initiated again as a vertical program, alongside but separate from the static health services. An initial treatment survey and a resurvey should bring the prevalence of active clinical yaws quickly below the 2% target.

Subsequently, two strategies are possible. First, treatment of yaws cases and contacts can be transferred to the static health care units, as in the previous mass campaigns. This strategy holds a considerable risk for resurgence of yaws in the near future because of nonexisting or poor active yaws surveillance. Second, the vertical yaws campaign can be utilized to implement a PHC system. For instance, in each village a person could be selected by the community to assist the yaws team in the initial treatment survey and resurvey. He or she could be made responsible for the census of the population in collaboration with local community leaders and for health education of the population, and he could assist in the clinical examinations and treatment.

Subsequently he could become the community health worker after appropriate training to take up the functions previously described. In this way, yaws control could reshape the organization of health services in a country by effectively establishing a PHC system. This approach is similar to the use of the djuru-frambesia in the Treponematosis Control Program Simplified (TCPs) in Indonesia in the 1950s [18]. For the yaws vigilante to become the community health worker, it is important that he be sponsored by the community from the beginning. If he has been administratively a full member of the yaws team (paid on the budget of the vertical yaws program), it is difficult to integrate him afterward as the health worker in the PHC program. He has not been accustomed to depending on and reporting to community leaders, and as a community worker he does not have the same amount of incentive in cash or kind that is usual in many of the (internationally sponsored) vertical programs. This problem arose with the auxiliaries in the previous yaws campaigns and in the smallpox eradication program.

In areas where static basic health services are not available or are poorly functioning, a vertical yaws control program must not be implemented because it will be ineffective in the long term. In areas with a PHC system in place, the yaws program can be partially or fully integrated into PHC (figure 1). The degree of integration depends on the importance of yaws as a public health problem but mainly on the control capabilities of the PHC system.

Where PHC is an efficiently working system, all yaws control activities are normally part of the daily routine activities of both the community health worker and the health workers at the health center. The community worker sees the villagers during his home visits at regular intervals. He has learned how to cope with skin conditions and knows which he can treat himself and which should be referred to the health center. In the WHO working guide for primary health workers [13], no mention is made of yaws, and this should be changed with specific adaptations in the chapter on skin diseases. The community health worker is responsible for active yaws surveillance, for follow-up of cases treated at the health center, and for contact tracing and treatment (selective mass treatment).

Knowledge of yaws should be updated for the workers at the health center and particularly for the supervisors of the PHC workers. At the central level, a yaws control unit should monitor the progress made by the PHC system in controlling the disease.

In areas where the PHC system as yet cannot cope with yaws control, a semi-integrated approach can be used. The initial treatment survey and resurvey is carried out by a special yaws team. The local PHC personnel must be actively involved also in this stage of the program. They have the responsibility for postcampaign yaws surveillance fully integrated with PHC activities. This approach was recently implemented in the Republic of Ghana [9, 19].

Conclusion

In areas where the PHC system is fully operational (community health workers and a health center as the first referral level), yaws control must be part of the routine functions of that system. As the whole population is covered through the health worker, early detection of cases of active clinical yaws, their treatment and follow-up, and treatment and follow-up of contacts are done through the PHC system. Unfortunately, in areas of high prevalence of yaws, successful PHC programs will be the exception rather than the rule.

In areas with nonexisting or poorly functioning static rural health services, yaws control could be implemented as a purely vertical program as in the past. But results obtained can hardly be consolidated, and such an effort is probably not effective. Nevertheless, a mass treatment campaign should be considered because it is unacceptable that affected popu-
lations should await action until peripheral health services are well established [20].

A vertical yaws control program could be implemented in those areas with well-functioning rural health services or with a nascent PHC system. The vertical program should be limited to an initial treatment survey and a resurvey in which the activities of a community health worker must be actively involved. With a nascent PHC system, yaws control is immediately integrated into that system; otherwise, the activities against yaws could be the starting point of a PHC system. In this way yaws control could repeat its historical role of shaping the rural health services. Yaws eradication requires active surveillance for the “last infectious cases” during many years, particularly in the most remote areas, and this is hardly feasible in Africa now. Therefore, eradication of yaws is problematic, but control should be attempted through the activities outlined above.

References

11. King M. Medical care in developing countries; a primer on the medicine of poverty and a symposium from Makerere. Nairobi: Oxford University Press, 1966
Research: The Prerequisite for Innovative Strategies and Technologies

Peter G. Janssens

From the Institute of Tropical Medicine "Prince Leopold," Antwerpen, Belgium

The search for new strategies and technologies for the control of yaws, a genuine but much neglected tropical disease problem, has been largely unsuccessful. This disease, with conspicuous early symptoms and a late crippling pathology, attracted the attention of the first generation of tropical doctors. As soon as specific therapy became available in the early part of the 20th century, mass treatment campaigns were started. The availability and efficacy of penicillin led some to anticipate yaws eradication; this expectation was not met but rather induced a false sense of security. After varying intervals resurgence occurred in several endemic regions. It is important to analyze this failure so that mistakes and underestimated or overlooked factors can be identified. On the whole, the main difficulty has been a lack of interest in a presumably disappearing disease and a consequent failure to take advantage of the benefits offered by recent advances in basic biomedical technology. Solid clinical, epidemiologic, and sociocultural data in connection with mass treatment and control are still needed. Research of high quality, with continuous assessment in the field, is a prerequisite for innovative strategies and technologies.

Yaws is one of the few genuinely tropical diseases. Although its prevalence in childhood and its crippling consequences in adulthood are appalling, yaws has not gotten the attention that some other exotic diseases have received. It is a rural disease, located at the "end of the road." Moreover, the nonvenereal treponematoses (yaws, endemic syphilis, and pinta) pose no threat to developed countries since there is no danger of these diseases becoming established after importation.

Yaws is a primitive treponematosis that seems to have originated and to have been preserved in Asian aborigines and African Pygmies [1]. These human beings and the affected communities do recognize this exuberant, florid, cutaneous disease as a distinct entity and give it vernacular names [2, 3]. The traditional healers recognize the disease as contagious. They recommend waiting until the outbreak of lesions is completed before starting treatment, which consists mainly of the washing or rubbing of lesions with herbs soaked in a poultice of bark, roots, or seeds and then powdering with similar crushed ingredients; cauterization with powder of malachite; applying of iron rust in lime juice; or even fumigation by burning of pulverized resinous roots.

The first generation of tropical doctors, practicing in urban areas, encountered patients with yaws only infrequently [4]. As soon as rural dispensaries were established, however, passive detection of yaws became routine in endemic areas. When arsenical drugs became the treatment of choice for syphilis, they were tried with great success against yaws, rendering therapy with mercury ointment and potassium iodide obsolete. By producing a quick disappearance of disturbing skin and mucosal lesions, salvarsan became a spearhead for the eager acceptance of modern medicine by rural communities. However, the rural dispensaries were still too few and far apart to have a real impact on the prevalence of yaws.

With the progressive improvement of the arsenical drugs and the introduction of cheaper bismuth compounds, attempts were made almost everywhere—e.g., in Indonesia, the western Pacific, and tropical Africa—to control yaws by means of mobile teams. The indispensable multidose regimen compelled team leaders to split the yaws teams into subunits that remained on the spot to complete the treatment, to monitor the evolution of treated cases, and to detect new or missed cases. This follow-up phase of the "vertical" program became both an incentive and a means for the gradual implementation of a "horizontal" system of fixed health centers, which in turn became the first phase of a primary health care system. Yaws campaigns thus became associated in some endemic areas of tropical Africa with the control of sleeping sickness, leprosy, and other diseases.

In Zaire, formerly the Belgian Congo, where I acquired my own experience, yaws was by ordinance
a notifiable disease. Its treatment was compulsory but, with the exception of the FOREAMI zone (i.e., the area covered by the Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge), its detection was mainly passive. Thus, notwithstanding these measures, the number of cases recorded annually remained at ~250,000 throughout the 1940s and early 1950s. With the introduction of penicillin treatment, the number dropped to 150,000 in 1955 and to <100,000 in 1958. In the FOREAMI-Kwango area [5], systematic active detection of cases and penicillin treatment became standard procedures and reduced the number of cases to five per 10,000 inhabitants. Still, although the prevalence was dramatically reduced, eradication was not achieved.

In general, as in Zaire, mass treatment of yaws with penicillin is followed by an impressive reduction in the number of new infections and clinically active cases. Moreover, such therapy brings about a strikingly fast transition from the prevailing epidemiologic pattern to a new pattern with a much lower prevalence (e.g., from hyper- to hypendemicity). Nevertheless, this approach, however useful it may be, does not stop transmission at a low level. This fact raises the obvious question: Why does a carefully managed mass campaign of treatment with a drug that is easy to administer and effective against a readily recognizable communicable disease fail to eradicate the disease? An unbiased look at all aspects of the problem is needed. Among the many factors involved in the answer to this question, one or more may have been underestimated, overlooked, or even ignored.

The Organisms

The reproducibility of yaws in humans by inoculation with secretions from patients with frambesia was demonstrated by Paulet in 1848 [6] and by Charlouis in 1881 [7], well before the identification of Treponema pertenue by Castellani in 1905 [8] in two Ceylonese patients with “parangi.” Treponema pallidum and T. pertenue are morphologically identical and are not cultivable but can be passaged in a number of laboratory animals. The discovery of T. pertenue a short time after the identification of T. pallidum by Schaudinn and Hoffmann [9] started straight away an unceasing controversy about the identity or plurality of the treponemes [10-15]. Does one treponeme produce different clinical patterns under different environmental conditions, or are the various diseases brought about by different spirochetes? A definitive answer still eludes us.

By modern standards our knowledge of the treponemes is plainly inadequate. The indispensable requirements go far beyond current data on viability, infectivity, metabolism, cross-immunity, behavior after years of passaging in animals, and capacity for survival for short periods in vitro in a cellular or cell-free culture medium. Fresh strains must be isolated from different geographic areas, from patients with dermatotrope or visceroptrope syndromes (e.g., pinta or endemic syphilis), and from patients whose spirochetes appear to vary in their resistance to antibiotics. The existence of a profusion of strains, as observed among leptospires, is unlikely. Nevertheless, the study of a number of strains might afford useful information about the existence of subspecies and variants. These strains should be kept, if possible, as stabilities. Whatever the final aim, the immediate need is to develop as fast as possible a scientifically sound, modern knowledge of the treponemes. Such fundamental research implies full use of the techniques of modern molecular biology for identification of the surface and core biochemical components, the organelles, the DNA sequences, the enzymatic pathways, and the metabolic and genetic makeup of the treponemes; for renewed attempts at in vitro cultivation of these organisms; for the selection of new and efficient drugs for the treatment of infected patients; and for the improvement of our understanding of immunologic responses to treponemal infection.

The Disease

The host factors involved in treponemal infection have long been presumed to be well known. However, not enough attention has been paid to the significance of a clinical evolution characterized by active waves interspersed with periods of latency or to the fact that not every infection is followed by active clinical lesions. In seroepidemiologic surveys the percentage of seropositivity is always higher than that of active cases; these two values can be as discrepant as 60%-70% vs. 20%-30%.

A certain degree of cross-immunity between T. pallidum and T. pertenue has often been observed. In
treponematoses, however, immunity is a slow process, developing during alternating active and latent periods, but the importance of successive relapses declines gradually. The immunity built up in children with extensive, profuse lesions is eventually very strong. Parents, being aware of the fact that yaws in childhood protects from infection in later life, have been known to expose their children to contagious contacts.

The nonvenereal tropical endemic treponematoses show different clinical patterns under different climatic conditions. Yaws is the disease of warm, humid, and mainly equatorial climates, prevailing in tropical forests and along coastal areas. Endemic syphilis is limited mainly to arid, semidesert climates. However, the presence and high prevalence of yaws on the high plateaus of the tropics call attention to the fact that the climatologic clearance is not so clear-cut. Moreover, between the humid and dry poles are transitional zones, such as degraded forests, gallery forests, and savannas. As a consequence, the occurrence of other geography-related clinical variations is plausible. In addition, it is worthwhile to remember that in the tropics even venereal syphilis is characterized by an abundance of mucosal plaques in cutaneous areas exposed to excessive sweating.

The influence of climatic conditions on symptomatology goes further. The percentage of active cases is higher during the rainy seasons or periods of high humidity in tropical areas, while the course of the disease remains more uniform in equatorial regions. Relapses occur mainly during the rainy season, and more infections are acquired when the humidity is high.

Since the start of the penicillin campaigns, a change in the clinical picture has been generally observed. Lesions tend to be less florid, with macules, micropapules in plaques, and less hyperkeratosis. These atypical, less abundant lesions are easily missed.

**Diagnosis**

The host factors underlying the degree of receptivity to infection, the clinical or subclinical evolution of infection, and the proneness to relapse or reinfection also have not received enough attention. These factors are important for postcampaign surveillance. In addition, more accurate clinical diagnostic techniques are needed for identification of the prevalent milder, attenuated treponematoses and for follow-up of patients after treatment. The practical meaning of a positive serologic reaction to lipoidal agents or to *T. pallidum* antigens has never been satisfactorily ascertained. In light of the possible interference of biologic factors inducing false reagin seroreactors, it is unreasonable to administer treatment on the basis of seroreactivity alone.

Diagnostic needs are even more pressing with regard to epidemiologic surveys. Some improved tools are available [16], such as the demonstration of treponemes in exudates by means of immunostaining mediated by specific fluorescent antibodies. The serologic method adapted to finger-prick blood collection on glass-fiber disks is well accepted. The humoral immune response can be detected through the intermediary of antibodies to lipoidal agents or *T. pallidum* antigens. The rapid plasma reagin card test or the Wellcome Syphacard Reagin (Wellcome Research Laboratories, Beckenham, England) is commendable, but the cheaper Venereal Disease Research Laboratory test is still in use and is also recommended. A positive reaction on routine screening can be quantified for confirmation. Both extracted and cloned *T. pallidum* can be used for more specific tests. The *T. pallidum* hemagglutination test, the Wellcome Syphatest, and the fluorescent treponemal antibody absorption test are available in kits. The enzyme-linked immunosorbent assay approach, well adapted for seroepidemiologic screenings, can be made operational. The *T. pallidum* immobilization test is obsolete for diagnosis.

By the currently available techniques, no differences can be demonstrated among *T. pallidum*, *T. pertenue*, and *Treponema carateum*. More specific serologic tools are needed; to this end, modern immunologic and genetic engineering techniques should be used to their fullest extent. Again, it remains an open question whether use of the most advanced technology on treponemal strains that have been passaged in animals for decades (e.g., the Nichols strain of *T. pallidum*) is the soundest approach to determining the profile of the antigenic mosaic, identifying the correct monospecific antigens, and producing monoclonal antibodies.

**Epidemiology**

The distribution of the nonvenereal treponematoses is uneven, regardless of living conditions. In endemic
areas some foci are more heavily affected than others. Although microfoci or isolated areas of infection, such as nearly inaccessible areas and closed valleys, should not be overlooked, this patchiness in distribution may keep some foci beyond the reach of the health services.

In endemic areas every child or young adolescent has somehow been in skin-to-skin contact with infectious lesions. (This mode of transmission excludes the likelihood that the infection will become venereal.) However, it is well known that under similar circumstances not every member of a household or a community develops clinically overt disease; the rate can be as low as 10%–30%. Some patients develop attenuated, subclinical, or latent infections. Their serologic identification among the 60%–70% of individuals who are seroreactive is highly desirable. Likewise, more information should be gathered about the late residua of early latent infections—the so-called last cases, which are the usual source of suddenly reappearing active cases.

These and many other unknowns about the geographic distribution of yaws and bejel (independent of any apparent difference in living conditions), about the dangerous latent form of infection, and about the puzzling resurgence of disease are in need of a careful, ongoing, in-depth investigation. Such an effort might pinpoint or provide some clues about overlooked epidemiologic factors.

Humans are believed to be the only significant reservoir of yaws. Concurrently with the occurrence of contagious cases in the population of endemic areas, a treponeme reservoir remains present among aborigines in Asia and Africa. Because of their nomadism, aborigines are often technically inaccessible to health services and remain a potential source of reinfection for other populations living in regular contact with them. In this context, it is not wise to pay some attention to the observations among pri-mates by Fribourg-Blanc et al. [17], Mollaret and Fribourg-Blanc [18], Baylet et al. [19], and Paris-Hamelin et al. [20]? Among baboons captured in Senegal, 47% showed the presence of treponemal antibodies; among those originating in Guinea, the percentage amounted to 75%. Moreover, 33% of tested chimpanzees from Zaire also had treponemal antibodies. The isolation of T. pertenue-like organisms from popliteal lymph nodes of 27.5% of 58 seropositive baboons and the regular passage of these organisms in hamsters raise the possibility of an animal reservoir living in close contact with infected populations. These facts are probably of only marginal importance but should not be ignored.

Treatment/Vaccination

As was mentioned earlier, the efficacy of penicillin against the nonvenereal treponematoses was so great and single-session therapy with long-acting penicillin so easy and so cheap that programs of mass treatment resulted in an impressive drop in prevalence; these programs did not, however, end transmission. Smoldering, latent infections and even the occasional emergence of an active case did not attract attention until unexpected and perplexing resurgences appeared. Forthwith, the possibility of penicillin resistance was invoked. However, variation in the responsiveness of treponemes to arsenicals and penicillin is not novel. In some patients treponemes have remained present after two or more administrations. No antimicrobial drug is 100% effective. Not much attention has been paid to these supposedly insignificant differences among the drug responses of different individuals. Nonetheless, these differences may be the origin of or play a role in the maintenance of subclinical infections and the resurgence of a focus.

The pharmacokinetic characteristics of penicillin—its absorption, distribution, metabolism, and elimination—are well known. As a result, the claim that those who respond poorly are fast excreters is admissible but not entirely satisfactory until scientifically proven. The pharmacodynamics of penicillin have received less attention, although the interaction of the drug and/or its metabolites with the defense mechanisms of the host is of capital importance. It is known that some invading pathogens evade recognition by the immune defense system by altering the molecular structure of their surface. The metabolic basis of this capability also needs to be explored.

Scientifically sound information in the field of pharmacodynamics might facilitate the search for drugs that are synergistic with the currently used efficient drugs and/or capable of enhancing the ability of the host defense system to play its role at full capacity. In addition, advances in this field would further the design of more effective drug regimens and might eventually be helpful in the control of the low percentage of nonresponding latent cases of dis-
ease; such control is the key to eradication. Finally, attention must be paid to the question of why some individuals in a community do not comply with the prescribed drug treatment.

Immunoprophylaxis is much in vogue, as is vaccination. However, the production of a treponemal vaccine, even when viewed most optimistically, is still far off. The maintenance of treponemes in animals offers no opportunity for collection of the most elementary basic data necessary for the elaboration of a vaccine. Prolonged survival of treponemes in vitro does provide useful information about the requirements and capabilities of the organisms but is no substitute for their cultivation in a cell-free medium. Identification of some biochemical components will not be a sufficient basis for attempts at genetic engineering, an approach that is indispensable for the production of antigens. A realistic look at the present situation gives rise to the thought that it might be more useful to direct efforts toward the development of more reliable tools for the detection of antibodies and circulating antigens. More solid data are also needed for assessment of protective roles of humoral and cellular immunity.

The prevailing propensity to regard vaccination as a master key for the prevention of all of the communicable diseases is naive. A basic scientist and a theorist can play with the idea of vaccinating all people against all potential pathogens: bacteria, viruses, parasites, mycetes. Public health professionals and field workers are eager to have vaccines to include in their immunization programs but are aware that unless more universal immunogenic substances become available, there must be a limit on the number of different antigens that can be administered. However, over and above worries about the existence of a saturation point or the risk of reducing defense capacities by “overvaccination” is the main concern: the difficulty of getting new and old vaccines to the target at-risk groups.

Control

An impressive reduction in the prevalence of yaws and other endemic treponematoses, referred to somewhat prematurely as a “disappearing” form of disease by Guthie et al. [21], followed the mass treatment campaigns of the 1950s and 1960s. Instead of eradication, however, a false sense of security resulted; clinicians, epidemiologists, public health authorities, and others lost interest in yaws. This situation emphasizes the need for yaws-oriented training or recycling of the professional auxiliary personnel of mobile teams, health centers and posts, and even hospitals. The training should draw special attention to the mild, subclinical, attenuated, atypical symptomatology and the high prevalence of latency. It should also emphasize the patchy epidemiologic pattern and the possible existence of neglected microfoci.

The need to stimulate the consciousness and active participation of the community has become common knowledge. Less often acknowledged, however, are the benefits of using this opportunity to get valuable hints from the community itself. Rural communities possess a striking perception of environmental ingredients and human attitudes. They are a source of information that too often remains untapped. Villagers are acquainted with yaws—both the early active form and some of the late painful or disabling symptoms. In his monograph on goundou, Botreau-Roussel [22] gave a good example of the use of villagers’ knowledge to gather correct information. Being a surgeon, he restored two patients with goundou by a successful face-lift. According to the medical profession, this disease was supposed to be very rare. In less than two years, however, Botreau-Roussel operated on 130 such patients who were brought forth as a result of the communities’ realization that a successful treatment was available.

Contacts at the grassroots level can also provide a suitable background for the collection of fundamental sociocultural data that will permit a more rational approach to health education, which is the key to active community participation. Yaws and other endemic treponematoses are maintained through underdevelopment. This situation can be solved only by the people concerned. They must be motivated to give up their traditional apathy and resignation. Health education can help to stimulate active participation, a problem-solving attitude, and a will to take the future into one’s own hands.

In summary, in order to overcome our present problems regarding the endemic treponematoses, we must increase our basic knowledge and continue to analyze in depth the current policies of yaws control programs. Both of these processes require basic and health-services research of high quality and continuous assessment in the field.
References

8. Castellani A. On the presence of Spirochaetae in two cases of ulcerated parangi (yaws). Journal of Tropical Medicine 1905;8:253
11. Van den Branden P. Le pian et la syphilis sero-ent-l-us une seule et même affection? Bruxelles Médical 1930;5:120
New Technologies for Use in the Surveillance and Control of Yaws


From the Centers for Disease Control, Atlanta, Georgia; the Epidemiology Division, Ministry of Health, Republic of Ghana; Genetics Systems, Seattle, Washington; and the Molecular Biology Institute, University of California School of Medicine, Los Angeles, California

In the Republic of Ghana, treponemal antigen tests performed on finger-prick blood from patients with yaws proved to be as sensitive as those tests performed on whole sera, and this mode of collection was more economical and acceptable than venipuncture. Under field conditions, dark-field microscopic examination of suspect yaws lesions was difficult as compared with collection of serous exudate in heparinized capillary tubes examined later in a reference laboratory. Direct staining of lesion exudate fixed on microscope slides with fluorescein-conjugated human or mouse monoclonal antibody against Treponema pallidum was more sensitive than dark-field examination. However, these techniques could not distinguish between the early lesions of venereal syphilis and those of yaws. An equally sensitive technique used a cloned segment of the T. pallidum (Nichols strain) genome to detect homologous DNA in lesion exudate fixed on nitrocellulose filter paper. The fixation of lesion exudates on microscope slides or nitrocellulose papers may prove to be the easiest method of collecting and transporting such materials to reference laboratories.

The clinical manifestations of early yaws are usually sufficient to distinguish it from other diseases when yaws is endemic in a population. The morphology of both early and late yaws lesions, however, is not unique and they cannot be easily differentiated except by certain epidemiologic criteria and laboratory tests [1]. The laboratory tests traditionally used for yaws surveillance are the same as those used to diagnose venereal syphilis. Serologic tests for active or latent yaws are often difficult to perform and to interpret under field conditions; test reagents are labile, and special equipment is usually required to get reproducible results.

We describe in this report the diagnostic tests used during an ongoing yaws control program in Ghana [2] that were designed to simplify collection, transportation, and testing of specimens. We also describe the preliminary results of new techniques designed to detect pathogenic treponemes in lesion exudate by direct antibody staining or by DNA hybridization with use of a cloned segment of the genome of Treponema pallidum.

Patients and Methods

Patients. Between 1979 and 1981, sera for nontreponemal and treponemal antigen tests were collected in “vacutainer” tubes by venipuncture or by finger-stick, with use of aseptic techniques, from 255 Ghanaians ranging in age from six months to 90 years. They resided in one of two villages in the Ashanti Region (total population, 103) or attended a local primary school (student population, 107) in an area where yaws was endemic. Another 45 patients presented to district clinics for treatment of active yaws lesions. The clinical diagnosis of yaws [3] and its treatment with benzathine penicillin were based on criteria established by the World Health Organization [4]. Lesion exudate and sera were also collected from six patients attending a clinic for sexually transmitted diseases in Seattle, Washington, who had dark-field-positive, primary venereal syphilis lesions.

Serologic tests. The nontreponemal antigen rapid plasma reagin (RPR) 18-nm (circle) and “teardrop” card tests were performed with serum or
plasma according to the procedures described by the manufacturer (Hyson, Westcott and Dunning, Baltimore, Md.) [5]. All sera were screened for treponemal antibodies by the microhemagglutination assay (MHA-TP; Miles Laboratories, Elkhart, Ind.) at a serum dilution of 1:20 in sorbent [6]. The fluorescent treponemal antibody-absorption (FTA-ABS) test was done using standardized reagents and procedures [5].

Finger-prick blood, collected on 1 x 3 inch rectangular filter papers (ROPACO no. 1023-.038; James River Rochester, Rochester, Mich.) was eluted from a 5-mm punched-out blood-soaked section and placed in the first well of a microtiter plate containing 0.1 ml of absorbing diluent from the MHA-TP kit [7]. The disk was incubated for at least 1 hr or overnight at room temperature. After incubation, the disk was removed from the well with forceps, carefully squeezed, and discarded. Approximately 75 µl of dark brown eluate at an approximate dilution of 1:20 was used as the starting dilution for the MHA-TP test. The FTA-ABS test was done on samples of whole sera in which the RPR test of the same sera was reactive at a dilution of 1:20 and the MHA-TP test was nonreactive.

Detection of Treponema pertenue in lesions. Suspected yaws lesions were cleaned with a cotton sponge soaked in sterile saline to remove any debris and eschar. The lesion was kept moistened with saline until any gross bleeding had abated. Heparinized, blood capillary tubes were filled by capillary action with lesion exudate and plugged at both ends with plastic sealant (Seal-ease, Clay Adams, Parsippany, N.J.). Sealed capillary tubes were transported inside labeled, capped 100 x 17-mm polystyrene tubes. In some patients, smears of lesion exudate were made on clean glass microscope slides, allowed to dry, and fixed for 1-3 min in acetone. Both capillary tubes and slides were stored at 4°C until tested, the former for more than one year. Lesion exudate was also examined within minutes after collection in the field by use of a Cooke-McArthur microscope (Cooke, Troughton and Simms, York, England) equipped with a dark-field condenser.

Slides made and fixed in the above manner from exudate contained in capillary tubes were examined with use of a fluorescein (fluorescein isothiocyanate) or rhodamine (tetramethylrhodamine isothiocyanate)-labeled human globulin from a patient with secondary syphilis that had been absorbed with Treponema phagedenis biotype Reiter [8] or with use of a monoclonal antibody that recognizes an epitope shared by both T. pallidum and T. pertenue (Genetic Systems, Seattle, Wash). This monoclonal antibody (H9-1) reacts with T. pallidum (Nichols strain) and T. pertenue, but not with T. phagedenis (Reiter strain), Treponema refringens, Treponema vincentii, Treponema denticola, Treponema hyodysenteriae, Leptospira species, or Borrelia species [8a].

A cloned segment (pAW305) of T. pallidum (Nichols strain) DNA [9] was used as a probe to detect homologous DNA in yaws-lesion exudate collected on nitrocellulose filters. The probe was radiolabeled by nick-translation with 32P-labeled nucleotides and tested at a reference laboratory by a procedure described in detail elsewhere [10]. The probe detected between 1 x 10^4 and 1 x 10^5 T. pallidum (Nichols strain) and from 5 x 10^3 to 1 x 10^4 T. pertenue (CDC1 and CDC2, respectively) [11] extracted from infected rabbit testes. The specificity of the DNA probe is still being determined; it does not react with 500 pg of meningococcal or T. phagedenis DNA. Because the probe contains some pBR 322 plasmid DNA, it reacts with >50 ng of pBR 322 DNA.

Results

Clinical diagnosis. A clinical diagnosis of primary or secondary yaws was made for 62 of the 255 persons examined. In 54 of the 62 cases, serologic tests and/or dark-field examinations were performed. These tests confirmed the diagnosis in 46 (85%) of the 54 patients. All but four of the patients with infectious yaws were between five and 14 years old. The sex ratio was 2.2:1 in favor of male patients. The most common yaws lesions observed consisted of papillomas or maculopapular eruptions on the face or extremities. Macular and plantar yaws lesions were uncommon and often difficult to distinguish from dermatophytosis or other causes of plantar hyperkeratosis and fissures. In the field, examination of specimens with a Cooke-McArthur microscope usually confirmed the clinical diagnosis of papillomatous or maculopapular yaws but could not contribute to the diagnosis of the disease in patients with macular and/or plantar lesions. Dark-field examination helped to differentiate the etiology of ulcers on the lower extremities in children who also had reactive yaws serology.

The morphology and antigenicity of T. pertenue
Figure 1. Treponemes in lesion exudate stained with fluorescein-conjugated murine monoclonal antibody (Genetic Systems, Seattle, Wash.).

could be preserved for at least one year in specimens collected in heparinized capillary tubes and stored at 4°C. Although the organisms were nonmotile and presumably nonviable, they could be recognized easily by immunofluorescence when stained by either the human antiserum or murine monoclonal antibodies (figure 1).

Serologic diagnosis. Of the 255 persons examined for yaws, conventional serologic tests were done for 76 residents of one village where infectious yaws was endemic (table 1), for 106 students in a local primary school, and for 45 patients attending one of four local primary health clinics. The qualitative RPR teardrop card test was performed in the field for 34 randomly selected village residents or students (three had infectious yaws lesions) and sera were reactive in 10 (29%) cases, including the three active cases of yaws. However, the sensitivity and specificity of the RPR teardrop test on the same 34 specimens were 71% and 78%, respectively, when compared with the results of RPR (18-mm) circle card test done on the same sera by a reference laboratory.

When the 241 sera were tested by the quantitative RPR (18-mm) circle card test in the reference laboratory, 107 (44.4%) were reactive. However, four of the 107 positive sera were only weakly reactive. A prozone phenomenon was not observed. The RPR titers for persons with infectious yaws were relatively high; for the 54 persons with clinically diagnosed infectious yaws, the RPR titer was $\geq 1:16$ dilutions in all but four patients. Of the 241 patients tested, 49 (20.3%) showed serologic but no clinical evidence of active yaws (RPR titer $\geq 1:8$).

The MHA-TP test for treponemal antibody was reactive at $\geq 1:2$ dilutions in 155 (64.3%) of the 241 sera tested, and there was total agreement between MHA-TP tests done on whole sera and on sera eluted from blood on filter paper. The MHA-TP test was nonreactive in five sera that were reactive in the quantitative RPR card test; however, each of these sera was reactive when tested by the FTA-ABS test. Reactivity in the MHA-TP tests increased with the age of the patients. These and the other serologic results in a yaws-endemic community are shown in table 1.

Direct assays for treponemal antigens. Direct fluorescent-antibody staining of lesion exudate fixed on microscope slides in the field or prepared from exudate collected in capillary tubes proved to be a sensitive method for detecting \textit{T. pertenue}. The fluorescent antibody detected treponemes with a morphology identical to that of \textit{T. pertenue} (and \textit{T. pallidum}) in lesion exudate from 26 (84%) of 31 patients with clinically diagnosed cases of infectious yaws. Similarly, the monoclonal antibody detected treponemes in the lesion exudate from eight (80%) of 10 patients. As shown in table 2, the monoclonal antibody also reacted with \textit{T. pallidum} in chancroid exudate from patients from the United States with venereal syphilis.

The treponemal DNA probe detected homologous DNA in lesion exudate fixed on nitrocellulose filters.

<table>
<thead>
<tr>
<th>Examination/test result</th>
<th>0-4</th>
<th>5-9</th>
<th>10-14</th>
<th>$\geq 15$</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Infectious yaws</td>
<td>2/25 (8)</td>
<td>2/28 (7.1)</td>
<td>2/7 (28.6)</td>
<td>0/16</td>
<td>6/76 (7.9)</td>
</tr>
<tr>
<td>(2) Seroreactivity, by RPR</td>
<td>6/21 (28.6)</td>
<td>8/27 (29.6)</td>
<td>3/7 (42.5)</td>
<td>9/16 (56.3)</td>
<td>26/71 (36.7)</td>
</tr>
<tr>
<td>(3) Titer $\geq 1:8$, no yaws lesions</td>
<td>1/21 (4.8)</td>
<td>3/27 (11.1)</td>
<td>1/7 (14.3)</td>
<td>1/16 (6.3)</td>
<td>6/76 (7.9)</td>
</tr>
<tr>
<td>Active yaws: (1) + (3)</td>
<td>3/25 (12)</td>
<td>5/28 (17.9)</td>
<td>3/7 (42.5)</td>
<td>1/16 (6.3)</td>
<td>12/76 (15.8)</td>
</tr>
<tr>
<td>(4) Seroreactivity by MHA-TP</td>
<td>4/21 (19)</td>
<td>15/27 (55.6)</td>
<td>5/7 (71.4)</td>
<td>14/16 (87.5)</td>
<td>38/76 (50)</td>
</tr>
</tbody>
</table>

NOTE. RPR = rapid plasma reagin test, MHA-TP = microhemagglutination assay.
Table 2. Diagnosis of infectious yaws and venereal syphilis by direct fluorescent monoclonal antibody staining and DNA hybridization.

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>No. of persons tested</th>
<th>No. of patients positive/ no. of patients tested with indicated method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dark-field microscopy</td>
<td>Monoclonal antibody staining</td>
</tr>
<tr>
<td>Primary syphilis</td>
<td>6</td>
<td>6/6</td>
</tr>
<tr>
<td>Secondary yaws</td>
<td>16</td>
<td>Not determined</td>
</tr>
</tbody>
</table>

for 13 (81.3%) of 16 patients with yaws, including all eight whose specimens were positive by monoclonal antibody staining (table 2). These preliminary data indicated that *T. pallidum* and *T. pertenue* are very closely related organisms.

Discussion

The clinical diagnosis of early (primary and secondary) yaws lesions can be made with a high degree of accuracy in populations where yaws is endemic, and laboratory confirmation of the diagnosis is seldom necessary. The problem, repeatedly stressed in earlier mass treatment campaigns against yaws, is identification and treatment of persons with active latent yaws infections, who are frequently subject to infectious relapses [12]. Serologic surveillance for active latent yaws is relegated to the consolidation phase of mass campaigns as a method of evaluating the long-term outcome of the campaign. Field-adapted nontreponemal antigen serologic tests together with appropriate population sampling techniques were implemented for this purpose [12, 13]. Although we tested several methods that simplified collection and transportation of serum for laboratory testing, the problems of variable sensitivity and lack of specificity for yaws remained.

The most practical method for collecting blood for serologic tests for detecting antibodies to *T. pertenue* is that of placing blood on a 1 × 3-inch rectangular filter papers. This method of blood collection has been used in the past for both treponemal and nontreponemal antigen serologic tests [14, 15] and produces results that are comparable to those obtained on whole-blood specimens tested in reference laboratories. ELISAs for treponemal antibodies that use antigens extracted [16, 17] or cloned [9] from

*T. pallidum* might be adapted and quantitated for the surveillance of yaws once the antigens have been stabilized for field use.

In this study, detection of *T. pertenue* in lesion exudate on microscope slides by direct fluorescent antibody staining with use of human syphilitic serum [18] or murine monoclonal antibody or in exudate placed on nitrocellulose paper by a radiolabeled DNA probe was quite sensitive; however, the specificity of these methods was not established. Nevertheless, these tests have great potential in terms of simplicity of specimen collection and shipment to a reference laboratory. They can establish the prevalence of infectious yaws in a given community—assuming that the suspect lesions are not those of venereal or endemic syphilis. Indeed, the results reported in this study support the concept that the treponemes that cause venereal syphilis, endemic syphilis, and yaws are closely related organisms belonging to a single species. If this is the case, then epidemiologic and clinical criteria may continue to be the only means to differentiate yaws from endemic and venereal syphilis in many parts of the world.

References

8. Liska SL. The direct fluorescent antibody technique with *Treponema pertenue*. PhD diss, Chapel Hill, NC: University of North Carolina, 1981


SESSION III

Prospects for Improved Laboratory Diagnoses of Treponemal Infections and Species Differentiation

Paul H. Hardy

From the Department of Molecular Biology and Genetics,
The Johns Hopkins University School of Medicine,
Baltimore, Maryland

The serologic diagnosis of treponemal infections has depended in the past on a variety of tests in which specificity was defined on an epidemiologic rather than on an immunologic basis. The lipoidal antigen tests possess no immunologic specificity. Tests based on whole treponemal antigens, although they do have some immunologic specificity, react with antibodies other than those generated in the course of syphilis and yaws infections. Recent developments in biotechnology now permit the identification of immunologically specific antigens in Treponema pallidum, and cloning of appropriate genetic information in Escherichia coli has led to the production of pure specific reagents. These developments will finally place the serologic diagnosis of treponemal infections on a sound immunologic basis.

Initial observation of the spirochete now known as Treponema pallidum and the association of this organism with syphilis are usually credited to Schaudin and Hoffmann [1] in 1905. That same year Castellani [2] recognized Treponema pertenue as the causative agent of yaws. A year later Wassermann et al. [3] described the first serologic test for the diagnosis of these treponemal infections. The test was a complement-fixation reaction that employed syphilitic tissues rich in treponemes as its antigenic component. In the following year Marie and Levaditi [4] demonstrated that the Wassermann test unfortunately lacked specificity with respect to the detection of antitreponemal antibodies. Although not appreciated at the time, it was eventually shown that the antibodies detected by the Wassermann test were directed against glycosphingolipid(s) present in the host tissue that was used as the source of treponemes. Despite this finding, the Wassermann test — and the many subsequent variations on its initial theme — were found to possess remarkable epidemiologic specificity, i.e., a positive test correlated well with the presence of syphilitic infection, and within a few years laboratories throughout the world were routinely using one or another of the lipoidal antigen tests for the diagnosis of syphilis. However, these tests had their limitations — they were occasionally negative in individuals with late syphilitic infection and sometimes were falsely positive in uninfected individuals.

The limitations of the lipoidal antigen tests, together with their lack of immunologic specificity — as demonstrated by Marie and Levaditi [4] — stimulated a search for a more specific and reliable test. However, roughly 40 years passed before the presence of antitreponemal antibodies was clearly demonstrated in serum from individuals with syphilitic infection. In fact, efforts to this end were so fruitless that for a period the prevailing belief was that no specific humoral immune response occurred in this disease. The first strong evidence to the contrary was probably the demonstration by Turner and his colleagues [5, 6] that in vitro incubation of T. pallidum with serum from syphilitic patients rendered the organisms nonpathogenic. This finding provided the basis for the subsequent development of the T. pallidum immobilization (TPI) test by Nelson and Mayer [7] in Turner's laboratory. The TPI test was a complement-dependent treponemical reaction that demonstrated beyond any doubt the development of specific antitreponemal antibodies in the course of syphilitic infection. The test was also technically difficult and expensive to perform. It survived only because it arrived when the prevalence of syphilis was at its peak in the United States and most other coun-
tries, and it documented the therapeutic efficacy of penicillin when the use of this antibiotic was just beginning to produce a precipitous fall in the incidence of early syphilis. However, within a few years new cases of syphilis were occurring so infrequently that performance of the TPI test was no longer cost-effective, and laboratories began to abandon it. It had served its purpose, not only by demonstrating the development of specific antibodies to *T. pallidum* but also by generating a renewed interest in the development of other, simpler tests for detecting these antibodies, and several such tests became available to replace the TPI test.

The second generation of serologic tests included the short-lived *T. pallidum* agglutination test [8], the several variations of the fluorescent treponemal antibody (FTA and FTA-ABS) test [9–11], the *T. pallidum* hemagglutination (TPHA) tests [12, 13], and the Reiter protein complement fixation (RPCF) test [14]. All but the latter used whole treponemes extracted from rabbit testicular syphilomias, and the development of these tests was due, in part, to advancements in methods for stimulating more intense experimental infections and, in part, in procedures for recovering cleaner suspensions of treponemes from the lesions. The RPCF test relied upon antigenic cross-reactivity between the nonpathogenic Reiter treponeme (*Treponema phagedenis*, var. Reiter) and *T. pallidum*; the test was soon discarded because of its unreliability. The second-generation *T. pallidum* tests were all more sensitive (in terms of antibody titer) than the TPI test but all of them possessed less immunologic specificity than the TPI test. In retrospect the remarkable specificity of the TPI test may have been a reflection of its low sensitivity, which was the result of suboptimal test conditions, i.e., the presence of sulfhydryl compounds at concentrations sufficient to impair complement activity and to hydrolyze IgM antibodies. In any event, all of the newer *T. pallidum* tests had the disadvantage of producing false-positive reactions as a result of the presence of antibodies to nonspecific antigens within the treponeme, e.g., shared axial-filament proteins and nucleic acids, or to host-tissue components tightly adsorbed to the surface of the treponeme, e.g., albumin and immunoglobulins. Despite the sometimes nonspecific reactions, several of these tests possessed sufficient epidemiologic specificity to justify their routine use as confirmatory diagnostic procedures for sera of suitably screened patients. For a number of years, the FTA-ABS was the test of choice for such purposes, but in the past several years it has lost favor and has slowly been replaced by the TPHA test.

As noted above, all of the *T. pallidum* tests to date have used whole treponemes from experimental lesions, and this has been their major weakness. Until very recently there have been few attempts to develop more defined antigens for the detection of antibodies to treponemes. A few years ago we recognized that the major antigenic component that the Reiter treponeme shared with *T. pallidum* was a protein constituent of the axial filaments (endoflagella) [15]. We subsequently used purified preparations of the organelles as the antigen in both counterimmunoelectrophoresis [16] and an ELISA assay [17] to detect treponemal antibodies in serum from syphilitic patients. Although the results correlated well with the presence of infection, they were based on immunologic cross-reactions only, and we did not feel this reaction warranted further study. This subject has been reexamined recently by investigators in Denmark, who made observations similar to ours, but they concluded that despite the cross-reactivity this reaction may have considerable diagnostic potential [18].

Obviously, efforts to obtain purified microbial antigens for use in a serologic test should be directed at the microorganism responsible for the disease. Unfortunately, for many years this effort was not practical for *T. pallidum* because this spirochete could not be cultured in vitro, and the relatively small quantity of treponemes that could be recovered from lesions in experimental animals were insufficient for such studies. However, this situation has now changed. Recent developments in biotechnology have made it possible to dissect and analyze small quantities of organisms so that culture of *T. pallidum* in vitro is no longer a necessary prerequisite. New genetic-engineering techniques are perhaps of even greater importance to the development of a specific diagnostic procedure because once the treponemal components of greatest value for this purpose have been identified they can be produced in quantity by cloning the appropriate genetic information into a surrogate host such as *Escherichia coli*. There seems to be no doubt that we now have on hand all the methodology necessary for the development of a simple but specific and relatively inexpensive serologic test for the diagnosis of syphilis.
Nevertheless, such a test has been slow to arrive, primarily because the necessary antigen has been difficult to identify.

Dissection and analysis of *T. pallidum* at the molecular level has been studied primarily by polyacrylamide gel electrophoresis (PAGE), which permits the separation of individual cellular components on the basis of molecular size. Most investigators have focused on the polypeptide composition of this organism, and as many as 85 different peptides have been demonstrated [19]. The potential immunogenicity of these components has been studied by Western blotting [20]. In this procedure components separated by PAGE are electrophoretically transferred to a solid matrix, such as nitrocellulose, where they are immobilized in their separated state. These components can then be exposed to an immune serum, and any immune complexes that form can subsequently be identified by isotope- or enzyme-labeled detection reagents. As one might expect this approach has revealed that in the course of syphilitic infection antibodies develop to almost every distinguishable treponemal peptide [19].

There are therefore a multitude of candidate proteins from which the most specific and significant antigen for diagnostic purposes must be chosen. It is reasonable to assume that the great majority of these antigens are located within the organism and are not encountered by the host until treponemes are killed and digested by phagocytes. Such internally located components are also unlikely to play a major role in pathogenesis of disease — or in host defenses against it. Surface proteins, on the other hand, are almost certainly of importance to both disease production and the immune state generated by the host. If, as has been suggested, attachment to host cells is an essential first step in infection by *T. pallidum* [21], the receptor site on the treponeme must by necessity be located on its surface. In the same vein, the well-recognized close association between host proteins and the lipoprotein outer membrane of *T. pallidum* [22] is undoubtedly due to properties of the constituents of the treponeme’s surface. These properties may, in fact, represent a virulence factor for *T. pallidum* by converting it, in essence, to a wolf in sheep’s clothing, thereby masking the organism and hiding it from the host’s defense mechanisms. As mentioned earlier, complement-dependent treponemical antibodies develop in syphilitic infection, and by extrapolation from the situation with other bacteria, these antibodies are most probably directed against surface constituents. It may be concluded from this that the search for an ideal diagnostic antigen in *T. pallidum* should focus on the surface of the treponeme, a conclusion recognized by a number of investigators who have attempted to identify the surface proteins of *T. pallidum*.

Several investigators have used brief radiiodination to achieve preferential labeling of surface proteins of *T. pallidum*, but results have varied somewhat [19, 23, 24]. As Norris and Sell [19] have emphasized, the iodination process is not necessarily limited to the surface of the treponeme, and the results are dependent on the specific procedure employed and the duration of labeling, with virtually all of the organism’s polypeptides becoming labeled in time. Baseman and Hayes [25] combined the intrinsic labeling of treponemes with [*35S]*methionine and the adhesion of treponemal proteins to tissue culture cells as a means of identifying three surface proteins believed to be involved in host cell attachment by *T. pallidum*. In other studies Alderette and Baseman [22] reported that trypsin digestion of whole treponemes removed five treponemal proteins as well as various host-derived proteins bound to the surface of the treponeme; they assumed the treponemal proteins were also on the surface of the organism. In recent studies Moskophidis and Müller [26] identified four treponemal glycoproteins by means of [*14C]*glucosamine incorporation and concluded that these glycoproteins also were surface constituents of *T. pallidum*. From all these studies there appear to be at least a dozen different proteins that may be located on the outer envelope of *T. pallidum*. Unfortunately, the molecular weights calculated and reported by different investigators have shown sufficient variation to make it difficult to compare the findings of one laboratory with those of another. However, it should only be a matter of time until these differences are resolved and a small number of significant surface proteins are unequivocally identified.

As the above studies have been in progress, several other groups have undertaken the cloning of *T. pallidum* DNA in *E. coli* [27–30], and libraries of recombinant DNA clones that cover the entire treponemal genome have been developed. It has not been difficult to recover from these collections a number of clones that synthesize *T. pallidum* proteins, as identified immunologically with syphilitic serum. However, to date there has been little progress in associating these *E. coli*-synthesized proteins with the
corresponding native T. pallidum proteins. The first such association has just been reported [31]. It is synthesized in E. coli as a 190,000-dalton polypeptide that corresponds to a protease-released 90,000-dalton peptide from T. pallidum. It is significant that immune rabbit serum produced with the E. coli-synthesized protein has given a positive TPI reaction, a finding indicative of the production of treponemal antibodies. This activity is also a strong indication of a surface location for the T. pallidum counterpart, a point the authors have apparently confirmed by immunostaining at the ultrastructural level. Quite predictably, preliminary studies using this polypeptide as an antigen in an ELISA reaction have indicated that it has great potential as a diagnostic reagent. This test system may well be the fabled pot of gold at the end of the rainbow. The 190,000-dalton protein could also be a good protective immunogen as well as a diagnostic reagent.

With this development it should not be long before competition from other clone-synthesized surface proteins of T. pallidum appears. As surface proteins on T. pallidum are identified, it will be possible to recover them from preparative polycrylamide gels in sufficient quantity for production of monospecific antibodies—either monoclonal or polyclonal. These antibodies, in turn, will provide the immunologic probes necessary for identification of the corresponding E. coli-synthesized product. Then it will be necessary only to ascertain which of several protein reagents is most satisfactory. The future for the serologic diagnosis of syphilis looks very bright insofar as the prospects for the development of a relatively simple and highly specific test is concerned. It is quite probable that several prospective antigens of equal specificity will be found and that the factor eventually defining superiority may simply be the ease with which the antigen is recovered from E. coli. As for the development of a test that might differentiate T. pertenue from T. pallidum, this is unlikely. Available genetic evidence indicates that these are basically the same organism, and their differentiation into two species is no longer warranted [32]. If this is the case, the differences in clinical manifestations of yaws and syphilis may simply reflect phenotypic changes in the organism resulting from host-environmental selective pressures. This is not a new idea; it was proposed by Hudson 25 years ago [33].

References

1. Schaudinn F, Hoffmann E. Vorläufiger Bericht über das Vor-

kommen von Spirohaeten in syphilitischen Krankheits-
produkten und bei Papillomen. Arbeiten Kaiserlichen
Geiisheitsamtes 1905:22:527-34

2. Castellani A. On the presence of spirochaetes in two cases of

3. Wassermann A, Neisser A, Bruck C. Eine serodiagnostische
Reaktion bei Syphilis. Dtsch Med Wochenscr 1906:32:
743-6

4. Marie A, Levaditi C. Les "anticorps syphilitiques" dans le
liquide céphalo-rachidien des paralytiques généraux et des
tabéqués. Annales Institut Pasteur 1907;21:138-53

5. Turner TB. Protective antibodies in the serum of syphilitic

6. Turner TB, Kluth FC, McLeod C, Winsor CP. Protective anti-
obodies in the serum of syphilitic patients. Am J Hgy
1948;48:173-81

7. Nelson RA Jr, Mayer MM. Immobilization of Treponema
pallidum in vitro by antibody produced in syphilitic in-

8. Hardy PH Jr, Nell EE. Specific agglutination of Treponema
pallidum by sera from rabbits and human beings with

9. Deacon WE, Falcone VH, Harris A. A fluorescent test for
477-80

10. Hunter EF, Deacon WE, Meyer PE. An improved FTA test
for syphilis, the absorption procedure (FTA-ABS) Public
Health Rep 1964;79:410-2

11. Deacon WE, Lucas JB, Price EV. Fluorescent treponemal
antibody-absorption (FTA-ABS) test for syphilis. JAMA
1966;198:624-8

12. Tomizawa T, Kasamatsu S. Hemagglutination tests for diag-
1966;19:305-8

13. Sequence PJL, Eldridge AE. Treponemal haemaggultination

14. D'Alessandro G, Dardanoni L. Isolation and purification of
the protein antigen of the Reiter treponeme. Am J Syph
Gonor Vener Dis 1953;37:171-70

15. Hardy PH Jr, Fredericks WR, Nell EE. Isolation and anti-
genic characteristics of axial filaments from the Reiter

16. Nell EE, Hardy PH Jr. Counterimmunoelectrophoresis of
Reiter treponeme axial filaments as a diagnostic test for

17. Hardy PH, Nell EE, O'Beirne AJ. An enzyme linked im-
munospecific assay for diagnosis of syphilis [abstract]. In:
Abstracts of Annual Meeting American Society for Mi-
crobiology. Washington, DC: American Society for Mi-
crobiology, 1978:308

18. Strandberg Pedersen N, Sand Petersen C, Vejtorp M, Axel-
sen NH. Serodiagnosis of syphilis by an enzyme-linked
immunosorbent assay for IgG antibodies against the Reiter

19. Norris SJ, Sell S. Antigenic complexity of Treponema pali-
dum. Antigenicity and surface localization of major poly-

20. Towbin H, Staehelin T, Gordon J. Electrophoretic transfer
of proteins from polyacrylamide gels to nitrocellulose
sheets: procedure and some applications. Proc Natl Acad
Sci USA 1979;76:4350-4
Prospects for Development of a Treponemal Vaccine
Sheila A. Lukehart

From the Department of Medicine, Division of Infectious Diseases, University of Washington School of Medicine, Seattle, Washington

The numbers of people affected by treponemal diseases and the degree of resultant morbidity and mortality emphasize the need for improved methods for controlling these infections. The existence of identifiable infectious stages, the relatively low infectivity rates coupled with long incubation periods, the noninfectious nature of the latent stage, and the lack of a known animal reservoir make treponemal diseases good candidates for control by active immunization. The development of a practical, effective vaccine against the treponematoses is dependent on an understanding of the pathogenesis of the diseases, a knowledge of the immunologic mechanisms of resistance, a definition of the protective antigens, and a readily available source of these antigens. Recent contributions to our knowledge in these areas include the application of state-of-the-art techniques such as Western blotting, radioimmunoprecipitation, gene cloning, and monoclonal antibody production. The scope of potential vaccines, target populations, safety, and efficacy are topics of discussion.

Venereal syphilis and the nonvenereal treponemal infections (yaws, pinta, and endemic syphilis) pose significant health risks to millions of persons, particularly in developing countries. Permanent disfigurement and deformity result from untreated disease, and venereal syphilis can affect the central nervous and cardiovascular systems, as well as fetuses and neonates. Although the total number of children and adults afflicted with treponemal diseases is not known, the prevalence is quite high in some geographic regions. Rates of reactive serologic tests for syphilis in antenatal clinics in developing countries range from <1% to >20% [1], and congenital syphilis is thought to contribute to 25%–30% of perinatal deaths in areas of Africa [2]. A recent survey by the World Health Organization detected clinical yaws in 20% and reactive serologic tests in 80% of the Pygmy population in the Central African Republic, the Congo, and Gabon [1]. It is estimated that more than 325,000 people in the United States have untreated syphilis [3].

Treponemal infections, transmitted primarily by direct contact with skin or mucous membrane lesions, are characterized by two infectious stages (primary and secondary) and long periods of latency. The attack rate for the nonvenereal treponematoses is not known; however, 30%–60% of known contacts of patients with infectious lesions of venereal syphilis become infected [4, 5]. Approximately three to six weeks elapse between contact and development of the primary chancre. The infectious lesions generally heal spontaneously after several weeks or months, although the lesions of pinta and endemic syphilis can persist for longer periods and recurrent lesions are common in yaws. Patients in the latent and tertiary stages of disease are not considered to be infectious except by the transplacental route in the case of venereal syphilis. Humans are the only proven reservoir for the etiologic agents' of venereal and endemic syphilis, yaws, and pinta. Although treponemes have been isolated from primates in Africa [6], the significance of this observation with regard to human disease is unclear.

The numbers of people affected by treponemal diseases and the degree of resultant morbidity and mortality emphasize the need for improved methods for controlling these infections. The existence of identifiable infectious stages, the relatively low infectivity rates coupled with long incubation periods, the noninfectious nature of the latent stage, and the lack of a known animal reservoir make treponemal diseases good candidates for control by active immunization.

* Treponema pertenue has been reclassified as Treponema pallidum subsp. pertenue, and the etiologic agent of endemic syphilis has been classified as *T. pallidum* subsp. endemicum. In this paper, the nomenclature employed in the original references will be used.
Early Attempts to Develop Treponemal Vaccines

Numerous investigators have attempted to immunize rabbits against syphilitic infection with preparations of killed or attenuated Treponema pallidum and nonpathogenic treponemes (table 1). In most cases, the results have been disappointing. Challenge of rabbits immunized with nonpathogenic treponemes has resulted, at best, in only slight delays or alterations in lesion development. Immunization with heat-killed, lyophilized, or sonicated preparations of T. pallidum has provided no protection against subsequent challenge. Partial protection has been achieved with preparations of Antiformin-treated [10] or “aged” [12, 13] treponemes; some of the animals immunized with these organisms were completely resistant to intradermal challenge, and others developed only asymptomatic infection. The most promising vaccine studies to date, conducted by Miller, have employed γ-irradiated, attenuated, motile treponemes as the immunizing preparation. In an elegant experiment, Miller [14] demonstrated that iv immunization with 3.7 × 10⁶ T. pallidum cells over a 37-week period resulted in complete resistance to intradermal challenge with 10⁵ and 10⁶ homologous organisms. No asymptomatic infection was detected in these animals, and complete protection persisted for at least one year following immunization. Subsequent attempts to make the immunization protocol more practical by reducing the number of injections and using stored treponemal preparations resulted in only partial protection characterized by delayed lesion development, atypical lesions, and accelerated healing [15].

In a small study on yaws, Schöbl et al. [17] demonstrated that sc immunization of monkeys with heated (50°C for 1 hr) Treponema pertenue conferred complete protection against homologous challenge. This protection persisted for two years following immunization.

Prerequisites for Development of a Treponemal Vaccine

The development of a practical, effective vaccine against the treponematoses is dependent on an understanding of the pathogenesis of the diseases, a knowledge of the immunologic mechanisms of resistance, a definition of the protective antigens, and a readily available source of these antigens. Most of the basic research to date has addressed these points with regard to venereal syphilis. The treponematoses differ in terms of affected organ systems, the presence or degree of tertiary involvement, and transplacental transmission; however, the natural histories of the infections and the histologic appearance of their lesions are similar. Consequently, the information gained in the examination of one treponemal infection may be applicable to the others.

Pathogenesis of treponemal infections. The pathogenic mechanisms of treponemal infections are not well defined. The organisms enter the body through mucous membrane or abraded skin and begin to multiply locally. They also rapidly gain access to the circulatory and lymphatic systems and disseminate throughout the body. It has been hypothesized that one of the first steps in infection is the attachment of the treponeme to the mammalian cell by specific receptor sites on the tip of the bacterium [23–25]. Most treponemes are seen in the extracellular spaces; however, they may also be found within cells [26–30]. The intracellular residence of treponemes may contribute to their ability to evade the host immune response and persist during the period of latency. The actual manifestations of syphilis (primary chancre, secondary skin rash, late destructive processes) are characterized by local active inflammatory reactions. Because the treponeme is not known to elaborate any toxin or to have any clear cytotoxic or cytopathic capability, the individual lesions and the tissue damage are thought to be due to the host’s immune response to the persisting bacteria.

Development of resistance during treponemal infections. The development of resistance to symptomatic reinfection has been recognized in venereal syphilis for many years, even before the discovery of T. pallidum as the causative agent. Hunter [31] reported in 1810 that persons with secondary syphilis no longer developed primary lesions following reinoculation, and subsequent studies by other investigators (reviewed in [32]) have confirmed and extended this observation. In a classic study, Magnuson et al. [32] demonstrated that persons with a history of treated or untreated syphilis showed responses to intradermal challenge with virulent T. pallidum that differed from responses in persons with no history of syphilis. Five patients with untreated late latent syphilis showed neither clinical nor serologic evidence of reinfection following challenge, and
Table 1. Description of early studies on the development of a treponemal vaccine.

<table>
<thead>
<tr>
<th>Immunizing preparation</th>
<th>Route*</th>
<th>Duration</th>
<th>Total dose†</th>
<th>Protection‡</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Treponema pallidum</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heated</td>
<td>id, im, ip, iv</td>
<td>≤4 months</td>
<td>&lt;3.8 × 10⁴</td>
<td>None</td>
<td>Eagle and Fleischman [7]</td>
</tr>
<tr>
<td>Stored frozen</td>
<td>sc, im</td>
<td>&lt;10 weeks</td>
<td>&lt;10⁷</td>
<td>None</td>
<td>Magnuson et al. [8]</td>
</tr>
<tr>
<td>Treated with Merthiolate§</td>
<td>id</td>
<td>12 weeks</td>
<td>3.6 × 10⁷</td>
<td>Partial</td>
<td>Waring and Fleming [9]</td>
</tr>
<tr>
<td>Dried in vacuo</td>
<td>im</td>
<td>26 weeks</td>
<td>1.2 × 10⁷</td>
<td>Partial</td>
<td>Waring and Fleming [9]</td>
</tr>
<tr>
<td>Lyophilized</td>
<td>sc</td>
<td>20 days</td>
<td>8.4 × 10⁷</td>
<td>Complete or partial</td>
<td>Tani et al. [10]</td>
</tr>
<tr>
<td>Treated with Antiformin‖</td>
<td>im, iv, footpad</td>
<td>16 weeks</td>
<td>6.9 × 10⁷</td>
<td>None</td>
<td>Izzat et al. [11]</td>
</tr>
<tr>
<td>Sonicated</td>
<td>im</td>
<td>7 weeks</td>
<td>3.12 × 10⁷</td>
<td>Complete or partial</td>
<td>Metzger and Smogór [12]</td>
</tr>
<tr>
<td>Aged with or without penicillin</td>
<td>iv</td>
<td>7 weeks</td>
<td>1.2 × 10⁷</td>
<td>Complete or partial</td>
<td>Metzger et al. [13]</td>
</tr>
<tr>
<td>Aged, 100°C for 1 hr</td>
<td>iv</td>
<td>7 weeks</td>
<td>1.2 × 10⁷</td>
<td>Complete or partial</td>
<td>Metzger et al. [13]</td>
</tr>
<tr>
<td>γ-Irradiated</td>
<td>iv</td>
<td>32 weeks</td>
<td>3.7 × 10⁷</td>
<td>Partial</td>
<td>Miller [14]</td>
</tr>
<tr>
<td>γ-Irradiated, stored at −200°C</td>
<td>iv, im</td>
<td>9 weeks</td>
<td>1.2 × 10⁸</td>
<td>Questionable</td>
<td>Miller [15]</td>
</tr>
<tr>
<td>Treated with glutaraldehyde</td>
<td>ip, iv</td>
<td>1 day</td>
<td>3 × 10⁷</td>
<td></td>
<td>Jones et al. [16]</td>
</tr>
<tr>
<td><em>Treponema pertenue</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heated, 60°C</td>
<td>sc</td>
<td>3–4 weeks</td>
<td>Not reported</td>
<td>Complete§</td>
<td>Schöbl et al. [17]</td>
</tr>
<tr>
<td>Heated, 80°C</td>
<td>sc</td>
<td>3–4 weeks</td>
<td>Not reported</td>
<td>None</td>
<td>Schöbl et al. [17]</td>
</tr>
<tr>
<td>Heated, 100°C</td>
<td>sc</td>
<td>3–4 weeks</td>
<td>Not reported</td>
<td>None</td>
<td>Schöbl et al. [17]</td>
</tr>
<tr>
<td><em>Treponema phagedenis</em> (Reiter)</td>
<td>iv, ip, sc</td>
<td>11 weeks</td>
<td>Not reported</td>
<td>Partial</td>
<td>Gelperin [18]</td>
</tr>
<tr>
<td><em>Treponema refringens</em> (Nichols)</td>
<td>sc</td>
<td>10–53 weeks</td>
<td>Not reported</td>
<td>None</td>
<td>Izzat et al. [19]</td>
</tr>
<tr>
<td>Sonicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with Merthiolate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with lysozyme</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>T. refringens</em> (Nichols)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>T. phagedenis</em> (Kazan)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Treponema minutum</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Treponema ambiguum</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Treponema microdentium</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Treponema paralitus-curvuli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spirocheta aurantia</td>
<td>id</td>
<td>1 day</td>
<td>10⁶–2 × 10⁸</td>
<td>Partial</td>
<td>Graves [21]</td>
</tr>
<tr>
<td>§ Merthiolate is a trade name for preparations of thimerosal.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>‡ Protection is defined as resistance to challenge with <em>T. pallidum</em>, unless otherwise indicated. Complete = no clinical or asymptomatic infection; partial = prolonged incubation period and/or altered lesion progression, or asymptomatic infection; and none = lesion development equivalent to that in immunized control animals.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>† Doses are expressed as numbers of organisms.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Abbreviations: id = intradermal; it = intratesticular.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>‣ Protection is defined as resistance to challenge with <em>T. pertenue</em>.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
13 of 26 persons with treated late latent syphilis showed no response to challenge. These observations demonstrate the development of active immunity during the course of infection and the persistence of that immunity following therapy. In the experimental rabbit model, the development of resistance has been shown to be dependent on the duration of infection as well as on the number of organisms contained in the initial inoculum [33]. Resistance persists throughout the course of untreated infection and, depending on the duration of untreated infection, can last for many months or years following antibiotic therapy. Immunity also develops during the course of yaws and endemic syphilis infection in humans [34], rabbits [35], and hamsters [36, 37].

**Mechanisms of immunity.** The role of antibody in protection against treponematid infection has been examined by the techniques of passive protection [38-44], in vitro-in vivo neutralization [45-47], and in vitro immobilization [48]. Generally, these studies have shown that antibody, in concert with complement, can immobilize *T. pallidum* in vitro [48] and render the organism noninfectious [47]. Passive immunization of hamsters with homologous immune serum completely protects the animals from endemic syphilis infection (i.e., infection with *T. pallidum*, Badia A strain) [49] and prevents the development of yaws lesions but does not protect against asymptomatic yaws infection [50]. Passive immunization of rabbits with antiserum to *T. pallidum* (Nichols strain) delays and alters lesion development following homologous challenge [38-44] but does not eradicate the challenge organisms.

There are several possible mechanisms for the protection provided by antibody. The most obvious mechanism is the direct killing of the organism by antibody and complement, as shown in vitro in immobilization and neutralization experiments. Miller [14], however, provided definitive evidence that immobilizing antibody is not required for resistance by his demonstration that animals immunized one year earlier with y-irradiated *T. pallidum* were completely immune to challenge but lacked demonstrable immobilizing antibody. Metzger and Smogor [12] also demonstrated resistance to challenge in immunized rabbits that lacked immobilizing antibody. These observations and the fact that passive administration of immune serum does not eliminate the infecting organisms indicate that the major contribution of antibody to resistance to primary treponematid infections may be not its bactericidal capability but its ability to interfere in other ways with a pathogenic mechanism.

Immune serum, presumably the immunoglobulin component, has been demonstrated to block the attachment of *T. pallidum* to mammalian cells [24, 25] and to extracellular matrix components [51] in vitro and may thus contribute to the partial protection demonstrated in the studies of passive immunization mentioned earlier. Opsonization may also be an important function of antibody in treponematid infections; immune serum has been shown to enhance significantly the phagocytosis of *T. pallidum* by rabbit macrophages [52]. Blockage of attachment and opsonization appear to be complement-independent functions. Azadegan et al. recently demonstrated that treatment with cobra venom factor abrogates protection in recipients of passively administered immune serum [53] but has no effect on resistance to challenge in animals cured of their primary infection [54]. These observations imply that the mechanisms of resistance operative in the two situations are different. That is, while bactericidal activity may play a role in protection from initial infection, complement-independent mechanisms are also capable of conferring resistance.

The persistence of organisms despite high antibody titers in natural infection illustrates that antibody alone is not sufficient to eradicate existing treponematid infection. Numerous investigators have examined aspects of cellular immunity in an attempt to broaden our understanding of the mechanisms of resistance; these workers have used lymphocyte blast transformation and lymphokine release assays as well as adoptive transfer. Their studies (reviewed in [55]) have shown that T lymphocyte sensitization occurs during the course of treponematid infection in humans and experimental animals and that these lymphocytes release soluble factors that activate macrophages [56]. Attempts to confer resistance by adoptive transfer of immune lymphocytes to naive recipients have met with mixed results. While Metzger and Smogor [57] demonstrated partial protection following challenge of rabbit recipients of immune spleen cells, Baughn and co-workers [58] were unable to transfer resistance to *T. pallidum* infection with immune cells, even in syngeneic rabbits. Schell and co-workers [59-61] showed that the adoptive transfer of T lymphocytes in the hamster models of
yaws and endemic syphilis did not prohibit primary lesion development but did result in accelerated healing.

The mechanisms of T cell–mediated protection in treponemal infection are not clear. Although no one has demonstrated a direct cytotoxic effect of lymphocytes on treponemes, Podwinska and Metzger [62] have recently shown that supernatant preparations from cultured, sensitized lymphocytes can kill *T. pallidum* in vitro. In other infections, T lymphocytes contribute to resistance by the elaboration of soluble factors that localize and activate macrophages for ingestion and destruction of the bacteria. The production of macrophage migration inhibitory factors (reviewed in [55]) and macrophage-activating factors [56] by *T. pallidum*–sensitized lymphocytes and the capacity of macrophages to phagocytize *T. pallidum* in vitro [52] have been demonstrated. Histologic studies have strongly implicated the T lymphocyte and the macrophage as the major infiltrating cells present in healing primary lesions in rabbits [63–65], and treponemes have been identified in macrophages in healing lesions by immunofluorescence [65, 66] and electron microscopy [67]. It appears that both humoral and cellular components of the host response have important roles to play in immunity to treponemal infection; future investigations of vaccine development should reflect our new awareness of the role of both arms of the immune response.

The search for protective antigens. Because the protective antigens of pathogenic treponemes have not been defined, a well-directed attempt to produce a treponemal vaccine is not yet possible. Although the vaccine studies already described have provided some information concerning the nature of the protective antigens, the hypotheses reached by the various investigators are contradictory. Tani et al. [10] hypothesized that the protective components are buried deep within the treponeme and that harsh treatment (such as that with Antiformin) is required to unmask the antigens for presentation to the immune system. Metzger et al. [13] demonstrated that the protective capacity of their “aged” vaccine was destroyed by incubation at 100°C for 1 hr and concluded that the important immunogen is a heat-labile protein. Schöbel et al. [17] showed that the protective capacity of their preparation of *T. pertenue* was also lost following heating at 80°C or 100°C for 1 hr. Miller, on the other hand, stated that the protective component is a loosely associated, heat-stable polysaccharide [14].

In recent years, the antigentic structure of *T. pallidum* has been examined by means of SDS-PAGE and Western blotting techniques [68–72], radioimmunoprecipitation [73–76], pathogenic and monoclonal antibody studies [77–79]. As a result of these studies, a fairly clear antigentic profile of the Nichols strain of *T. pallidum* has emerged; this profile includes the identification of at least 22 separate antigentic polypeptides (figure 1). A number of these molecules have been shown to contain antigentic determinants also found in the nonpathogenic *Treponema phagedenis*.

![Figure 1. Antigenic profile of Treponema pallidum. Nichols strain, as revealed by autoradiography with pooled human syphilitic sera and 125I-labeled protein A. Treponemes were disrupted by sonication, solubilized in SDS, and electrophoresed on 12.5% polyacrylamide gels prior to electrophoretic transfer onto nitrocellulose paper for reaction with antibody and 125I-labeled protein A. Twenty-two antigenic molecules were identified; approximate molecular weights are shown.](image-url)
biotype Reiter [68, 69, 76], pathogenic T. pertenue [80, 81], and other spirochetes [82]. Two molecules that have been identified only in T. pallidum, T. pertenue, and Treponema paraluis-cuniculi appear to contain pathogen-specific determinants. Other molecules appear to contain both common and pathogen-specific determinants on the same polypeptide. It is not yet known whether these antigenic determinants are protein or carbohydrate moieties.

Although the ability of these molecules to stimulate the host immune response is being examined in several laboratories, our current knowledge of the participation of any of these specific antigens in pathogenesis or resistance is limited. Baseman and Hayes [73] have identified three proteins (of 72,000, 28,000, and 26,000 daltons, respectively) that are thought to be associated with the attachment of treponemes to mammalian cells. Jones et al. [83] have recently shown that a monoclonal antibody with specificity for a determinant on a 47,000-dalton molecule can immobilize T. pallidum in the presence of complement. However, much work remains to be done in the definition and characterization of treponemal antigens.

Source of treponemal antigens. In the past, treponemes for antigenic analysis or vaccine studies have been obtained by extraction from infected rabbit testes. Consequently, the acquisition of large quantities of organisms has been an expensive and time-consuming process. Although significant progress has been made in the retention of viability and short-term propagation of T. pallidum in tissue culture systems [84], continuous cultivation has not been achieved. The recent application of gene-cloning techniques to treponemal research may finally provide investigators with a ready source of treponemal antigens, thus facilitating studies of potentially important molecules. Several laboratories have reported the expression of treponemal antigens in Escherichia coli [85–87]; investigations are currently underway to determine the immunogenic potential of these molecules. Gene-cloning technology will unquestionably be useful in the production of large quantities of antigens for future vaccine preparations.

Scope of Potential Vaccines

The pathogenic treponemes have numerous antigens in common, and active infection with one strain or subspecies provides some protection against infection with another treponeme in humans [34] and experimental animals [35, 88]. The relative absence of venereal syphilis in areas with a high prevalence of yaws has been postulated to be due to this cross-protection. Significant differences between the protective antigens of various strains and subspecies of T. pallidum are revealed, however, by the lack of complete resistance to heterologous organisms. Miller [14] demonstrated that animals immunized with γ-irradiated T. pallidum (Nichols strain) were completely resistant to homologous challenge but experienced only a slightly extended incubation period following intradermal challenge with the Haiti B strain of T. pertenue. Conversely, Schöbl et al. [17] demonstrated that T. pertenue-immunized monkeys that were resistant to homologous challenge were susceptible to infection with T. pallidum. This antigenic heterogeneity has important implications for vaccine development. A multivalent preparation may be required to protect against different strains of T. pallidum as well as against different subspecies. The eradication of one treponemal disease by immunization of a population may simply open the door for establishment of another treponemal infection if the vaccine is not cross-protective.

Target Population for Immunization

Young children are at highest risk for acquiring nonvenereal treponemal infections, and exposure to venereal syphilis usually occurs after puberty. The administration of a vaccine preparation to infants and young children would thus be an appropriate approach for interrupting the spread of treponemal disease to susceptible persons. Clearly, infected persons must be treated, and a combination of mass treatment and immunization may be the optimal approach in areas of high prevalence. In regions in which a high proportion of treponemal infection is found in a particular subset of the population (i.e., venereal syphilis in homosexual males in the United States and Europe), vaccine administration may be targeted more precisely to the populations at highest risk, as is currently done with hepatitis B vaccine.

Practical Considerations for Treponemal Vaccines

The safety and efficacy of candidate vaccines for treponemal infections are of obvious concern.
First, the noninfectious nature of the vaccine preparation and the safety of administration to persons with past or present treponemal infection would need to be demonstrated. Magnuson et al. [32] demonstrated the development of gummatus lesions at the site of reinoculation in persons with past tertiary syphilis; thus, the potential exists for inducing serious hypersensitivity reactions by immunization of sensitized individuals. Secondly, a vaccine preparation that provided partial, rather than complete, protection might have the unfortunate effect of modifying the disease in subsequently infected individuals to a very subtle or asymptomatic form that could go unrecognized. This effect was noted in early studies of treponemal vaccine in rabbits. Finally, the effect of artificial immunization on interpretation of the results of screening tests for treponemal infection is important. If the antibody response to immunization cannot be differentiated from that to active infection, an important means of diagnosis of the treponematoses will be lost.

Summary and Conclusions

The high level of morbidity and mortality attributable to treponemal infections throughout the world demands the application of vigorous control efforts; artificial immunization is potentially an appropriate component of such efforts. Because the development of immunity following active infection or immunization with attenuated *T. pallidum* has been demonstrated, the production of an effective vaccine appears to be an attainable goal. Before a practical vaccine can become a reality, however, basic investigations of the antigenic structure of the etiologic agents and the mechanisms of immunity to treponemal infections must continue. Newly developed techniques in immunology and molecular biology have resulted in significant progress in the past decade. Continued funding for the training and support of young scientists and for the performance of basic and applied research is mandatory if the control of treponemal diseases is to be realized.

References

8. Magnuson HJ, Halbert SP, Rosenau BJ. Attempted immunization of rabbits against syphilis with killed *Treponema pallidum* and adjuvants. Journal of Venerable Disease Information 1947;28:267-71
17. Schöbel O, Tanabe B, Miyao I. Preventive immunization against treponematoses infections and experiments which indicate the possibility of antitreponematosus immunization. Phil J Sci 1930;42:219-37
27. Azar HA, Pham TD, Kurban AK. An electron microscopic study of a syphilitic chancre. Archives of Pathology 1976;90:143-50
34. Turner TB The resistance of yaws and syphilis patients to reinoculation with yaws spirochetes. American Journal of Hygiene 1936;23:431-48
44. Titus RG, Weiser RS. Experimental syphilis in the rabbit: passive transfer of immunity with immunoglobulin G from immune serum. J Infect Dis 1979;140:904-13
51. Fitzgerald TJ, Repesh LA, Blanco DR, Miller JN. Attachment of Treponema pallidum to fibronectin, laminin, collagen IV, and collagen I and blockage by immune rabbit IgG. Br J Vener Dis, 1984 (in press)
55. Washington, DC: American Society for Microbiology, 1984
57. Lukehart SA. Activation of macrophages by products of lymphocytes from normal and syphilitic rabbits. Infect Immun 1982;37:64-9
61. Schell RF, Chan JK, LeFrock JL, Bagasra O. Endemic syphilis:
transfer of resistance to *Treponema pallidum* strain Bonnia A in hamsters with a cell suspension enriched in thymus-derived cells. J Infect Dis 1980;141:752–8


72. Van Eijk RVW, van Embden JDA. Molecular characterization of *Treponema pallidum* proteins responsible for the human immune response to syphilis. Antonie Van Leeuwenhoek 1982;48:486–8


Potential for Development of Antibiotic Resistance in Pathogenic Treponemes


Penicillin has been widely used for many years for the treatment of yaws and other human treponematoses without the emergence of penicillin-resistant treponemal strains. However, experience with various bacterial pathogens serves to emphasize that resistance to penicillin and other antibiotics can suddenly appear after decades of exquisite sensitivity. The finding of plasmid DNA in at least one strain of Treponema pallidum, the reporting of several instances in which antibiotic treatment of syphilis has failed, and the demonstration that a recent clinical isolate of T. pallidum is resistant to erythromycin indicate that the pathogenic treponemes do have the potential to develop antibiotic resistance. Although it is impossible to predict when antibiotic resistance might become a significant problem in dealing with infections caused by these organisms, the vigorous pursuit of alternatives to antibiotic therapy for the control of human treponematoses seems prudent.

The efficacy of virtually every new antibiotic introduced into clinical practice has been compromised by the emergence of resistant organisms. However, despite the widespread use of penicillin in the treatment of yaws, syphilis, and other human treponematoses, penicillin-resistant strains of the pathogenic treponemal species have never been demonstrated. This situation has led some investigators to question whether or not the pathogenic treponemes have the genetic capacity to develop antibiotic resistance [1]. The finding of plasmid DNA in at least one strain of Treponema pallidum [2], the description of several cases in which antibiotic treatment of syphilis has failed, and recent experimental data from our laboratory indicate that treponemes do have the ability to acquire antibiotic resistance. Clearly, the development of antibiotic resistance is a potential threat in any bacterial system, and there is as yet no convincing reason to believe that pathogenic treponemal species will prove to be the exception. It is impossible to predict when or if antibiotic resistance will become a significant problem in dealing with infections caused by Treponema pertenue, T. pallidum, and other pathogenic treponemes. The purpose of this brief review is to discuss the potential for and consequences of the emergence of antibiotic-resistant strains of treponemes.

Humans constitute the only known reservoir for T. pertenue, and infection with this organism can be effectively eliminated with penicillin. Mass penicillin treatment campaigns in the 1950s and 1960s resulted in drastic reductions in the incidence of yaws and other nonvenerale treponematoses [1]. At one point the eradication of yaws was deemed possible if intensive surveillance for active cases were vigorously maintained. Unfortunately, often as a result of economic factors, adequate surveillance was not uniformly maintained, and endemic foci of yaws have again emerged in a number of countries [1]. Current therapy for yaws still depends almost entirely on penicillin; alternative drugs have not been tested extensively. The tetracyclines and chloramphenicol were used successfully for the treatment of yaws in limited clinical trials in the 1950s [3, 4]. However, we could find no recent information concerning the efficacy of tetracycline, chloramphenicol, erythromycin, or the cephalosporins in the treatment of yaws. Thus, in the event that penicillin-resistant strains of T. pertenue do become a problem, well-tested alternative antimicrobial agents may not be readily available.

Considerably more information has been obtained concerning the susceptibility to antibiotics of the
syphilis agent *T. pallidum*. Since this pathogenic treponemal species is virtually indistinguishable from *T. pertenue* by a number of criteria [5–8], such information is most likely applicable to the yaws agent as well. Because of the inability of researchers to cultivate treponemes in vitro for sustained periods, antibiotic sensitivity testing has been largely confined to empirical clinical trials, in vivo experiments examining the rate of clearance of treponemes from infected rabbit tissues in the presence of various antibiotics, and in vitro observations of the effect of antibiotics on the motility of treponemes extracted from infected rabbit testes [9, 10]. Almost all of these experiments have employed the Nichols strain of *T. pallidum*, first isolated from the cerebrospinal fluid of a syphilitic patient in 1912 and maintained since that time by passage in rabbits. As far as can be ascertained, this strain has never lost its pathogenicity for humans [5].

On the basis of many studies, penicillin remains the antibiotic of choice for the treatment of infection with *T. pallidum* [5, 9–11], and there seems to be little concern that resistance to penicillin will develop in this bacterium [1]. We found two reports of instances in which penicillin treatment of syphilis failed. In one of these cases, the infection was subsequently cured by extended retreatment with penicillin; this pattern may suggest chromosomally encoded, low-level resistance to the antibiotic [12]. The second reported case was that of a child who died of congenital syphilis [13]. Viable, virulent organisms were recovered from this child at autopsy in spite of 17 days of high-dose penicillin treatment. Although such a finding certainly suggests that this instance of treatment failure resulted from infection with a *T. pallidum* strain exhibiting high-level penicillin resistance, such resistance was not in fact demonstrated, and the lack of subsequent reports of similar cases probably indicates that resistance is not the correct explanation.

Alternative antibiotics for use in patients with syphilis who are allergic to penicillin are limited. Chloramphenicol, tetracycline, erythromycin, and cephalosporins have all been shown to be efficacious for therapy [10, 14]. However, chloramphenicol is not currently used because of its potential toxicity, and tetracycline is not recommended for use in pregnant patients or young children because of its effect on bones and teeth [14]. Instances of erythromycin treatment failure have been well documented, and congenital syphilis has occurred in infants whose mothers responded to erythromycin treatment [15–17]. Cephalosporins have not been extensively tested but—except for cost and potential cross-reaction allergic responses in penicillin-allergic patients—appear to be acceptable alternative agents [14, 19–21]. Streptomycin has been effective against syphilis in experimental rabbits, but only at doses toxic for humans, and rifampin has been ineffective in similar studies [10, 11, 14].

An important question would appear to be whether or not strains of *T. pallidum* that are currently responsible for causing syphilis are as sensitive to antibiotics as the original Nichols strain. We recently compared the in vitro sensitivity of three pathogenic treponemal strains to several antibiotics that either directly or indirectly inhibit protein synthesis (authors’ unpublished observations). The three strains tested were the Nichols strain of *T. pallidum*, a recent (1977) clinical isolate of *T. pallidum* designated street strain 14 (provided by Sandra Larsen of the Centers for Disease Control, Atlanta), and the Gauthier strain of *T. pertenue*. To test these strains we devised a medium for the efficient radiolabeling of pathogenic treponemes with [35S]methionine [8]. Under our experimental conditions radiolabel was incorporated linearly into treponemes freshly extracted from infected rabbit testes for at least 16 hr.

It appeared that a full complement of treponemal proteins was synthesized throughout this period [8]. For antibiotic susceptibility testing treponemes were incubated in the presence of the test antibiotic for 4 hr prior to the addition of radiolabel. [35S]Methionine was then added to each sample, and incubation was continued for another 4 hr. The incorporation of radiolabel into protein was then determined and compared with that in a control sample incubated without antibiotics. Our results are presented in Table 1.

In this experiment we employed two concentrations of each antibiotic. The lower concentration represented a level achievable in the serum of patients taking the drug according to currently recommended regimens. The higher concentration represented 10 times the "therapeutic" level and was chosen in the hope that we did not overlook an effect of the drug. The results for each of the treponemal strains tested generally corroborated the results of earlier studies. Chloramphenicol and tetracycline effectively inhibited protein synthesis in vitro in all three strains. Interestingly, treponemes exposed to inhibitory concentrations of these antibiotics for 8 hr remained fully motile; therefore, motility does not appear to
Table 1. In vitro sensitivity of three pathogenic treponemal strains to various antibiotics.

<table>
<thead>
<tr>
<th>Antibiotic, concentration (µg/ml)</th>
<th>Treponema pallidum</th>
<th>Treponema pertenue, Gauthieri</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nichols</td>
<td>Street 14</td>
</tr>
<tr>
<td>None</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>92.5</td>
<td>68.9</td>
</tr>
<tr>
<td>200</td>
<td>93.3</td>
<td>87.9</td>
</tr>
<tr>
<td>Tetracycline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>86.9</td>
<td>78.3</td>
</tr>
<tr>
<td>40</td>
<td>94.5</td>
<td>96.9</td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>86.8</td>
<td>0.0</td>
</tr>
<tr>
<td>130</td>
<td>89.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Streptomycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>32.6</td>
<td>6.4</td>
</tr>
<tr>
<td>500</td>
<td>60.9</td>
<td>8.3</td>
</tr>
<tr>
<td>Rifampin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>24.8</td>
<td>0.0</td>
</tr>
<tr>
<td>100</td>
<td>41.5</td>
<td>3.0</td>
</tr>
</tbody>
</table>

NOTE. Freshly extracted treponemes were washed and resuspended in the radiolabeling medium [8] to a density of 3–6 x 10^6 cells/ml. The treponemes were next incubated in the presence of an antibiotic for 4 hr and then radiolabeled with [35S]methionine for 4 hr (see text). The incorporation of label into protein was measured by precipitation with trichloroacetic acid (TCA). The inhibition of protein synthesis was calculated as a percentage based on a comparison of TCA-precipitable counts per minute (cpm)/ml of the antibiotic-treated sample with that of the untreated control sample. Each control sample yielded TCA-precipitable counts in excess of 10^6 cpm/ml.

be a sensitive or valid in vitro indicator of antibiotic sensitivity. Rifampin had little effect on protein synthesis, and streptomycin had only a modest effect at the higher (toxic) concentration. Erythromycin effectively inhibited protein synthesis in T. pertenue and the Nichols strain of T. pallidum. However, somewhat surprisingly, this antibiotic had virtually no effect on protein synthesis in T. pallidium street strain 14, even at the higher concentration tested. Thus, this treponemal strain appeared to exhibit high-level resistance to erythromycin.

We subsequently learned in a personal communication from D. S. Kellogg of the Centers for Disease Control that T. pallidum street strain 14 was originally isolated from a penicillin-allergic patient with an active case of secondary syphilis against which erythromycin therapy had failed. This patient received first a total of 10 g of erythromycin over a five-day period in the hospital and then a total of 20 g over a 10-day period as an outpatient. Because of a persistent vasculitic skin rash and a positive result in the Venereal Disease Research Laboratory test, the patient was treated in the hospital for 30 additional days, with 500 mg of erythromycin administered four times per day. While still under hospital observation after this additional therapy, the patient developed scrotal lesions that were dark-field positive. It was at this time that street strain 14 was isolated. Since street strain 14 is clearly resistant to erythromycin in vitro, the evidence strongly indicates that erythromycin-resistant strains are responsible for at least some of the reported episodes of erythromycin treatment failure. This case represents the first demonstration of the appearance of clinically relevant antibiotic resistance among the pathogenic treponemes.

The mechanism of erythromycin resistance in street strain 14 is currently being investigated. At this point we cannot say whether or not the resistance determinant in this strain is an acquired one. There certainly are examples of transferable determinants of erythromycin resistance in both gram-positive and gram-negative bacteria; some of these determinants are located on transposons (as reviewed in [22]). An observation of some importance in this regard was the finding of a multicopy 7.5-megadalton plasmid in the Nichols strain of T. pallidum [2]. The demonstration of a plasmid in a pathogenic treponeme suggests that these organisms may have the potential to exchange genetic information via conjugation or other mechanisms. Furthermore, since plasmids are likely targets of transposons, treponemes may have the potential to acquire plasmid- and/or transposon-mediated antibiotic resistance. Such a potential should not be unexpected since resistance of these types has been found in numerous bacterial pathogens. (For reviews, see [23, 24].)

It is difficult to assess accurately the potential consequences of the appearance of antibiotic-resistant strains of T. pertenue or T. pallidum. Certainly, the development or acquisition by these strains of resistance to agents other than penicillin should not have a major effect on the control of human treponematoses. On the other hand, the appearance of strains with high-level penicillin resistance would require a substantial change in treatment practices and would probably have an adverse economic effect on control efforts. Because a sufficient number of effective antibiotics are available and have been tested against T. pallidum, the development of penicillin
resistance in this organism would not portend disaster. However, antibiotics other than penicillin, tetracycline, and chloramphenicol have not been tested in T. pertenue infections, and no relevant clinical or experimental antibiotic testing has been done since 1956. In 1982 a World Health Organization scientific group indicated that alternative antibiotics for the treatment of yaws in penicillin-allergic patients needed to be evaluated [1], but to our knowledge such studies still have not been reported. Should high-level penicillin resistance emerge in *T. pertenue*, there will be an urgent need for large-scale trials of alternative antibiotics and further in vitro testing in systems such as the one we have recently developed.

In summary, the fact that penicillin-resistant treponemal strains have not yet been encountered after many years of reliance on this one antibiotic should not give anyone a feeling of complacency. Experience with *Neisseria gonorrhoeae*, *Streptococcus pneumoniae*, and (more recently) viridans *Streptococcus* [25] serves to emphasize that resistance to penicillin can suddenly appear after decades of exquisite sensitivity. Penicillin-resistant strains of *S. pneumoniae* and viridans *Streptococcus* were originally isolated in Africa and may well represent “survivor” strains selected by the massive penicillin campaigns of the 1950s and 1960s. We have presented sufficient evidence at least to strongly suggest that treponemes do have the potential to acquire resistance determinants. For this reason, and since total eradication of yaws with penicillin has been tried and has not been achieved, the vigorous pursuit of alternatives to antibiotic therapy (i.e., vaccines) for the control of human treponematoses seems prudent.

References

16. South MA, Short DH, Knox JM. Failure of erythromycin etolate therapy in uto syphilis. JAMA 1964;190:70-1
Therapy for Nonvenereal Treponematoses: Review of the Efficacy of Penicillin and Consideration of Alternatives

Stuart T. Brown

Penicillin therapy has been a crucial element in public health programs for control of nonvenereal treponematoses. The recommendations made by the World Health Organization on penicillin therapy and the literature substantiating the effectiveness of penicillin therapy are reviewed. In mass public health programs, the recommended penicillin regimen can confidently be used. Although penicillin is the drug of choice for all treponemal infections, some individuals will be allergic to this drug. For these persons tetracyclines are the most thoroughly evaluated alternative antimicrobial agent and seem highly effective. However, further comparative evaluations of various tetracycline regimens are needed if tetracyclines are required by more than the occasional individual. The long-acting tetracyclines may be particularly appropriate in minimizing problems of compliance.

Penicillin was established as an effective treatment for treponematoses in the 1940s. Subsequent laboratory experiments, controlled clinical trials, and public health programs all underscored the effectiveness of penicillin in the therapy for nonvenereal treponemal infections. On the basis of these observations, various expert groups have recommended penicillin as the drug of choice for the treatment of treponematoses [1-4]. In this article these recommendations are reviewed and supporting information on penicillin from both control programs and clinical trials is examined.

Allergy to penicillin may be more common today than in the 1950s and 1960s, since it is possible that populations suffering from nonvenereal treponematoses have had more exposure to penicillin today than during the era before mass treatment campaigns. Therapeutic alternatives for penicillin-allergic individuals with nonvenereal treponematoses have not been recommended. Information related to the effectiveness of potential alternatives is reviewed, and agents for further consideration and possible study are proposed.

Recommendations for Therapy: Summary

By the time of the meeting of the World Health Organization (WHO) Expert Group in 1952, information was available on the susceptibility of the treponemes to penicillin [1]. In addition, penicillin had become widely available. A stable, repository form of penicillin, procaine penicillin in 2% aluminum monostearate (PAM), had been developed and standardized; and the pharmacology of this preparation was known. Studies of the clinical efficacy of PAM for the treatment of venereal syphilis and nonvenereal treponematoses had been conducted. Thus, this committee was able to consider recommendations for therapy in mass campaigns against treponematoses. Since penicillin was one of the most expensive aspects of these campaigns, the committee focused on the minimum therapeutic regimen that would both halt disease progression and limit continued transmission of disease. The minimum dose of PAM recommended for adults was 1.2 million units given in a single dose; appropriately lower doses were recommended for children (table 1). The committee also noted that many new cases of treponemal infection found on reexamination of populations resulted from patients who were incubating infection or who had latent infection at the time of the initial mass survey and therapy. Therefore, the committee felt that it was feasible to treat physical or family contacts or latent cases in addition to the clinically apparent cases. One-half of the total dose used to treat an active case was considered adequate for these contacts and latent cases.

The Second International Conference on the Control of Yaws was held in 1955 after control programs had been implemented in many countries (table I) [2]. The stat dose of 1.2 million units of
Table 1. Highlights of recommendations for therapy in programs to control nonvenereal treponematoses.

<table>
<thead>
<tr>
<th>Recommending group, year [reference]</th>
<th>Drug and dose for treatment of active yaws in adults (in children)</th>
<th>Policy on contacts and latent cases (dose)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO Expert Committee on Venereal Infections and Treponematoses, 1952 [1]</td>
<td>PAM: 1.2 million units im stat (appropriately smaller dose)</td>
<td>Feasible to treat (use one-half dose for active cases)</td>
<td>Specifications for PAM proposed</td>
</tr>
<tr>
<td>Second International Conference on Control of Yaws, 1955 [2]</td>
<td>PAM: 1.2 million units im stat (younger than 15 years; use one-half dose)</td>
<td>Should treat</td>
<td>Operational definition of whom to treat as latent cases or contacts based on disease prevalence: total mass treatment (&gt;10%), juvenile mass treatment (5%-10%), and selective mass treatment (&lt;5%)</td>
</tr>
<tr>
<td>WHO Expert Committee on Venereal Infections and Treponematoses, 1960 [3]</td>
<td>PAM: 1.2 million units stat (younger than 15 years; use one-half dose)</td>
<td>Should treat (use one-half dose for active cases)</td>
<td>Penicillin allergy reviewed</td>
</tr>
<tr>
<td>WHO Scientific Group on Treponemal Infections, 1980 [4]</td>
<td>Benzathine penicillin: 1.2 million units im stat (younger than 10 years; use one-half dose)</td>
<td>Should treat (use full dose for active cases)</td>
<td>Potential drugs for penicillin-allergic patients: tetracycline, chloramphenicol, erythromycin</td>
</tr>
</tbody>
</table>

NOTE. WHO = World Health Organization; PAM = procaine penicillin in oil with aluminum monostearate.

PAM was found to be effective for cases of active yaws and both safe and applicable to field settings. Although data were available from Haiti on the effectiveness of one-half of this dose (600,000 units of PAM), most participants thought that the margin of safety of the larger dose was preferable for control programs. The participants simplified recommendations for treatment of children by suggesting that all persons younger than 15 years of age be treated with one-half of the adult dose. By the time of this meeting, participants felt more confident that contacts and patients with latent yaws should receive preventive treatment and recommended that they receive one-half of the dose given to those with active yaws. Moreover, a more specific operational definition of persons who needed such treatment based on the prevalence of active disease in the population was proposed by participants. Treatment of the entire population, total mass treatment, was proposed for settings where >10% of the population had active yaws; treatment of active cases and all contacts and pubertal children, juvenile mass treatment, was recommended where disease prevalence was 5%-10% and only treatment of active cases and household and other obvious contacts, so-called selective mass treatment, was recommended for areas where disease prevalence was <5%. There was no perceived need to consider alternatives to penicillin; therefore, conference participants did not discuss alternative regimens for patients allergic to penicillin.

The 1960 WHO Expert Committee endorsed the recommendations made at the 1955 international conference (table 1) [3]. Again, although the effectiveness of the regimen used in Haiti was noted, the regimen using the larger dose was adopted. The committee report contained a sizable section devoted to reactions to penicillin and cited unpublished information from the United States that suggested the frequency of reactions to penicillin injections had nearly doubled between 1954 and 1959. Neither anaphylactic nor accelerated allergic reactions were separated from other types of reactions in these data. The report went on to note that although serious reactions had been rare in programs for the endemic treponematoses, "the possibility of these becoming a problem of wider public health importance should not be underestimated." The report continued with a section devoted to drugs other than penicillin and noted that no suitable parenteral preparations that could be considered practical were available.

The 1980 WHO Scientific Group noted the de-
creased availability of PAM in countries throughout the world [4]. Furthermore, the information on quality control concerning adherence of commercially available PAM preparations to WHO specifications was classified as incomplete. Because of these concerns and because benzathine penicillin was generally available, the group recommended benzathine penicillin rather than PAM (table 1). In addition, it advised that contacts and patients with latent yaws should receive doses equal to those administered to patients with active yaws. Finally, the definition of a child, for purposes of therapy, was changed from one younger than 15 years to younger than 10 years. Alternative modes of therapy for penicillin-allergic patients were not recommended, although the group indicated that such alternatives needed to be evaluated. This group did make recommendations for the treatment of penicillin-allergic persons with venereal syphilis.

The Use of Penicillin in Public Health Programs

The effectiveness of the treatment recommendations and of some management principles can be inferred from the experiences in public health programs. Considerable information was available to the groups that formulated program policies. Although only a portion of these data were published, these reports provide valuable evidence supporting the recommendations.

Efficacy of PAM. In the Bosnia, Yugoslavia, campaign against endemic syphilis, a single dose of PAM was as effective as a multiple-dose regimen of PAM [5]. This observation had great practical importance for public health programs. In addition, the Bosnia campaign was the first large-scale control program undertaken by WHO. As a consequence, the regimen of a single dose of PAM was quickly adopted by many of the new treponematoses control programs. Programs in Western Samoa and Netherlands New Guinea (Irian) used the recommended single dose of 1.2 million units of PAM to treat >95% of the total population at an initial treatment survey [6, 7]. When resurveys were conducted a year later, the prevalence of active yaws in Western Samoa had declined from 11% to 0.06% [6]. In Irian, the estimates of yaws incidence before and after the mass treatment campaign declined from 820 to 40 per 100,000 population [7]. Most of the cases of yaws identified during the resurveys in Irian were persons who had been absent when the initial survey team visited their homes or who had emigrated from areas not covered by the initial treatment campaign. A one-year follow-up of a selected group of treated patients with yaws found that the failure rate was <1% in this country [7]. A dose of 1.2 million units of PAM was also used successfully in the program in Iraq to treat 2,500 patients with bejel [8]. Clinical cures occurred in all cases observed for three months after treatment.

Treatment of contacts and latent cases. Initial efforts for disease control focused on mass clinical screening to identify symptomatic infected patients; these patients were then treated. However, many people in Bosnia who developed disease between the initial and follow-up examinations had apparently acquired disease from other family members who had been asymptomatic at the time of the initial examination [5]. Persons who transmitted disease either had latent cases and an infectious relapse or had developed infectious disease from an incubating infection; data from several family trees supported this hypothesis. In addition, 96 families in which there was a case of infectious endemic syphilis were entered into a special study. These families were divided into two groups. Seventy-two children were in one group in which all family members received treatment; none of the children in these families had developed syphilis at the time of the six-month follow-up. Seventy-eight children were from the group of families in which only active cases were treated; 28 of the 78 children in these families had developed syphilis at the time of the six-month follow-up evaluation.

Program experiences also supported the value of treating contacts and patients with latent yaws. As noted above, the Irian and Western Samoan programs recorded a decline of >95% in the prevalence of yaws in one-year follow-up surveys [6, 7]. In these programs, patients with latent yaws and contacts were all treated, thus assuring that all patients with latent yaws and contacts received therapy. In contrast, the Indonesian program recorded a more modest decline in the prevalence of yaws from 10% to 3.4% at the one-year follow-up [9]. Although there are many differences in the programs conducted in these three different sites, one striking difference was that in Indonesia only patients with active yaws received treatment; no patients with latent yaws and few contacts received treatment. The Indonesians also noted that only 90% of yaws cases were cured with a stat dose of 2.4 million units of PAM. Thus,
the large stat dose of PAM resulted in a lower cure rate than that observed in the other programs. The lower cure rates and the modest effect on yaws prevalence noted in Indonesia may reflect the greater opportunity for reinfection from untreated contacts and patients with latent yaws.

Clinical Trials with Penicillin

Shortly after penicillin was found to be highly effective in the therapy for early syphilis, investigators found that this drug was equally effective in the treatment of nonvenereal treponematoses. Although nonvenereal treponematoses are considered to be more sensitive to penicillin therapy than is syphilis, serologic response to treatment is much less rapid and complete. Thus, one year after penicillin therapy, which cured early yaws infections, only 16% of the patients became seronegative [10]. In contrast, 70% of patients with early syphilis became seronegative one year after curative therapy with penicillin. Because seroresponse is so much slower in yaws, criteria for cure are limited to clinical findings, rather than the combined clinical and serologic criteria so widely used in trials against syphilis.

A trial of therapy for yaws in 1948 compared two regimens of penicillin in oil with beeswax (POB) with a regimen of sodium penicillin (table 2) [10]. A total of 500 patients with primary or secondary yaws were entered into the trial; 447 (89%) were observed for a year. Lesions became dark-field negative 8–10 hr after treatment, and patients’ bone and joint pains remitted in 24–48 hr. All patients were clinically cured at the time of their first follow-up visit, but no mention is made of late relapses and/or reinfection. The serologic tests (Kahn) became nonreactive in 16% of patients overall. Patients who were hospitalized for treatment with sodium penicillin were noted to develop a brief fever of 100–104°F shortly after penicillin injections began, apparently a Jarisch-Herxheimer response.

A second, larger study of the use of three different POB regimens for treatment of early yaws was reported in 1952 (table 2). Nearly two-thirds of these patients were observed for a year; the overall clinical cure rate for the year exceeded 95%. Small differences were noted between the regimens. Since these were not randomized trials and no other comparison of these groups is made, it is uncertain whether the small differences noted are important.

The effectiveness of penicillin in the treatment of yaws was evaluated in studies conducted in Mexico (table 2) [12]. Although four different regimens of PAM were used, only two regimens, both of which used a total dose of 1.2 million units of PAM, were evaluated in groups of ≥100 patients. Only 53% of the patients were observed for a full year. The clinical and serologic cure rates for these two regimens were similar even though one was a single-dose regimen and the other was a regimen of four weekly doses. Substantial differences were noted in clinical response according to the stage of disease: 100% of patients with primary disease were cured, 69% of those with secondary yaws lesions were cured, and only 40% of those with late yaws lesions were cured. It should be noted that most patients improved, but the restitution of normal epithelium was incomplete.

The most extensive and carefully controlled study of the efficacy of PAM for the treatment of early yaws involved 1,049 Haitian patients who had dark-field-positive primary or secondary yaws lesions (table 2) [13]. Patients were treated with single-dose PAM regimens of 150,000–600,000 units and observed for ≥24 months. Outcomes of cumulative retreatment and cumulative seroconversion rates were studied as in previous investigations of syphilis therapy, but only clinical criteria were used to decide whether to re-treat patients. Because the collection of data, total size of the study, and methods of analysis were so complete, several crucial variables could be examined for their effect on the outcomes of treatment. Hume and Facio [13] found no differences in either cumulative retreatment rates or seroconversion rates by sex. However, a greater seroconversion rate occurred for younger patients than for those older than age 10. Hume and Facio postulate that these findings reflect the somewhat shorter durations of disease in children, hence a greater tendency for seroconversion. Paradoxically, they also noted higher retreatment rates for these younger patients. This finding was explained on the grounds that young children have greater exposure to active disease than do older patients. During the course of this work, two PAM preparations had been used; only one met the standards set by WHO. The cumulative retreatment rate for those treated with PAM of good quality was 0.6% at two years, whereas the retreatment rate for those treated with the PAM of poor quality was 5%. The small group of patients with primary yaws had a 24-month cumulative seroconversion rate of 73% compared with a seroconversion rate of 28%.
# Table 2. Clinical trials with penicillin therapy for nonvenereal treponematoses.

<table>
<thead>
<tr>
<th>Country, year [reference]</th>
<th>No., type of case</th>
<th>Treatment regimen</th>
<th>Percentage of cases with indicated results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clinical cure</td>
</tr>
<tr>
<td>Haiti, 1948 [10]</td>
<td>200, primary or secondary yaws</td>
<td>Sodium penicillin: 40,000 units im q 3 hr × 4 days</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>151, primary or secondary yaws</td>
<td>POB: 600,000 units im daily × 2 days</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>149, primary or secondary yaws</td>
<td>POB: 1.2 million units im stat</td>
<td>100</td>
</tr>
<tr>
<td>Haiti, 1952 [11]</td>
<td>450, early yaws</td>
<td>POB: 300,000 units im daily × 4 days</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>492, early yaws</td>
<td>POB: 600,000 units im daily × 2 days</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>258, early yaws</td>
<td>POB: 600,000 units im daily × 4 days</td>
<td>98</td>
</tr>
<tr>
<td>Mexico, 1952 [12]</td>
<td>392, pinta 11, pinta</td>
<td>PAM: 1.2 million units im stat × 4 days</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>29, pinta 233, pinta</td>
<td>PAM: 1.2 million units im weekly × 4 weeks</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAM: 300,000 units im daily × 4 days</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAM: 300,000 units im weekly × 4 weeks</td>
<td>53</td>
</tr>
<tr>
<td>Haiti, 1956 [13]</td>
<td>51, primary yaws</td>
<td>PAM: 600,000 units im stat</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>43, secondary yaws</td>
<td>PAM: 150,000 units im stat</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>129, secondary yaws</td>
<td>PAM: 300,000 units im stat</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>826, secondary yaws</td>
<td>PAM: 600,000 units im stat</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>17, yaws hyperkeratosis</td>
<td>Benzathine penicillin: 1.2 million units im</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>35, early yaws</td>
<td>Benzathine penicillin: 0.6 million units im</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>22, yaws hyperkeratosis</td>
<td>Benzathine penicillin: 0.6 million units im</td>
<td>86</td>
</tr>
</tbody>
</table>

**NOTE.** POB = penicillin in oil and beeswax; and PAM = procaine penicillin in oil with aluminum monostearate.

for patients with secondary yaws; however, the retreatment rates were similar for these two groups.

Despite the excellent efficacy of PAM, Grin et al. [14] continued to search for other penicillin preparations that produced prolonged levels of penicillin in serum after administration. Dibenzylethylene-diaminedipenicillin G (benzathine penicillin G) was one salt that appeared promising. In the yaws program in Thailand, the effectiveness of stat doses of 1.2 million or 600,000 units of benzathine penicillin was excellent for patients with early yaws (table 2) [14]. Clinical cure rates were 97% and 100%, respectively, when assessed six months after treatment. Although few patients had become seronegative at six months, virtually all had decreases in their VDRL (Venereal Disease Research Laboratory) titer. Grin et al. [14] noted that the efficacy of this preparation was comparable with their earlier studies using.
1.2 million units of PAM, but they did not conduct direct comparative clinical trials. Patients with late yaws with hyperkeratosis responded less completely than did patients with early yaws to both PAM and benzathine penicillin, although the latter was more effective in the small study groups observed.

**Controlled Clinical Trials: Nonpenicillins**

Drugs that are considered potentially useful for treating penicillin-allergic patients with nonvenereal treponematoses include tetracyclines, chloramphenicol, and erythromycin [3]. These drugs may be ranked according to decreasing efficacy against treponematoses on the basis of experimental animal studies: (1) penicillin, (2) erythromycin, (3) tetracyclines, and (4) chloramphenicol [15]. Although penicillin causes more rapid disappearance of treponemes from lesions than do other drugs, clinical healing of lesions occurs in the same time for penicillin and for other drugs. Study of the short-term effectiveness of alternative antimicrobial agents can provide some insight into their efficacy; nonetheless, long-term studies of these agents are necessary. It is regrettable that few such studies have been conducted. Furthermore, direct comparison of regimens of PAM or benzathine penicillin with these alternatives is necessary to address problems of the comparability of various drugs.

More patients with nonvenereal treponematoses have been treated with tetracyclines than with any of the alternatives proposed for penicillin-allergic patients (table 3). Various regimens of tetracyclines

<table>
<thead>
<tr>
<th>Country, date [reference]</th>
<th>No., type of case</th>
<th>Treatment regimen</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold Coast, 1950 [16]</td>
<td>3 children, secondary yaws</td>
<td>Tetracycline: 500 mg po TID × 7 days</td>
<td>Clinical cure at 6 weeks</td>
</tr>
<tr>
<td>Gold Coast, 1950 [17]</td>
<td>5 children, secondary yaws</td>
<td>Tetracycline: 250 mg po TID × 7 days</td>
<td>Clinical cure at 3-6 months</td>
</tr>
<tr>
<td>Gold Coast, 1951 [18]</td>
<td>2 children, tertiary yaws</td>
<td>Tetracycline: 500 mg po TID × 7 days</td>
<td>Clinical cure at 4-6 weeks</td>
</tr>
<tr>
<td>Gold Coast, 1951 [18]</td>
<td>6 children, secondary yaws</td>
<td>Tetracycline: 0.75 or 1 g po BID × 7 days</td>
<td>Clinical cure at 3 months</td>
</tr>
<tr>
<td>Haiti, 1951 [19]</td>
<td>30 patients, all ages and all stages of yaws; cases received the 10-g dose in either the 3-day or the 5-day regimen</td>
<td>Tetracycline: 5 g, 3 g, and 2 g on successive days</td>
<td>Two clinical relapses at 3 months</td>
</tr>
<tr>
<td>Haiti, 1951 [19] (addendum)</td>
<td>70 yaws patients</td>
<td>Tetracycline: 2 g po daily × 5 days</td>
<td>Clinical cure at 3 months</td>
</tr>
<tr>
<td>Haiti, 1951 [20]</td>
<td>65 yaws patients, all ages and stages</td>
<td>Tetracycline: 2 g po daily × 5 days</td>
<td>Clinical cure at 3 months</td>
</tr>
<tr>
<td>Jamaica, 1951 [21]</td>
<td>85 yaws patients, all ages and stages</td>
<td>Tetracycline: 3 g, 2 g, and 2 g po on successive days</td>
<td>Two reinfections and 2 relapses by 2 months</td>
</tr>
<tr>
<td>Jamaica, 1951 [21]</td>
<td>41 yaws patients</td>
<td>Tetracycline: 2 g po daily × 5 days</td>
<td>Clinical cure at 2 months</td>
</tr>
<tr>
<td>Jamaica, 1951 [22]</td>
<td>10 yaws patients</td>
<td>Tetracycline: 250 mg po QID × 14 days</td>
<td>83% clinical cure and 25% seroreversion (1 year)</td>
</tr>
<tr>
<td>Jamaica, 1953 [23]</td>
<td>8 yaws patients</td>
<td>Tetracycline: 250 mg po QID × 14 days</td>
<td>Clinical cure at 1 year</td>
</tr>
<tr>
<td>Haiti, 1954 [24]</td>
<td>120 yaws patients all ages and stages</td>
<td>Tetracycline: 250 mg im daily × 5 days</td>
<td>4 reinfections and 2 relapse/failures after 3-4 months</td>
</tr>
<tr>
<td>Jamaica, 1951 [21]</td>
<td>99 yaws patients</td>
<td>Chloramphenicol: 1 g po daily × 14 days</td>
<td>79% clinical cure and 29% seroreversion (1 year)</td>
</tr>
<tr>
<td>Haiti, 1951 [25]</td>
<td>36 yaws patients, all ages and stages</td>
<td>Chloramphenicol: various iv and po regimens</td>
<td>3 of 21 patients observed for 6 weeks had no healing of ulcers</td>
</tr>
</tbody>
</table>
eradicate treponemes from lesions, relieve bone and joint pains, and lead to healing of lesions [16–24]. The minimum duration of effective tetracycline therapy appears to be five days; three-day regimens were associated with clinical failures even in short-term studies [17, 19, 20]. The minimum daily dose required is uncertain but a 1-g or 2-g dose seems to be adequate.

The semisynthetic tetracyclines, doxycycline and minocycline, may be particularly useful to consider as alternative drugs for penicillin-allergic patients. At least doxycycline is now available as a generic preparation in some countries; thus, the cost per patient treated may be nearly as low as for standard tetracycline. Oral doses of these drugs are rapidly absorbed, with no effect of concomitant food administration on resultant serum levels. Serum levels are prolonged, allowing effective dosage schedules of two daily administrations. Finally, doxycycline has been effective for treatment of syphilis when administered twice daily [26–28].

Studies with chloramphenicol demonstrate that this drug has some activity against yaws infections (table 3). However, Hill [21] found that >20% of the patients treated and observed after a 14-g regimen had relapse. Results of clinical trials do not suggest that this regimen is sufficiently effective.

Discussion

Penicillins with prolonged action given in a single-session im dose are highly effective for treponemal infections. A 1.2-million-unit dose of PAM or benzathine penicillin G is adequate for cure of the nonvenereal treponematoses. The PAM regimen has been extensively evaluated in clinical trials and in public health control programs; the regimen with benzathine penicillin has been less extensively evaluated, but there is no doubt as to its efficacy. Therefore, mass public health programs can confidently use the recommended penicillin regimen.

There is widespread agreement that public health programs to control nonvenereal treponematoses are more effective when treatment is extended beyond the clinically apparent cases. Direct observations made in the Bosnia campaign and the indirect observations made in yaws programs emphasize the value of treating contacts and patients with latent yaws [5–8]. When such treatment is used, it is now recommended that contacts and patients with latent yaws receive the same dose as that for patients with active yaws. This practice will assure that persons with late incubating disease or with early, clinically inapparent primary lesions receive adequate therapy. Likewise, the use of full doses assures that persons with latent disease who have a clinically inapparent relapse receive a full curative dose.

The difficult problems of standardizing PAM preparations and of assuring that preparations meet the WHO specifications were noted by the fourth WHO Expert Committee in 1952 [1]. The greater biologic effectiveness of preparations of PAM that conform to these specifications was demonstrated in Haiti, where the two-year cumulative retreatment rates were 0.6% and 5% for those treated initially with PAM preparations that did and did not meet these specifications, respectively [9]. It is notable that the WHO Scientific Group of 1980 mentioned that, even today, some commercially available PAM preparations may not meet the WHO specifications [4]. Thus, the problem of adequate adherence to WHO specifications has continued for three decades. Use of PAM for the treatment of all infections has declined; as a consequence, PAM preparations are not available in many countries [4]. Since problems of quality assurance and availability are not as serious for benzathine penicillin as for PAM, the shift in recommendations may ensure general use of more effective therapy.

Although penicillin remains the drug of choice for public health programs to control nonvenereal treponematoses, the penicillin-allergic individual will require an alternative antimicrobial regimen. The magnitude of the problem of allergy to penicillin is uncertain. Since many severe allergic reactions to penicillin would have been immediately apparent to survey/treatment teams, the failure of reports to mention this as a problem is remarkable. It was suggested in 1960 that increasing availability and use of penicillin for medicinal, agricultural, and other purposes would result in large numbers of persons newly sensitized to penicillin. Is this possibility now a reality and, if so, would such an observation apply to the population affected by yaws, the people at "the end of the road"? More than 700,000 individuals received penicillin treatment in 1981–1983 in the program in Ghana; no anaphylactoid reactions were noted [26].

Tetracyclines are the most thoroughly evaluated alternative antimicrobial agents for the treatment of treponemal infections. In experimental animal
Penicillin Therapy for Yaws

studies, tetracycline has had good activity; clinical trials in syphilis have likewise proved the effectiveness of this agent [27, 28]. The few long-term follow-up studies of nonvenereal treponematoses identify tetracycline as also effective for treatment of these diseases. It is noteworthy that a five-day regimen seems an adequate duration of therapy for nonvenereal treponematoses when a daily dose of 2 g of tetracycline is used. Studies have not evaluated the effectiveness of the long-acting tetracycline, doxycycline, for the treatment of nonvenereal treponematoses. The advantages of a dosage schedule of two administrations daily make this a particularly attractive alternative. Parenteral tetracyclines have not been adequately evaluated to clarify whether a preparation could be developed that would lead to an effective single-dose regimen.

Among other antimicrobial alternatives, erythromycin has exhibited high activity in experimental animal studies, but its clinical effectiveness for syphilis is no greater than 90% [28]. Studies with this drug in the treatment of nonvenereal treponematoses have not been reported. Chloramphenicol, despite experimental effectiveness, appears ineffective for nonvenereal treponematoses. Although cephalosporins have activity in experimental studies [30, 31], their activity against nonvenereal treponematoses has not been evaluated in clinical trials. Their cost, the probable need for multiple-dose regimens, and the potential cross-reactivity in penicillin-allergic patients make the cephalosporins unlikely candidates as alternatives to penicillin.

Clinical trials need to be conducted that directly compare the recommended regimens of benzathine penicillin (or PAM) with regimens of alternative antimicrobial agents. These studies should address the question of efficacy and examine issues of compliance as well. The toxicity of these regimens should also be reviewed, emphasizing the bone and tooth effects in children and perhaps the effects in pregnant women.

Finally, there is the general growing problem of antimicrobial resistance in bacteria. The observation that one Treponema pallidum strain contains plasmid DNA material [32] is worrisome. Further, the documentation of erythromycin resistance in a treponeme emphasizes that this general problem may extend to these organisms [33]. Fortunately, resistance to penicillin has not yet been clearly demonstrated in laboratory studies, clinical trials, or control efforts. There is an urgent need to implement control programs, however, before this organism acquires resistance to penicillin.

References

Clinical Diagnosis and Changing Manifestations of Treponemal Infection

Ferdinand A. Vorst

From the Department of Public Health, University of Limburg, Maastricht, The Netherlands

The symptomatology of the papillomas of yaws as described in the literature pertains to the disease in highly endemic areas only. Yaws with milder symptoms—attenuated yaws—occurs in areas that, possibly because of climatic influences, have a low endemicity of yaws. Receding yaws that follows mass treatment in previously highly endemic areas also has the features of attenuated yaws. Yaws symptomatology during the early papillomatous stage may assume any variation within two extreme clinical syndromes: holoendemic yaws, which is characterized by innumerable large, elevated, exuding papillomas of long duration (up to three years), relatively short latent periods, and high reagin levels; and attenuated yaws, which is characterized by scanty—or only one—small, dry papilloma(s) of short duration (only a few weeks), a dominance of latency, and low reagin levels. The public health importance of attenuated receding yaws lies in its potential to revert to classic yaws with high rates of transmission.

Control of endemic treponematoses in a population is based on mass treatment with penicillin. Treatment policies for yaws—as established at the Second International Conference on Yaws in Enugu, Nigeria, in 1955 and described by Hackett and Guthc [1]—differ according to the extent of the treponemal reservoir in the population. The reservoir of infection consists of infectious clinical cases, latent cases that may give rise to new infectious clinical cases, and incubating cases. Incubating cases cannot be detected by any technique available, and latent cases can be detected only by serologic investigation. Large-scale serologic investigations are impractical in field situations, however, and were used in only one mass campaign (that against endemic syphilis in Bosnia, Yugoslavia [2]).

Fortunately, the prevalence of latent cases of yaws may be assessed by determining the prevalence of active clinical cases. Li and Soebekti [3] demonstrated that, for every person with a clinically active case of yaws, there are a total of three to four seropositive persons in the population, whatever the prevalence of clinical cases.

To allow for easy assessment of the treponemal reservoir in populations to be covered by mass treatment, the Enugu conference distinguished three levels of endemicity of yaws. (1) Hyperendemic yaws: >10% of the population have clinically active cases, a prevalence implying that up to 60% of the remaining population are seropositive—total mass treatment is needed to reduce the treponemal reservoir; (2) mesoendemic yaws: 5%–10% of the population have clinically active cases and 20%–40% are seropositive, both occurring primarily in children up to 15 years of age—juvenile mass treatment (treatment of all children and other obvious contacts) is considered adequate; and (3) hypoendemic yaws: <5% of the population have clinically active cases and <10% are seropositive—selective mass treatment (treatment of all with active cases plus household, school, and other obvious contacts) is necessary.

For the purposes of control campaigns, this protocol turned out to be adequate and to lead to impressive results in all the endemic areas. Yaws could be reduced to low prevalence—approaching eradication—or total eradication could be attained. This reduction was demonstrated, for instance, in Indonesia and Nigeria. Similar results were achieved for endemic syphilis in Bosnia.

The failure of control campaigns could be attributed, whenever it occurred, to insufficient coverage of the population, overly long intervals between consecutive surveys, or inadequate consolidation measures. Where coverage of at least 80% of the population was attained initially and during regular resurveys and where consolidation measures were adequate, the treatment protocols recommended by the Enugu conference, which were based on prevalence of clinical cases, were most effective.
Clinical Prevalence as a Criterion for Mass Treatment Policy

The value of the setting of three different levels of endemicity as established at Enugu was great; however, theoretical and even practical questions arise [1]. For instance, holoendemic yaws might be considered a distinct category, with a prevalence of clinical cases of $\geq 30\%$ and seropositivity reached at the age of five to six years in all individuals. The interval between resurveys has to be shorter in such areas unless coverage of at least $90\% - 95\%$ of the population has been attained at the initial treatment survey. Mesoendemic yaws, with a prevalence of clinical cases approaching $10\%$, may call for total mass treatment, which in fact was carried out in many such areas. Finally, hypoendemic yaws, with a prevalence of clinical cases of $\leq 5\%$, may describe, on one hand, the situation in populations with fairly active transmission, leading to active lesions in $3\% - 4\%$ of the population and to a substantial latent treponemal reservoir, and, on the other hand, may describe the situation in populations with very low transmission, leading to not more than a few lesions in thousands of individuals. The latter situation merits particular attention.

Value of Clinical Diagnosis

The publication by the World Health Organization (WHO) of the International Nomenclature of Yaws Lesions [4] helped considerably to attain international comparability for diagnostic categories. However, even for experienced auxiliary field staff, diagnosis of some of the lesions described was difficult, even in hyperendemic areas, where many lesions of all kinds were regularly encountered. Doubt also arose in situations where some of the other early lesions, such as macular, papular, and nodular yaws, were encountered. Also, it appears that the prevalence of early hyperkeratoses varies considerably in areas with the same endemic level. Furthermore, hyperkeratoses are likely to be either underdiagnosed or overdiagnosed by many staff because differential diagnosis is difficult.

The most easily identified lesions in many campaigns were therefore the papillomas and those of late active cases; the former are epidemiologically the most important lesions as sources of transmission of treponemes to susceptible persons and as indicators of recent transmission.

Characteristics of Papillomas

In all the textbooks and in almost all papers on yaws, papillomas are described as having a typical raspberry appearance, a diameter of $\leq 20$ mm, a yellowish color and as being elevated and moist. They can be present in large numbers (multiple papillomas) on all parts of the body except the scalp. Less typically, these lesions are described as flatter, with less of a raspberry appearance, a diameter of $\leq 10$ mm, as drier, as not being present in large numbers but still multiple, and as sometimes being limited to the moist skin folds of the neck, armpits, buttocks, and around the genitals. The literature abounds with excellent illustrations of such papillomas (see [4], for example).

Few authors have reported on papillomas with atypical features. Wilson [5], however, described cases of "atypical yaws" in Panama with almost no secondary eruptions and cases with only one papilloma. Fawkes [6] commented on the milder type of disease found since organized treatment began in Trinidad. Hackett [7], discussing the epidemiology of receding yaws, states that previously many patients in hyperendemic areas had numerous lesions, but, he writes, "Such abundance is not often seen now," and, he continues, "A characteristic of the papillomatous stage of receding yaws is the scantiness of papillomata in even the most heavily affected patient; these lesions are usually dry, whereas previously they would have exuded an abundant infectious serous discharge." In 1979, Niemel [8] described similar attenuated cases of yaws in Suriname.

Receding or Attenuated Yaws

The clinical changes of yaws papillomas in geographic areas that previously had a considerably higher prevalence was noted in many countries, but not many observations found their way into the literature. Retrospectively, these changes can be inferred from descriptions and reports from earlier periods that are available in health services in many countries and from personal observations.

The same sources reveal that the characteristics of "atypical" or "mild" yaws, described by Hackett [7], were found in areas where the prevalence had not been reduced by treatment but had always been low because of climatic circumstances not conducive to the transmission of yaws. These are geographic areas with higher altitude, where yaws had a lower
prevalence than in the neighboring lower plains and a milder symptomatology. Low prevalence and mild symptomatology have also been found in areas with low humidity. Such high-altitude areas are to be found in many endemic areas, among others, the Caribbean, the Pacific, and Indonesia. Such low-humidity areas are found, for instance, in West Africa, where fully developed lesions were prevalent in the humid coastal forest belts, and atypical lesions were prevalent in the drier areas in the savannahs away from the coast, with yaws even disappearing completely in some areas.

In such areas, yaws lesions are often atypical. Papillomas are present but scanty; in many cases only one papilloma is found, and those present are mainly confined to the hidden, moist skin folds. The lesions may become atypical, a phenomenon that makes diagnosis hazardous in the field. In Togo, an epidemiologic survey conducted by WHO in 1963–1965 [9] revealed that such atypical lesions with reduced features were found in the coastal area, which previously had hyperendemic yaws. During the survey, there was a prevalence of 0.2% of cases with papillomas and of 0.1% of cases with active late lesions. A prevalence of 4% of inactive sequelae of late lesions, mainly in older adults, indicated active transmission during earlier periods. Most of the papillomas found were scanty; in the majority of cases there was only one papilloma, which was small, hidden in skin folds, dry, flat, and greyish in color. Such lesions should be classified as those of receding yaws, as Hackett [7] had described previously. The relation of receding yaws to attenuated yaws will be discussed later.

**Duration of the Papillomatous Stage in Yaws**

In the earlier literature on yaws, many publications deal with descriptions of yaws symptomatology and mention the duration of the papillomatous stage. A few papers cover yaws in endemic areas all over the world: Callanan [10], Montel [11], van Nitsen [12], Hermans [13], Cartron [14], and Hunt and Johnson [15]. These authors and others all state that the papillomatous stage lasts from some months to some years and that successive crops erupt during this stage.

Hackett mentions the duration of the papillomas several times in his various papers [4, 7]. He states: "papillomata tend to occur at intervals for 2 to 3, up to 5 years after the date of infection. Probably each person infected with yaws is an infectious patient for at most 12 to 18 months." He further indicates that the average duration of the first collection of papillomas is approximately six months and that subsequent eruptions last another six months.

Kranendonk [16] undertook an objective assessment of the duration of papillomas in the then hyperendemic Asmat area in Irian Barat (Indonesia) by relating the average duration of the papillomas to the prevalence found in his field investigations and the estimated average life expectancy in the area under study. This approach was also used, with some variation, by Sellards [17]. For the Asmat area, Kranendonk arrived at an average duration for the papillomas of 1.7–3.5 years, using for his calculations an average life expectancy of 25–30 years. It is essential to note that he collected data in an area in which no treatment had occurred. Treatment interferes, of course, with any calculation of the average duration of the papillomas. Because Kranendonk's calculation was carried out on data collected in an area in which virtually no treatment had been provided and with a very high prevalence (most of the region having been opened to outsiders a few years before and medical staff having never penetrated the region), it is important to bear in mind the very long average duration (up to 3.5 years) calculated for papillomas in an extremely highly infected community.

The only indication in the literature of a connection between the prevalence of yaws and the duration of the papillomas is found in the work of van der Hoff [18], who studied two areas with endemic yaws in southwest Borneo (Kalimantan, Indonesia) and compared the characteristics of yaws in the two areas, each showing different prevalence. He found a longer duration of the papillomas in the area with the higher prevalence. Duration of the papillomas can also be calculated if data on incidence—infected from serologic surveys—are available, as well as data on prevalence.

One of the best studies in the earlier period was carried out by Turner and Saunders in Jamaica in 1935 [19]. They investigated two areas with high prevalence, one higher than the other. This excellent study, in which duration of the papillomas was inferred from data collected on prevalence and incidence, indicates a longer duration of the papillomas in the area with the higher prevalence.

Interesting data from the previously mentioned WHO survey in Togo allow further insight into the
duration of papillomatous lesions because of the fact that almost no penicillin had been administered in the very lowly endemic savannah area of northern Togo. Reliable data on prevalence were available from the survey and from the yaws campaign that was carried out simultaneously. Also, specific rates of seropositivity were available from a random sample of the population. (Rates of seropositivity were calculated with use of the following tests and adjusted for biologic false-positive reactions by means of Treponema pallidum immobilization [TPI] testing: Venereal Disease Research Laboratory [VDRL], Kline, Kolmer, and Reiter protein complement fixation.) Of children up to 15 years of age, 0.2% showed infectious lesions. Data on prevalence for the children two to four years of age had not been collected separately, but prevalence may be assumed to have been <0.2%, since the age of onset of yaws is relatively late in such hypoendemic areas. The children two to four years of age had, however, an adjusted rate of seropositivity of 2%. These data suggest the presence of papillomatous lesions with a short duration (approximately one month or only slightly longer); otherwise the clinical prevalence at a certain point should have been greater than <0.1 of the rate of yaws infection measured serologically. These data indicate that the ratio of rates of seropositivity to those of clinical prevalence may be much higher in areas of low endemicity than the 4:1 ratio suggested by Li and Soebekti [3].

Serologic Data in Highly and Lowly Endemic Yaws

D'Mello and Krag [20] demonstrated that average reagin titers (VDRL) are lower in individuals with latent yaws than in those with clinically overt yaws, especially early infectious yaws with papillomas. These authors also showed that the administration of penicillin results in a lower average VDRL titer. The same phenomenon was discussed by Li and Soebekti [3], Klokke [21], and Kranendonk [16].

In the Togo survey, the average VDRL titer was still substantially higher in a previously hyperendemic area in which treatment had occurred than in a hypoendemic area without treatment, even after the rate of seropositivity by the VDRL test was adjusted for false positivity by means of the TPI test. Kranendonk [16] found the same difference between areas of high and low prevalence using the Chediak test. This finding leads to the assumption that lowly endemic yaws, where lesions are of reduced severity and of shorter duration, results in lower reagin levels in infected individuals than does hyperendemic yaws.

Classic and Attenuated Yaws

As previously mentioned, highly endemic yaws appears as a treponemal infection characterized by profuse collections of abundant, large, elevated, exuding papillomas of long duration that may relapse a certain number of times and that give rise to high titers of reagin in the serum of the infected individual. The age of onset in such highly endemic geographic areas is very low. The duration of papillomas in the most affected areas may extend to longer than three years.

Lowly endemic yaws, on the contrary, appears as a disease characterized by mostly solitary lesions, which—if multiple—will be very few in number, confined mostly to the protected skin folds, small in size, dry, flat, greyish in appearance or completely atypical, and of short duration—possibly as short as one month. Such infection gives rise to low reagin titers only in the serum of the individuals infected. In areas of such lowly endemic yaws, the age of onset is during childhood—spread equally among all age groups—but most of the infections start no earlier than after the first few years of life.

In areas with highly endemic yaws, if the disease is left untreated, the ratio between the rate of seropositivity and the prevalence of clinical cases will be low; in areas with lowly endemic yaws, this ratio will be much higher.

The picture of lowly endemic yaws presented is one of disease at reduced severity, i.e., attenuated disease. In areas with attenuated yaws, latency increases at the expense of periods of overt clinical lesions. Latency is a characteristic of all human treponemal infections. Even in areas with holoendemic yaws, many individuals periodically have no lesions during the early period of the infection. In attenuated yaws, latency is only occasionally interrupted by clinical activity, but lesions are then atypical; they are small, dry, few in number, and do not last long before disappearing spontaneously. The ratio between the rate of seropositivity and the rate of clinical cases is obviously much higher for attenuated than for highly endemic yaws.

Holoendemic yaws is the expression of maximal transmission of Treponema pertenue in extremely favorable (for the treponemel) circumstances. Most
susceptible persons are infected at an early age by frequent exposure to treponemes from the innumerable large, exuding papillomas present in the environment. The extreme manifestation of attenuated yaws, on the other hand, may be lesions of even shorter duration that are small and dry and barely produce treponemes. Asymptomatic yaws may possibly occur when latency replaces clinical manifestations altogether; reagins would no longer be produced, and only the presence of treponemal antibodies would reveal that infection had taken place. This would be the end of transmission. (Fribourg-Blanc et al. [22] found treponemes in asymptomatic African monkeys with positive results in TPI tests but negative results in VDRL tests.)

Public Health Importance of Attenuated Yaws

In natural circumstances, in dry areas, or at high altitudes, attenuated yaws does not present an important public health problem because of the low prevalence of clinical cases, the mild and scantly early lesions, and the low potential for transmission of treponemes. Late lesions, which are of the most importance for public health, are extremely rare in cases of attenuated yaws. Also, such attenuated yaws will most probably remain stable and not give rise to higher prevalences of early lesions with late lesions occurring at an older age.

In areas where prevalence of yaws was previously high, attenuated yaws will, however, most likely retain the potential to develop into clinically active disease, with florid early infectious lesions that exude treponemes in a population in which most of the younger generation are susceptible. Reports of increasing yaws prevalence from various countries seem to confirm the potential for relapse within a few years of yaws that had been reduced to a low prevalence with concomitant attenuation. In that respect, attenuated receding yaws merits close surveillance, for which serologic surveys are indispensable.

References

2. Grin El. Epidemiology and control of endemic syphilis.

15. Hunt D, Johnson AL. Yaws, a study based on over 2,000 cases treated in America Samoa. United States Naval Medical Bulletin 1923;18:599-607
Impact of the Control of Endemic Treponemal Diseases in Ghana on Other Diseases

From the Epidemiology Division, Ministry of Health Accra, Republic of Ghana; and the International Health Programs Office, Centers for Disease Control, Atlanta, Georgia

A program for control of yaws and yellow fever in the Republic of Ghana was initiated with the aims of reducing the sharp increase in the prevalence of yaws and preventing epidemics of yellow fever. In addition, the program included health education and mass immunization with single doses of measles, tetanus, and tuberculosis vaccines. An evaluation of the first three years of the program indicates that the multidisciplinary approach has benefited a large segment of the population, which previously had little or no access to medical care. This control program has also had an impact on other diseases and conditions.

Yaws is the most important of the endemic treponemal diseases known in the Republic of Ghana. It is the second most common notifiable communicable disease in Ghana (after measles). Over 90% of the active forms of yaws occur in children younger than 15 years of age [1]. The disease is most prevalent where there is overcrowding and where the standard of hygiene is low. The persons most commonly affected are those living in rural areas. Other treponemal diseases (bejel or endemic syphilis and venereal syphilis) occur in neighboring countries [2] but have not yet been recognized as problems in Ghana.

Control of Yaws in Ghana

The control of yaws in Ghana was first attempted as part of a vertical program involving members of mobile field unit teams who traveled from village to village examining patients for yaws, trypomosiasis, and other diseases. Yaws treatment campaigns in the late 1950s and early 1960s reduced the prevalence of this disease to negligible levels [3–5]. In recent years, however, the prevalence has reached epidemic proportions. This increase is the result of a redirection of the activities of medical field units from the control of yaws to that of cholera since the latter disease was introduced into Ghana in 1970. This redirection resulted in the failure to maintain yaws surveillance on a regular basis because of limited resources.

The resurgence of epidemic yaws in Ghana was noted by Ashitey in 1976 [6]. The sharp increase in the number of cases, the severity of disease in children, and the loss of productivity in the adult population with its attendant effect on the national economy compelled the government of Ghana, in collaboration with international donor agencies, to initiate another mass treatment campaign against yaws in 1981. The objective was to reduce the prevalence of yaws from the estimated rate of 400–500 cases per 100,000 population to <100 cases per 100,000 population by 1983.

A vertical program could not be justified because it was not feasible economically or technically. Rather, there was a need for an integrated, multipurpose approach that maximized the use of all available resources for the control of yaws as well as yellow fever, measles, neonatal tetanus, and tuberculosis. Other conditions, such as cholera and cerebrospinal meningitis, were also included in particular areas.

There was an urgent need for the inclusion of yellow fever vaccination in the campaign because focal epidemics of this disease were occurring simultaneously [7]. An epidemic of yellow fever was reported in northern Ghana in August 1977; by the end of

S332
1979, epidemics had occurred in some parts of the Eastern, Volta, and Brong-Ahafo regions. A total of 872 cases and 189 deaths, with a case-fatality rate of 21.7% were reported in 1979. After a campaign of selective mass immunization, no further epidemics occurred. In 1980, only eight cases and six deaths were reported from the Brong-Ahafo and Volta regions. A notable feature of the outbreak of yellow fever in northern Ghana in 1977 was that most of the cases (67%) and deaths (82%) were in children younger than 15 years of age—the same age group afflicted with yaws. The campaign against yaws offered an excellent opportunity to use available logistics to enhance the national Expanded Programme on Immunization (EPI) for children in Ghana. Because of a shortage of vaccine and other technical constraints, yellow fever vaccination coverage was lower than planned for the three-year operational period evaluated. However, no epidemics of yellow fever occurred in those areas where vaccination was performed.

After yellow fever had been chosen as a target disease, it was further decided to include measles, tetanus, and bacille Calmette-Guérin (BCG) vaccinations as campaign activities. This concept was in line with the general policy of the EPI—i.e., to increase vaccination coverage and to enhance herd immunity throughout the nation.

Methods of Control

Patients with yaws and their contacts were treated with single-dose IM injections of benzathine penicillin. Children aged one to five years received 300,000 units, those between six and 15 years received 600,000 units, and those older than 15 years received 1.2 million units. With few exceptions, all children between one and 15 years of age residing in villages where infectious yaws was present were given penicillin (juvenile mass treatment), as were adult contacts of patients with yaws [8].

Because the quantities of yellow fever vaccine were limited, the most susceptible age group was targeted, and all children younger than 10 years of age were vaccinated. Children between nine and 24 months of age received measles vaccine, and those younger than four years were given BCG vaccine. Women of childbearing age (15-45 years) were given one dose of tetanus toxoid to lessen the chance of neonatal tetanus in their children. These activities were preceded and followed by simple talks on health education, nutrition, and sanitation.

Results and Discussion

A survey of random communities that participated in the campaign against yaws and yellow fever was conducted after one year. The goals of the survey were to determine the completeness of vaccination coverage and to test the serologic response to yellow fever and measles vaccines. Of 1,925,912 persons examined in the survey, 77,818 (4.04%) had received treatment for active yaws, while another 1,556,360 persons had been given chemoprophylaxis (table 1). At the end of three years, morbidity due to yaws had been reduced from the estimated 400-500 cases per 100,000 population to 62 cases per 100,000 population.

The results of indirect fluorescent antibody tests [9] revealed that only 8.1% of 62 randomly selected children 10 years of age or younger had antibody

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws treatment</td>
<td>3,382,906</td>
<td>1,925,912</td>
<td>56.9</td>
<td>...</td>
</tr>
<tr>
<td>Measles vaccination</td>
<td>520,821</td>
<td>262,443</td>
<td>50.3</td>
<td>17.4</td>
</tr>
<tr>
<td>Yellow fever vaccination</td>
<td>3,471,143</td>
<td>1,475,554</td>
<td>42.5</td>
<td>12.4</td>
</tr>
<tr>
<td>Tetanus toxoid vaccination</td>
<td>2,314,759</td>
<td>558,453</td>
<td>24.1</td>
<td>3.8</td>
</tr>
<tr>
<td>Bacille Calmette-Guérin vaccination</td>
<td>2,314,759</td>
<td>494,791</td>
<td>21.4</td>
<td>1.7</td>
</tr>
</tbody>
</table>

* Includes 197,040 persons first examined during resurveys.
to yellow fever virus before immunization with strain 17D vaccine; in contrast, 86.7% of 53 children who had received the vaccine six months previously had antibody to the virus. Although the number of children tested for yellow fever antibody was small, the results indicated that yellow fever vaccination was efficacious.

The coverage achieved for measles vaccination was also lower than expected, with only 50.3% of the eligible population aged nine to 24 months immunized. Limited serologic studies indicated that ~80% of children in this age group were susceptible. Although the level of coverage was low, it was higher than at any other time since the beginning of the EPI in Ghana.

Activities for Control of Other Diseases
In 1981–1983 several epidemics of cholera occurred in Ghana. Because of the public health importance of these epidemics, medical field unit teams involved in the yaws–yellow fever program conducted surveillance programs and instigated immediate cholera containment measures. There were 943 cases of cholera and 64 deaths in 1981, 11,037 cases and 1,225 deaths in 1982, and 8,302 cases and 319 deaths during the first six months of 1983. Despite their widespread occurrence, these epidemics were contained through the logistics of the yaws–yellow fever program. Unfortunately, the time lost in combating cholera was detrimental to the yaws–yellow fever program because most cholera epidemics occurred outside the scheduled operational areas.

At the beginning of the yaws–yellow fever campaign, there was concern that the mass use of penicillin might increase the incidence of penicillinase-producing Neisseria gonorrhoeae in some parts of the country. This development has not yet been confirmed by any increase in the number of reported cases of gonorrhea or infection with penicillinase-producing gonococci, but reporting is inadequate and active surveillance is limited. An additional risk is that venereal syphilis, which is rare in Ghana, may appear in areas where yaws is eradicated or occurs at a very low prevalence.

References
8. World Health Organization. Treponemal infections. WHO Tech Rep Ser 1982; 674
SESSION IV

Feasibility of Eradicating Yaws

William H. Foege

The elimination of yaws from large geographic areas provides evidence that global elimination of person-to-person yaws transmission is feasible. The failure to reach that goal to date is the result of managerial rather than technical deficiencies. If the eradication of yaws can be accomplished, it should be done to reduce the suffering that is associated with the disease. In addition, a positive benefit-cost ratio is likely to be realized within a period of decades, and in areas endemic for yaws, its elimination could well provide a basis for the development of a strong system of primary health care. The decision to eliminate yaws must be made deliberately by the World Health Assembly with full knowledge of the implications of not making such a decision. A positive decision would result in enriched lives for countless potential victims of yaws and save the world money in the long term.

We would like to believe in disease eradication, and therefore we have all frequently asked the question, Can anything follow smallpox? On the one hand, we would like to believe in the possibility of disease eradication; on the other hand, we are afraid to commit ourselves to so radical a goal. Many who feel that smallpox was unique because it was easier to eradicate are not aware of the arguments that raged 20 years ago. It is safe to say that, even after the resolution of the World Health Assembly in 1966 that called for smallpox eradication, most scientists felt that this could not be accomplished. Most, if not all of them, have since changed their minds.

In 1978, as we debated whether to work toward a goal of interrupting measles transmission in this country, we reviewed the subject under three headings: Can we technically interrupt measles transmission? Should we interrupt measles transmission? Finally, Will we interrupt measles transmission? Since then the Centers for Disease Control (Atlanta) has held weekly meetings to review the cases of measles reported for the previous week and to ask the following questions: What has gone wrong? Why do we still have cases of measles?

I think it is interesting that despite a vast increase in our knowledge of measles epidemiology since 1978, there have been no surprises regarding the measles virus per se. Interrupting the transmission of measles virus is still a reasonable goal. However, we have become aware of many surprising aspects about the epidemiology of people that have helped measles virus survive. We have learned a great deal about those who are out of the mainstream of American life and we have seen that special approaches will be necessary to reach those people. But the point is, measles virus itself has not presented surprises. As we look at yaws, the same approach might be useful. To answer the question of whether yaws can be eradicated, one must ask the questions: Is the accumulation of knowledge and technology adequate? Should it be eradicated? Are the trade-offs acceptable? Will it be eradicated?

The first problem is the definition of yaws eradication. Do we mean eradication of the organism or eradication of the disease? How will we handle evidence and suggestions of the possibility of a non-human reservoir? What if we are dealing with minor variations of a single species? How should we define disease? How will we handle latency? I believe that these are all scientifically interesting and important questions, but I am going to change the terms of reference and say that these questions are really secondary. What is truly important and what we wish to achieve is to stop the transmission of yaws from person to person. Therefore, the question becomes, Is it possible technically to stop the human transmission of yaws? It seems that the powerful, persuasive, and almost overwhelming answer is found by looking at the places where transmission has been halted in the past 30 years—not necessarily the large geographic areas, but rather the small ones. I first ran a medical center in Nigeria in 1965.
in an area where Albert Zahra had been working to eliminate yaws and I saw the miracle of a population that had been overwhelmed by yaws enjoying its release from bondage. The elimination of the disease had been achieved within decades after the development of a good tool, namely, penicillin.

The world waited 180 years to avail itself of the benefits of smallpox vaccine. The fact that it has not fully used tools for the control of yaws after 40 years should not be a surprise and certainly should not be an argument that these tools cannot work. Yet we must ask: Why have these tools not worked better? Why have there been reversals in the eradication of yaws?

If one stands back a bit from the action and looks at the situation, it is clear that the reversals have been management failures rather than technical or scientific failures. In some ways, it is almost absurd to have a group of scientists meeting to discuss yaws. The meeting instead should be one of managers figuring out what to do next because, whether the questions concern getting penicillin to people, deciding on the standards for surveys, gettingatisfactions into villages, or deciding on what can in practice be done about diagnosis, the questions are managerial questions. The eradication of yaws can technically be accomplished. It was already technically possible in the 1950s, and since then we have learned a great deal about mass campaigns, surveillance, and standards.

It should be possible, as with smallpox, to gradually eliminate yaws from targeted geographic areas and follow up by concentrating resources into smaller and smaller remaining geographic areas. I'm convinced that it is easier from a managerial point of view to stop yaws transmission on this globe than it is to repair a satellite in space. The real question then becomes not just whether it can be done technically but also whether it can be done from a social point of view. Will we as a society make the decision and commit the resources? Such a decision would be much tougher than the decision to eliminate smallpox because it would be an unselfish one. The Western countries do not have to worry about importation of yaws; the leaders of developing countries are not themselves at risk. Such a decision is, in essence, a much greater test of civilization than that concerning smallpox because the decision would not provide personal gain to the decision-maker. Whatever the social problems, the answer to the technical problems is clear. Yaws transmission can be stopped.

The next questions are: Should it be done? Is it worth the effort? Does it detract from primary health care? I think three arguments are key. The first one has to do with quality of life. The extent of the suffering imposed on patients with yaws is well known. Humanitarian considerations dictate that the end of the road should never be so distant that we do not see those who suffer and share their burden. Cost factors provide a second argument. The world has already opted for control of yaws. That is, no country is willing to return to the situation in the 1940s as far as yaws is concerned. When there is a reversal in the control of yaws and when the prevalence reaches a given level, there will always be a response. Therefore, when we consider the cost of interrupting transmission, we are really talking about the incremental cost between that required for reaching some level of control as now practiced and that required for the interruption of transmission. Even if that increment resulted in a doubling of the resources devoted to yaws for 15 years, the end result would be to recoup all investments over the two decades following successful interruption of transmission. Even if the increment tripled for 15 years, the break-even point would occur within a lifetime, after which benefits would continue to accrue and costs end. The benefit-cost ratio would be positive at some point and would continue to grow. This is a key point whenever one can answer yes to the first question, Is it technically possible to eliminate the disease?

Failure to pursue health programs with a positive benefit-cost ratio, where a dollar invested will return more than a dollar in benefits to society, is ultimately a decision to spend more money on the condition in question and to increase suffering. So we must understand that to opt for only the control of yaws saves us money but costs our children money. To opt for interruption of transmission of yaws costs us money but saves our children money. Therefore, the interruption of yaws should be pursued from a cost perspective. Yet, the third argument for the eradication of yaws is that it would strengthen the public health structure of the world, i.e., primary health care. It is possible to stop the transmission of yaws without a preexisting primary health care structure, as discussed elsewhere in the symposium. The converse is not true; it is difficult to imagine yaws continuing to occur in areas that have adequate primary health care. Therefore, the interruption of yaws transmission could be used as an indicator in the following sense.
Smallpox eradication was an indicator of our ability to mobilize the community against a health problem for a limited period of time. The presence of guinea worm is becoming an indicator of inadequate water supplies, although the absence of guinea worm does not mean that the water supply is adequate. In a similar way, the presence of yaws could well be an indicator of an inadequate ongoing primary health care system, although the absence of yaws does not mean that primary health care is adequate.

Solving the yaws problem requires knowledge of the prevalence of the disease, the existence of a surveillance system, and the ability to join the right person with the correct essential drug. These are skills that one needs for an ongoing primary health care system. Responding to the problem of yaws is what a primary health care system should be doing, and breaking the transmission of yaws would provide the system with easily understood results, would build trust among the people, and would lift the spirits of the health workers themselves. It should be done without delay, before drug resistance adds one more problem and while we can still redeem the pledge made in the 1950s to eradicate yaws. It is exciting to consider that a concerted effort now could possibly prevent any yaws transmission in the 21st century.

Finally, whether transmission will be interrupted is a social rather than a technical question. But this answer very much hinges on the people at this symposium, who have the interest and information to educate the decision makers.

The decision to make a concerted effort to eradicate yaws would be a global decision like that made at the World Health Assembly in 1966 for smallpox. Such an effort will not just happen but rather requires a definite global commitment. Such a decision should be taken only with careful consideration, but at the same time careful consideration should be given to the implications of not making such a decision. The effort to eradicate yaws would take not only a decision but also the mobilization of resources and considerable managerial expertise. Unless the decision is made to interrupt transmission, we will never know the ultimate barriers to interruption of transmission no matter how carefully we study the disease. In summary, the eradication of yaws could be done, it should be done, and if we fail to make the effort, both victims of yaws and people in public health will be poorer for the opportunity lost.
Control of Yaws and Other Endemic Treponematoses: Implementation of Vertical and/or Integrated Programs

Donald R. Hopkins

Previous mass campaigns against the endemic treponematoses have taught investigators several lessons that, along with current constraints and altered circumstances, must be considered in the formulation of a contemporary strategy for the control or eradication of yaws, endemic syphilis, or pinta. A time-limited, vertical approach is necessary in highly endemic areas initially to reduce the level of transmission. Elsewhere, control activities should be integrated into other primary health care interventions, especially health education, water and sanitation programs, maternal and child health care, and provision of essential drugs. Control of the endemic treponematoses is an ideal means of strengthening primary health care in endemic areas.

In view of all the information that has been presented at this symposium about the status of the endemic treponematoses, strategies and technologies for their control, research needs, and the feasibility of yaws eradication, it is appropriate that this final presentation should focus on implementation. Given all that we know, what is to be done about yaws and its cousins, and how is it to be done?

In attempting to address these questions realistically, we must take several important facts into account. (1) Partly because of the great success of the mass campaigns of the 1950s and 1960s, the endemic treponematoses are widely thought to be “under control” already. (2) Since these diseases are not fatal and usually are restricted to poor, remote, rural populations, they are not perceived to be high-priority problems by many decision makers. (3) The price of continued apathy will be an even greater resurgence of these diseases and, potentially, the loss of our “magic bullet”—long-acting penicillin—through the development of resistance. (4) In areas where the endemic treponematoses still occur, medical services are inadequate or nonexistent. (5) Programs aimed at a single disease are now frowned upon by much of the international public-health establishment. (6) The world is committed to establishing broad-based primary health care services in all currently underserved areas as a means of achieving “Health for All by the Year 2000.”

The second observation—the low priority given to control of endemic treponematoses in most affected countries in recent years—deserves further emphasis. Of all the remaining endemic countries, only the Republic of Ghana, where yaws is now the second most commonly reported communicable disease (exceeded only by measles), appears to regard control of yaws as a high priority. Since a resolution calling for improved control of endemic treponematoses was adopted by the World Health Assembly in 1978, no affected country except Ghana has even mentioned yaws, endemic syphilis, or pinta at one of the annual assemblies. In some instances, it is alleged that the unpopularity and political impotence of the tribal group(s) affected encourage neglect of the problem. Colombia, Ghana, and Indonesia continue to support active, categorical campaigns against yaws. Endemic syphilis was identified as a target deserving high priority for control efforts in the Sahel in 1977 [1], but no effective action has yet resulted at national or regional levels. When public health workers from the Centers for Disease Control in Atlanta visited Ivory Coast, Ghana, Togo, and Mali in 1979 under the sponsorship of the U.S. Agency for International Development, all four countries expressed interest in a regional control program. However, significant support was mobilized only for the most severely affected country, Ghana.

In this paper, the term vertical is used to describe programs that are characterized by a narrow focus or a single target disease and by separate lines of supply, communication, and supervision; in addition, vertical programs usually are time limited. The term integrated is used to describe programs that seek to address many diseases or conditions simultaneously; these programs operate within the general supply, communication, and supervisory channels of the national health system concerned, and they are intended to continue indefinitely. Either type of pro-

Please address requests for reprints to Dr. Donald R. Hopkins, Building 1, Room 2000, Centers for Disease Control, Atlanta, Georgia 30333.
necessary in areas where the overall prevalence is lower but the affected populations are nomadic or live in regions that are exceedingly remote or difficult to reach [3].

Because of the need to reach >90% of the target population [4], some kind of mobile outreach component that goes beyond any conceivable density of fixed health centers will also be necessary in the more heavily endemic areas. Such a program must reach every village, at least in affected areas, and may need to reach each household [16]. Missed cases were the most frequent sources of continued transmission after mass treatment in former campaigns [4]. These special efforts will require an emphasis on the main disease with which they are concerned and special assurances of supplies, communication, and sufficient supervision; the programs should also be time limited. In other words, a classic vertical or categorical approach should be used. In return, these efforts should achieve a rapid reduction in prevalence more efficiently than would otherwise be possible, and afterward the same personnel and equipment could be used in a similar concentrated attack on another common high-priority problem, or could be immediately (re)integrated into the regular primary health care service. By the time the special effort ends in an area, specific arrangements for ongoing surveillance, for treatment of additional patients and contacts, and for prophylaxis must be in place.

This exact approach was chosen reluctantly despite a strong commitment to primary health care by Ghana in 1980. The program against yaws was combined with vaccination against yellow fever, tuberculosis, tetanus, and measles and was begun in the most affected regions of the country [11]. Precisely the same approach is required now in other areas where one of these diseases is highly endemic or epidemic. Those who insist that an integrated approach alone should be pursued in all instances must recall that in Indonesia the campaign against yaws was a part of the established health services from the start [12], and yet the disease is resurgence there too.

Something less than the special effort just described should be sufficient in areas where prevalences are low. Obviously, however, this "something less" must offer more than the prevailing situation. In these circumstances, two or three different levels of activity against yaws can be imagined.

At a bare minimum, it must be ensured that all of the fixed peripheral health posts in known or sus-

pected endemic areas are supplied regularly with adequate amounts of penicillin and that the peripheral health care workers at those posts are trained to diagnose yaws properly, to treat contacts as well as patients, and to report diagnosed cases routinely to appropriate health authorities. In areas where yaws or another of the endemic treponematoses occurs, it may well turn out that the steps just described will be the first of eight suggested elements of primary health care (as defined by the World Health Organization [WHO]) to be implemented. If so, these steps should prove to be a logical foundation upon which other priority services can be built.

In other areas, a "yaws component" may have to be added to other previously implemented elements of the WHO primary health care package: health education (instruction of villagers about how the disease spreads and how to prevent and treat it); implementation of safe water and sanitation practices (promotion of more frequent bathing, the use of soap, and perhaps more clothing); maternal and child health care (screening and treatment for all treponematoses); provision of essential drugs (including penicillin); treatment of common injuries and health conditions; and control of locally endemic diseases (including yaws) (figure 1) [4, 17-19]. Indeed, of the eight standard elements of primary health care defined by the WHO, only one—provision of childhood immunizations—is not directly related to control of the endemic treponematoses [20].

Some may object that the inclusion of efforts against yaws would be detrimental to the pursuit of more important primary health care activities or that such efforts, if begun too early, would complicate things too much at the peripheral level of the health system. In response, we note the proven popularity and efficacy of efforts against yaws in endemic com-

![Figure 1](https://via.placeholder.com/150)  
**Figure 1.** Interventions necessary to achieve control of the endemic treponematoses.
nunities [21]. In addition, we assert that few actions are more important than controlling an easily preventable cause of mutilation and crippling. Besides, if the public health care system cannot take the simple steps needed to control yaws, how will it control tuberculosis or leprosy, which require a much longer period of therapy; schistosomiasis and malaria, which are far more complicated; or the immunizable diseases, which require a cold chain?

Whether activities against yaws are added to other ongoing public health care services or whether the other services are added in the wake of yaws-related activities in any given endemic area is not nearly as important as a careful consideration of exactly which activities are to be combined and how. As has already been mentioned, there is much experience to draw on from earlier campaigns against yaws. Because of the great overlap in manifestations and control measures, for example, and because of concern that the control of endemic treponematoses increases the vulnerability of populations over time to venereal syphilis, it might be an attractive option in some areas to combine an attack on yaws with an effort to detect and prevent cases of congenital syphilis. Similarly, yaws surveillance and possibly treatment might be combined with other vertical disease-control efforts, such as onchocerciasis control, immunization programs, or diarrheal disease control [22].

At some point during the course of control programs, especially if elimination is the national goal, some form of active case finding (active surveillance) will become necessary to ensure that any continuing foci of infection are detected and controlled before they spread and thereby require more extensive counter measures. In many areas it should be possible—if full advantage is taken of fixed peripheral health centers, schoolteachers and pupils, markets that draw from a large area, and other ongoing institutions or activities of any type (including cooperation of agricultural extension workers, for example, or serologic surveys undertaken for other reasons)—to maintain a surveillance system that is sufficiently sensitive to detect new cases of disease before the disease spreads too far [13, 23]. If a fairly extensive network of peripheral health workers and/or centers that can treat cases and contacts detected by the surveillance system exists, it may be sufficient. In all likelihood, however, other arrangements will have to be made in order to follow up reports of cases or suspected cases and to ensure that patients and contacts are treated promptly, regardless of whether they live within reasonable walking distance of a health center. Thus, some kind of mobile capacity, which could perhaps simultaneously undertake other useful services (e.g., the surveillance of other high-priority problems, the transport of supplies, or an emergency response to epidemics), will also be needed. This mobile capacity may take the form of a single team covering a small country or several regionally based teams in larger countries.

Thus, in answer to the question of what should be done and how, I believe that vertical and integrated programs, appropriately stratified according to the epidemiologic situation and resources of each country where an endemic treponematosis still exists, should be implemented. Control of yaws and the other endemic treponematoses needs to be recognized as a vital step in the strengthening of primary health care. Such control efforts serve as an attractive spearhead in the neglected, remote populations concerned, helping to gain the cooperation of the people by producing visible improvement quickly. Control programs also provide a useful indicator of which populations are most underserved by the existing public health system [8, 24].

Whether the objective is to eliminate or to control the endemic treponematoses, the target group is still mainly children younger than 15 years, and the principal intervention strategies should include early detection and treatment of cases, prophylactic treatment of contacts, provision of water and soap, and health education. The principal support measures required include transportation both for mass treatment surveys and for active surveillance and containment in areas of high incidence, regular provision of drugs, training of health care workers in the proper diagnosis and treatment of the diseases, and—especially in areas of low incidence—laboratory diagnosis. The appropriate indicator of success or failure should be the number of cases or the incidence each country feels it should tolerate in its control program. In many of the areas concerned, even one active case should be intolerable in 1984.

References


10. Cruz AH. Integration of yaws control into the permanent health structure of the Philippines. Bull WHO 1953;8:345-53
15. World Health Organization. Treponema infections: report of a WHO scientific group. WHO Tech Rep Ser 1982;674
Summary and Recommendations

This symposium, the third such meeting on treponematoses, took place 29 years after the second meeting in Enugu, Nigeria, in 1955. The first meeting had been held in Bangkok, Thailand, in 1950. Several individuals who had participated in one or both of the preceding meetings were at the present one. It seems appropriate to mention three individuals unable to be present who have made major contributions to our knowledge of the treponematoses and to the control programs of the 1950s and 1960s—Drs. C. J. Hackett, Ellis Herndon Hudson, and Thomas B. Turner. The participants at the symposium made reference to the outstanding and influential work of these men and expressed regret that they were unable to attend.

Drs. Zahra, Haidar Abu Ahmed, and Widy-Wirsky, whose papers are included in this publication, were unable to attend the symposium because of last-minute complications.

Extent of the Problem and Status, Strategies, and Technologies of Control

The meeting opened with welcoming statements by Dr. Carlyle Guerra de Macedo, Director, Pan American Health Organization (PAHO), and Dr. Mark S. Beaubien, Deputy Director, Fogarty International Center. Both indicated that their organizations are supportive of renewed efforts to eliminate yaws and, by implication, the other endemic treponematoses. Dr. de Macedo stated: "if we consider the available knowledge and existing epidemiologic conditions, there is a real possibility that we can eradicate the disease and that this task can be carried out in the short term, at least, I am sure, with regard to the Americas."

The first two sessions were devoted to a review of the past efforts to control yaws, endemic syphilis, and pinta; their current extent; and the status of control programs. A discussion took place concerning the virtues and flaws of the mass campaigns, integration of control and primary health care activities, and some of the newer technologies available for use in surveillance and control. It was noted that in 1949, the Second World Health Assembly accepted the advantages of an epidemiologic approach to the control of the diseases, and with the availability of an effective, single-dose, long-acting penicillin—procaine penicillin with 2% aluminum monostearate (PAM)—the initiation of mass campaigns became feasible. By the time of the first international symposium in Bangkok, enough experience had been gained in pilot studies such as those against yaws in Haiti, endemic syphilis in Yugoslavia, and pinta in Mexico to allow the participants to identify several principles as essential to the successful conduct of such programs. First, it is necessary to examine at least 90% of the population in all screening surveys. Second, periodic resurveys should be carried out at intervals of six to 12 months to provide treatment of cases missed earlier as well as of reinfections and imported cases. Third, the total reservoir of treponemal infection—active, latent, and incubating cases—must be treated as well as all individuals assumed, on an epidemiologic basis, possibly to fall into these groups. Fourth, minimal effective doses of PAM must be utilized; those recommended at that time were 1.2 million units for adults with definite infections and 0.6 million units for those younger than 15 years of age. Contacts were to receive one-half these doses.

Five years later, in Enugu, certain refinements of these principles were encouraged, primarily in regard to treatment policies based on levels of endemicity. In hyperendemic areas, where >10% of the population had active disease, the entire population was to be treated (total mass treatment [TMT]). If the prevalence of active disease was 5%–10%, all prepubertal children and other contacts of infectious individuals, e.g., family or household contacts, in addition to those with active disease, were to be treated (juvenile mass treatment [JMT]). Where the prevalence of active disease was <5%, household and other obvious contacts were to be treated along with individuals with active disease (selective mass treatment [SMT]).

It is interesting that these principles and recommendations remain relatively unchanged.

Please address requests for reprints to Dr. John C. Hume, The Johns Hopkins University, School of Hygiene and Public Health, 615 North Wolfe Street, Baltimore, Maryland 21205.
ing in October 1980 did, however, recommend that all cases and contacts receive the same dosages and that benzathine penicillin be substituted for PAM. The current recommended therapy for individuals older than 10 years of age is a single injection of 1.2 million units and for individuals 10 years of age or younger, 0.6 million units.

These mass campaigns were instituted around the world in all areas recognized as having these diseases as a public health problem. It is estimated by WHO that during the global program, primarily in the 1950s and 1960s, ~160 million individuals were examined during the initial treatment surveys, >300 million were examined during the resurveys, and ~50 million cases and contacts were treated.

Throughout these symposium sessions the critically important role of WHO as conceptual planner, leader, and facilitator was repeatedly acknowledged. In addition, the indispensable role of the United Nations Children’s Fund (UNICEF) as a partner in supply and support services, along with the United States Agency for International Development (USAID) and other bilateral programs, was made abundantly evident. Furthermore, the remarkable effort and support of the nations bearing the social and economic burden of the treponematoses as well as the quality of the scientific and administrative leadership in program implementation became clear in the epidemiologic data presented.

The successes of these programs are impressive. Whereas in the 1950s it had been estimated that there were 50–100 million cases worldwide, the comparable estimate was 1–2 million in 1976. In Yugoslavia, endemic syphilis had been eradicated by the late 1960s. In the Americas, there was a marked reduction in the incidence of yaws throughout the affected areas, with apparent elimination of the disease from Central America and several of the Caribbean islands, such as Antigua, Barbados, Jamaica, St. Vincent, the Grenadines, and the Turks and Caicos Islands. In South America, while transmission still occurs in some countries, it is obviously found in increasingly remote, small foci and, where not eliminated, has become a relatively minor public health problem as compared with that in the 1950s. Pinta, while still present, for example, in Mexico and Colombia, is a rapidly dimishing problem.

In Asia, the mass campaigns carried out against yaws in Indonesia, Thailand, Malaysia, Papua New Guinea, and in areas of India greatly reduced the incidence and prevalence. The same was true of efforts directed at scattered foci of endemic syphilis in India. However, there continues to be low-level transmission in India, Malaysia, and Thailand. In Papua New Guinea, there have been reports of several localized outbreaks, and in Indonesia, there has been a disturbing resurgence of transmission in many areas of the country. Bejel, which had been recognized as a problem in sections of Iraq, Saudi Arabia, Syria, and other Asian countries, still exists in these areas, though transmission is apparently considerably reduced.

The picture in Africa is somewhat mixed. Successful campaigns were mounted in most of sub-Saharan Africa where yaws was a problem. It is clear that the mass approach was remarkably effective in achieving spectacular reductions in rates. However, there appears to be no nation where these programs were able to eradicate the disease, though in most the initial results were dramatic. Unfortunately, in some countries, such as Benin, the Central African Republic, Ghana, and Togo, there are areas where the proportion of children with infectious yaws now approaches that of the pre-campaign years. It can safely be stated that the situation is precarious in West and central Africa. As regards endemic syphilis, its incidence in the Sahel region approaches that of yaws in West Africa, highly endemic areas having been recognized in Senegal and Burkina Faso (formerly known as Upper Volta).

In their earlier stages these programs frequently were faced with problems, some unforeseen, which have taught valuable lessons. Those most frequently referred to and of most importance would include the following.

(1) While the availability of low-cost, long-acting, highly effective penicillin made possible the successful mass campaigns, the quality of the product is of vital importance. Numerous references were made to lack of quality control in the manufacture and storage of penicillin preparations. Similarly, improper administration of the drug, such as inadequate dosage, was noted. Thus, both governmental control in the pharmaceutical industry and appropriate supervision at every level of program administration and implementation are critically important to program success.

(2) The absolute necessity of assuring appropriate support services was emphasized. A major concern must be the availability of adequate transport vehicles and the facilities for their proper and timely repair and maintenance (including supplies of spare
tires and parts). Also essential is a system for obtaining and distributing a steady supply of drugs and equipment for diagnosis and for administration of medication.

(3) The creation and the maintenance of a corps of appropriately trained staff were emphasized. Not only is the preparation of health care workers competent in the diagnosis, treatment, and control of the endemic treponematosis important but so is the training of administrative personnel, drivers, mechanics, and other support staff.

(4) Because of emerging hints that current drugs may not remain effective (a subject covered in more detail later in this summary) and evidence that, in some areas, venereal syphilis has gradually been filling the vacuum caused by the elimination or reduction of the endemic treponematosis, frequent reference was made to the need for continued and expanded research in the basic microbiology of the treponemes and in the diagnosis, treatment, prevention, epidemiology, and control of the infection. Otherwise, it is feared that problems in the control of these diseases may outstrip our knowledge of how to cope with them.

(5) It was emphasized that public as well as professional support must be maintained to assure, at both the national and international levels, that public policy and resultant budgetary decisions provide continued support for the necessary control activities.

(6) Vital to ensuring public support and arriving at proper program decisions is a strong epidemiologic component in the administration of a program. Provision must be made for a constant and complete system of reporting of cases. With data regarding the incidence and prevalence of the diseases available, public support can be maintained, realistic budgetary requests supported, and health administrators can determine not only the extent and nature of the problem but also how best to attack it within the national system of health services.

(7) Finally, it was pointed out that it had been recognized early in these campaigns that, while undoubtedly remarkably effective, these campaigns were unlikely to eradicate the endemic treponematoses unless provision was made for constant surveillance and for widely available primary health care services. The very success of the programs resulted in a sense of complacency and lack of concern in many areas, a situation that led inevitably to a rerudescence of the problem. It was evident from the reports that the countries that had been able gradually to replace the vertical programs with adequate primary health care services that provided constant surveillance and containment activities were those where eradication or extremely low levels of transmission had been achieved. At the other extreme were those nations where mass campaigns, following initial successes, had been abandoned without the provision of a sound primary health care system. In other words, the failure to maintain control or reach the goal of eradication can, in most countries, be attributed to one or more of the following: a false hope that the diseases were under control and no longer a threat, an assumption leading to a change of health priorities; a switch from the mobile approach to the use of inadequate numbers of static clinics providing curative, clinical services but no real surveillance and consolidation activities; and often a slower than anticipated improvement in the socioeconomic status of the nation or, in some instances, an actual worsening of the situation.

In many areas, the mass campaigns provided many of the world's poor with their first encounter with modern medicine, providing a stimulus for the acceptance of later programs and assisting in the development or strengthening of rural health services. Frequently, the opportunity was seized after the attack phase to incorporate other public health activities into the functions of the mobile teams. For example, in West Africa, the teams were trained to recognize and deal appropriately with cases of leprosy or trypanosomiasis. Elsewhere, the teams added to their yaws control functions the administration of vaccinations against a variety of diseases, such as yellow fever, measles, smallpox, tetanus, and tuberculosis, or participation in diarrheal control programs. In other locations, such as Indonesia, efforts were made to incorporate even the initial treatment surveys and the subsequent resurveys into the basic rural health services. Depending on the adequacy of the surveillance and follow-up services available, the long-term results vary from poor to excellent.

With the adoption of the principle "Health for All by the Year 2000," there has been a worldwide recognition of the need for the development of primary health care services that are available to all citizens. In many areas this focus on primary health care has led to a certain disenchantment with vertical programs. However, it was the consensus of the speakers that, in areas where the treponematoses are hyperendemic, the vertical programs are still desirable and,
in fact, will make it possible for the primary health care system to cope with the overall health problems. In these situations particularly, the governments involved often may require outside financial and, possibly, technical assistance. Each country must determine as accurately as possible the distribution of the diseases within its borders as well as their prevalence and incidence in the affected areas. This information must be matched against the health service resources available, and decisions must be made as to the optimal mix of vertical and primary health care services. Where the latter seem reasonably adequate, it is essential that the health personnel, especially the village health workers, be trained in the recognition of the diseases and their management and be made aware of the need for treating all possible contacts and for educating the public in the communities to recognize the disease and seek assistance. The importance of having intercountry, regional, and concurrent control programs was also emphasized. Since in most areas there is considerable movement of persons across the borders, it is futile to expect the elimination of the problem in one country when an adjacent nation has no program and has an infected population.

Several authors made a plea that clearly formulated strategies, defined according to the degree of development of a nation’s health services, be developed. The importance of incorporating the successful combinations of the endemic treponematosis control programs with other programs of case finding, vaccination, or therapy was emphasized. Two other points were made. One was how to approach the situation in which there are areas of high endemicity in a country with totally inadequate primary health care services and where it is improbable that these could be made available in the foreseeable future. At least one speaker questioned the desirability of instituting a mass campaign in such circumstances. The other point was the increasing need for making serologic testing available. Techniques are available now that allow the use of finger-prick specimens collected in the field, the test being performed in central or regional laboratories. These tests are quite reliable and reasonably inexpensive. There is no doubt that they can be useful in epidemiologic surveys in the identification of untreated latent cases as well as previously treated cases for which therapy may have provided inadequate protection. Information can be acquired as to the geographic and age distribution of seropositive persons, which can be helpful in defining the problem more accurately and, especially, in noting trends. The practicality, however, will depend on the fiscal and human resources available, the nature of the problem, and specific factors existing in a given area.

Research Needs

The third session was devoted to a consideration of the current status of our knowledge concerning possible improvements in our antitreponemal armamentarium, potential hazards facing the programs, and the effect of efforts at treponemal disease control on other diseases.

One important requirement in dealing with treponemal infections is having available a cheap, simple, sensitive, and specific diagnostic laboratory test. While excellent tests have been developed to detect treponemal antibodies, these tests do not differentiate among the species (or, as the taxonomists now say, among the subspecies or variants of Treponema pallidum). A test that could make this differentiation would help in defining more precisely a nation’s problem, an understanding that, in turn, would make possible more intelligent planning for the control effort. Another problem has been the difficulty in making good serologic tests widely available in less-developed areas, especially in remote areas where the nonvenereal treponematoses are endemic. A final desideratum noted would be the availability of serologic tools that would distinguish new infections from old. The identification of pathogenic treponemes by dark-field examination or of their antigens by available techniques has not been generally applicable for a variety of obvious reasons.

Some progress has been made in the improvement of techniques for the identification of both treponemal antibodies and antigens. Efforts to simplify collection and transportation of serum for laboratory testing were described. In the field, however, the most practical current method of performing serologic tests for detecting treponemal antibodies remains the collecting of blood on filter paper and the transporting of samples to the laboratory.

A review of the application of newer techniques in treponemal research indicated encouraging progress. A considerable amount of work has been done in adapting the enzyme-linked immunosorbent assay (ELISA) to the detection of treponemal antibody.

It will be necessary to develop more refined antigenic reagents, however, before these techniques
achieve the desired degree of specificity. Happily, there are advances on this front as well. With modern electrophoretic procedures, it is possible to dissect treponemes and recover many of their individual structural components. This should permit the identification of antigens that are elegantly specific for pathogenic treponemes and the use of these antigens as immunogens in animals for the production of monospecific polyclonal antibodies. While relatively little has been published, some work has been done on production of monoclonal treponemal antibodies from hybridoma cell lines. Unfortunately, until these investigations make use of more refined, individual proteins, these techniques will suffer the disadvantages of relatively poor specificity.

Perhaps the most exciting work focuses on the development of potentially protective immunogens and on diagnostic reagents resulting from the cloning of polynucleotide sequences of treponemal DNA into another host that can be easily cultured in vitro. Several groups have reported the production of *T. pallidum* gene products in *Escherichia coli*. It is hoped that a single gene having the desired specificity will be identified by use of previously noted procedures. This advance, coupled with new, high-expression vectors and other improved cloning tools, should provide us quite soon with the ideal antigen in adequate amounts and, in time, at a reasonable price.

Some steps have also been taken to overcome the problems created by the inavailability of dark-field microscopy in the field. Studies have shown that *Treponema pertenue* can be detected in lesion exudate on slides by direct fluorescent-antibody staining with use of either human syphilitic serum or mouse monoclonal antibody or in exudate placed on nitrocellulose paper and identified with a radiolabeled DNA probe. While these methods were quite sensitive, their specificity was not established.

As regards the development of methods that will differentiate among the antibodies or antigens of *T. pallidum*, *T. pertenue*, and *Treponema carateum*, there seems to be little likelihood that this can be achieved in the near future.

A second matter, which could have most important implications for the control or elimination of the endemic treponematoses as well as of venereal syphilis, is the possibility of developing an effective vaccine. Immunity may result from treponemal infection, as demonstrated in animals and humans, and some vaccines utilizing attenuated strains of *T. pal-
native effective therapies be made available. The tetracyclines seem to be highly effective when used in appropriate regimens and have been more thoroughly evaluated than other antibiotics. It is essential that various tetracycline preparations be further evaluated, especially those that are long-acting. Similar studies of other agents, such as erythromycin, would be desirable.

The second problem is the potential development of treponemal resistance to penicillin. The demonstration of plasmid-mediated erythromycin resistance in a clinically isolated strain of *T. pallidum* in a new assay of protein synthesis that measures incorporation of $^{14}S$-methionine certainly brought home the possibility of such an occurrence. It makes even more urgent an intensive attack on the treponematoses with the currently available control methods, and underlines the need for support of basic research that would provide the foundation for the development of a safe and effective vaccine.

Discussion covered a variety of subjects related to research needs, some associated with the topics already mentioned. For example, it was pointed out that, as control efforts in a hyperendemic area are successful and yaws becomes hypoenendemic, transmission is at a low level; frequently the manifestations in individual patients become attenuated or less florid. This situation demands that close surveillance be undertaken, including serologic surveys where possible, and underlines the importance of developing simpler, less expensive serologic tests.

Several potential difficulties regarding vaccines were pointed out. For example, a vaccine that was only partially protective could modify the manifestations of the disease in such a manner in a subsequently infected individual as to allow the disease to go unnoticed or unrecognized. Administration of vaccine to individuals previously infected or to those in late stages of the disease might result in serious hypersensitivity reactions. Also, the antibody response to immunizing agents could provide a source of confusion in the interpretation of screening tests. Obviously, it is essential that the noninfectiousness of any preparation and the safety of administration to individuals with past or present treponemal infections be well established before vaccination is generally applied. The matter of the specific populations to be vaccinated also received attention. Clearly, the target groups would vary from area to area.

The impact of endemic treponematoses control programs on other disease problems was considered. The beneficial effects of multipurpose programs, such as those discussed earlier, were reiterated and emphasized. There was concern, however, that the elimination of the childhood endemic treponematoses would create an immunologic vacuum and that the prevalence of venereal syphilis would consequently increase. This situation may have already occurred in some areas.

Permeating the discussion in all sessions was recognition of the necessity for improved epidemiologic investigations not only to define the nature and extent of the problem in all affected areas but also to maintain surveillance of the results of therapy. Such investigations would permit the early identification of ineffectiveness due to poor drugs, inadequate regimens, or developing resistance. The need for decision-analysis models that could be used to modify established yaws control campaigns so that they met local or regional requirements was also stressed.

Finally, it was pointed out that the absence of good educational materials, including sets of color photographs of typical and atypical lesions of endemic treponematoses, should be rectified. These materials should be used in the training of field workers in vertical programs and personnel in primary health care programs who are to be responsible for surveillance activities after the mass campaigns. Such materials become especially important as the prevalences of the diseases drop and health workers are less familiar with their clinical manifestations.  

**Worldwide Control and/or Eradication**

The closing session was concerned with a consideration of the feasibility of eradication of the nonvenereal treponematoses and of the best ways to work toward that goal. Regarding the former, three questions were posed: (1) Is eradication technically possible? (2) Assuming it is technically feasible, should it be done, is it worth the effort, and does it detract from primary health care efforts? (3) Will transmission be interrupted? The answer to the first question as regards person-to-person transmission is

---

undoubtedly yes. Successful programs have demonstrated that transmission can be eliminated by administering penicillin to appropriate segments of a population. The failures in control programs have been the result of managerial deficiencies such as inappropriate coverage of the population, inadequate surveillance, and faulty logistics, e.g., interruption in the supplies of drugs, lack of spare parts for and maintenance of vehicles, or insufficient training of field workers in the recognition of the diseases.

One can hardly argue the fact that these infections cause much suffering, disfigurement, crippling, and disability in those affected—primarily children. The fact that these diseases occur for the most part in disadvantaged, remote, rural groups makes the burden even more difficult to bear. As Dr. W. H. Foege stated: “Humanitarian considerations dictate that the end of the road should never be so distant that we do not see those who suffer and share their burden.”

A related question concerns financial considerations. Certainly, in the short term there is an investment involved, which will to some extent divert support for other areas in a nation’s budget. However, the problem of these infections is resurgent, and if the prevalence increases sufficiently, the nations involved must respond. Thus, the benefit-cost ratio over a relatively short period will become positive, and the interruption of transmission should be pursued because of long-term financial benefits. There is urgency in this pursuit, since, if the spectre of penicillin resistance becomes a reality, the currently available, inexpensive weapons would become ineffective, leaving only much more expensive and relatively untested alternatives. The impact of endemic treponematosis control programs on primary health care is always a consideration in discussing feasibility of these programs. There is no doubt that when an adequate primary health care structure exists in an area it can cope with the endemic treponematoses. Until such facilities are available, the focused programs can actually stimulate the improvement of primary health care. It was pointed out that the presence of yaws is, in fact, an indicator of an inadequate primary health care system.

The last of the questions, “Will interruption of transmission be brought about?” is clearly a social and political question. A positive answer will depend on a commitment by the World Health Assembly and on global support from all nations and voluntary and official international organizations.

The discussion of implementation brought together much that had been brought out in earlier sessions. Dr. D. R. Hopkins, in answer to the question of what should be done and how, responded: “I believe that vertical and integrated programs, appropriately stratified according to the epidemiologic situation and resources of each country where an endemic treponematosis still exists, should be implemented.” Control of yaws and the other endemic treponematoses needs to be recognized as an ideal means toward the end of strengthening primary health care. The prevalence of these diseases is a useful indicator of which populations are most underserved by the public health system, and such a control program can serve as an effective spearhead in the neglected, remote populations concerned, helping to gain their cooperation by allowing visible improvement to be manifest quickly. Dr. Hopkins summarized the goals of such programs:

Whether the objective is to eliminate or to control the endemic treponematoses, the target group is still mainly children younger than 15 years, and the principal intervention strategies should include early detection and treatment of cases, prophylactic treatment of contacts, provision of water and soap, and health education. The principal supportive measures required include transportation both for mass treatment surveys and for active surveillance and containment in areas of high incidence, regular provision of drugs, training of health care workers in the proper diagnosis and treatment of the diseases, and—especially in areas of low incidence—laboratory diagnosis. The appropriate indicator of success or failure should be the number of cases or the incidence each country feels it should tolerate in its control program. In many of the areas concerned, even one active case should be intolerable in 1984.

Representatives of several international organizations and agencies, including WHO, UNICEF, PAHO, the Organization of Coordination for the Control of Endemic Diseases, the Commission of European Communities (CEC), USAID, and the International Union Against the Venereal Diseases and Treponematoses (IUVDT) commented on their interest in the problem.

The meeting concluded with the adoption of the following recommendations:

**Recommendation 1.** Health authorities and governments in tropical and subtropical countries should take special steps to assess and keep themselves fully informed of the status of the nonvenereal treponematoses and to report this information at least once a year to WHO and to the appropriate regional health authorities.
Recommendation 2. Summary reports of the status of the nonvenereal treponematoses as important childhood diseases and of efforts directed against them should be made annually to the general assemblies of WHO, UNICEF, and IUVDT.

Recommendation 3. International, regional, and bilateral agencies, as well as the countries concerned, should resolve to interrupt transmission of the nonvenereal treponematoses by vigorously implementing World Health Assembly Resolution 31.58, 24 May 1978 (Appendix 1). Implementation of this resolution will require different combinations of integrated and categorical efforts according to the circumstances of the different countries.

Recommendation 4. Several existing developments in fundamental research pertaining to the treponematoses were noted during the symposium. Support from government, university, and private sources will be required and should be encouraged to continue such sophisticated research.

Recommendation 5. The symposium participants acknowledge with gratitude the enormous progress to date regarding the nonvenereal treponematoses that has been accomplished as a result of generous assistance to affected countries by international and bilateral agencies, especially WHO, UNICEF, PAHO, IUVDT, CEC, and USAID. Similar renewed efforts are required to complete the task and prevent further deterioration of the current situation.

Postscript

As a result of the symposium and the information presented at the meeting indicating a resurgence of the endemic treponematoses in some areas and the presence of continuing foci of endemicity in others, efforts have been initiated to renew or intensify programs aimed at interrupting transmission of these diseases. Because of the various epidemiologic and financial circumstances in the affected nations, no single pattern of attack can be applied, but through the judicious combination of categorical and integrated programs, it should be possible to eliminate significant levels of transmission. All of the bilateral and international health agencies and associations represented at the meeting expressed their interest, in principle, in working toward this goal if the affected countries so decide. Subsequent meetings with representatives of several of these groups have borne this out, and the following are some of the developments.

At its annual meeting in Montreal on June 20, 1984, the IUVDT passed a resolution recommending that affected countries make a careful assessment of the extent of their problem and, with the technical assistance of WHO and IUVDT and the financial assistance of international agencies and industrialized countries, launch effective control efforts (Appendix 2).

Representatives of the Centers for Disease Control and the Fogarty International Center have met with appropriate health officials of several African countries; Indonesia; WHO in Geneva and its Regional Offices in Brazzaville, New Delhi, and Manilla; UNICEF; and the CEC. Interregional meetings are tentatively scheduled to be held in Cipanas, Indonesia, in July 1985; and in Brazzaville, Republic of the Congo, in late 1985. The purpose of these regional meetings will be to coordinate plans for action.

It seems certain that there will be a revitalization of activities designed to eliminate the endemic treponematoses. It is hoped that, as Dr. Hopkins stated in his informal discussion, "There should be no need for a fourth international symposium on the endemic treponematoses, except perhaps to celebrate their demise."

R. Duncan Catterall

James Pringle House
Middlesex Hospital

John C. Hume

The Johns Hopkins University
School of Hygiene and Public Health
Baltimore, Maryland, U.S.A.

Appendix 1. Resolution 31.58 of the Thirty-First World Health Assembly

Control of Endemic Treponematoses

The Thirty-First World Health Assembly,

Recognizing that the endemic treponematoses in general and yaws in particular are resurging as serious public health problems, especially in parts of the world where the diseases were once controlled by Member States in cooperation with WHO and UNICEF;

Recognizing the grave consequences, especially for children, of the deteriorating epidemiological situation in a number of countries;
Conscious of the seriousness of the present situation and the danger of further extension and entrenchment of the diseases;
Emphasizing the urgent need for prompt and vigorous action to control the diseases;

1. REQUESTS Member States:
   (1) to formulate and implement integrated treponematoses control programmes with particular emphasis on active surveillance so as to interrupt transmission of the diseases at the earliest possible time in the areas where they are still endemic and to prevent recurrence of the diseases in areas from which they have been eliminated or have never been endemic;
   (2) to report regularly to WHO on the current epidemiological situation of endemic treponematoses;

2. REQUESTS the Director-General:
   (1) to encourage the national and international surveillance of these diseases;
   (2) to cooperate with Member States, on the request of the governments concerned, in the planning, implementation and evaluation of control programmes;
   (3) to try to obtain from various sources within the United Nations system, as well as from governmental and private organizations extrabudgetary resources for the implementation of control programmes;
   (4) to report on this matter in the biennial reports to the World Health Assembly.

Thirteenth plenary meeting, 24 May 1978
A31/VR/13

Appendix 2. Resolution of the Thirty-Second General Assembly of the International Union against the Venereal Diseases and the Treponematoses

Whereas
Yaws and endemic syphilis are re-emerging as major public health problems in some countries of the world and
These non-venereal treponematoses are easily treated and particularly amenable to prevention and control

Be it resolved that
Those countries potentially experiencing a resurgence of yaws or endemic syphilis reestablish accurate reporting systems for these diseases with the assistance and coordination of WHO

and
Those countries experiencing a significant non-venereal treponematoses problem launch effective control measures in close cooperation with their primary health care systems and with the technical assistance of IUVD and WHO and the financial assistance of international agencies and industrialized countries and

This resolution of the IUVDT be brought to the immediate attention of the Director-General of WHO at the next World Health Assembly.

President of IUVDT
Hofrat Prof. Dr. A. Luger
Montreal, 20 June 1984
Infectious Diseases Society of America

OFFICERS AND COUNCIL
Paul G. Quie, President
Richard B. Hornick, President-Elect
Theodore C. Eickhoff, Past President
Herbert L. DuPont, Secretary
Pierce Gardner, Treasurer

COUNCILLORS
Vincent T. Andriole
John G. Bartlett
R. Gordon Douglas
P. Frederick Sparling
Morton N. Swartz
Lowell S. Young

PUBLICATIONS COMMITTEE
Harry N. Beaty
Vincent T. Andriole
Bascom F. Anthony
R. Gordon Douglas
David T. Durack
F. Marc LaForce
Morton N. Swartz
Herbert L. DuPont (ex officio)
Martha D. Yow (ex officio)
Edward H. Kass (ex officio)

The Infectious Diseases Society held its organizational meeting on October 26, 1963, at the Airlie House in Warrenton, Virginia. For several years prior to this, there had been increasing interest in the formation of such a society. A community of investigators interested in laboratory and clinical aspects of infectious diseases was becoming increasingly defined in many major academic centers. Certain of these investigators were meeting each year at Atlantic City at an informal dinner club, and a similar group had begun to meet for dinner and discussion at the time of the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Finally a decision was made to explore various ways in which an organization could be formed that would articulate the broad interests of those working in infectious diseases. An Organization Committee was formed and was charged with the responsibility of calling the first meeting, arranging for scientific program, and nominating the first slate of officers. A number of pharmaceutical firms provided financial assistance.

The organization clearly has met an important need. Its growth, its relationship to national and international activities in infectious disease, its unusual and broad scientific programs, and its relationship to the Interscience Conference have given the Society a unique and useful place in the academic and scientific community. Its decision to constitute itself as a meeting place for scientists from all of the Americas has also given it a potentially important role in unifying scientific activity in many neighboring countries.